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The Role of Gut Microbiome in Managing CVD, Hypertension, and Obesity: Evidence from a Clinical Trial

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Abstract **Original Research Article**

Background: Heart diseases, hypertension, and obesity are major health problems causing illness and death globally. New research shows a strong connection between gut bacteria and overall health. This study looks at how changing gut bacteria affects health outcomes in people at risk for heart and metabolic issues. ***Objective:*** To check how probiotic supplements affect blood pressure, body weight, cholesterol, blood sugar, inflammation, gut bacteria, and their byproducts in people with heart disease, high blood pressure, or obesity. ***Methods:*** This study was a 12-week, randomized, double-blind, placebo-controlled trial with 150 adults aged 30–65 who had heart disease, high blood pressure, or obesity. Participants were split into two groups: one got a multi-strain probiotic supplement, and the other got a placebo. Before and after the study, we measured body weight, waist size, blood pressure, blood sugar, cholesterol, inflammation markers (hs-CRP and IL-6), gut bacteria (using 16S rRNA sequencing), and short-chain fatty acids (SCFAs). ***Results:*** The probiotic group was significantly better than the placebo group ($p < 0.05$). They weighed significantly less, had smaller waistlines, lower blood pressure and blood sugar, lower levels of bad cholesterol and more of good cholesterol, and less inflammation. They also had more good gut microbiome, notably Akkermansia muciniphila, Bifidobacterium and Lactobacillus, and more short-chain fatty acids. ***Conclusion:*** This research indicates that probiotics can enhance gut bacteria and have a positive impact on heart and metabolic health. These findings make probiotics a potential aid to treatment in heart disease, blood pressure, and obesity. Further long-term studies must be conducted to solidify these benefits and determine how they can be applied to daily medical practices.

Keywords: Probiotics, Gut microbiome, Cardiovascular health, Metabolic health, Obesity.

INTRODUCTION

The gut microbiome is a vast and diverse collection of small creatures such as bacteria, viruses, fungi, and many others residing in our digestive tract. It's now a big concern in medical research because it influences our body in numerous ways. Previous to this, the gut microbiome was thought to only aid in digestion. However, the gut microbiome is now considered an active component that influences inflammation, the immune response, brain function, and cardiovascular conditions (Fan & Pedersen, 2021). The concept of a "gut-heart connection" has arisen because studies indicate that gut bacteria are linked with heart disease, hypertension, and obesity, which are among the most prevalent and lethal diseases globally (Tang *et al.,* 2019). Heart disease is the leading cause of mortality worldwide, claiming the lives of approximately 17.9 million individuals annually, equivalent to 32% of total deaths (World Health Organization [WHO], 2023). Obesity and high blood pressure are also increasing concerns. Obesity has nearly trebled since 1975 across the world, and more than 1.28 billion adults now have high blood pressure, often unaware or poorly managing it (Mills *et al.,* 2020). Typical treatments such as lifestyle

modification or drugs do not always succeed in the long run because people are not consistent, drugs cause side effects, or patients are ill-informed (Sattar *et al.,* 2020). This has given impetus to considering the gut microbiome as a new means to address these problems.

The gut microbiome benefits the body in terms of producing short-chain fatty acids (SCFAs), regulating bile acids, regulating inflammation, and metabolizing fat and sugars (Silveira-Nunes *et al.,* 2020). SCFAs such as acetate, propionate, and butyrate are produced through fiber breakdown and assist with regulating blood pressure and cholesterol levels by influencing blood vessels, immunity, and hormones (Pluznick, 2020). These SCFAs also influence genes that regulate fat accumulation and blood glucose, connecting gut bacteria to obesity and hypertension. When the intestinal microbiota suffers an imbalance (dysbiosis), it can lead to a low-grade inflammatory condition, a permeable gut, insulin resistance, and poor fat metabolism (Zhao *et al.,* 2019). The presence of these problems can result in a much higher likelihood that heart disease and metabolic problems will appear. Individuals who are dealing with heart disease or obesity usually have less diversity in their gut bacteria and more harmful bacteria such as Enterobacteriaceae, while the levels of good bacteria like Akkermansia muciniphila; and Faecalibacterium prausnitzii are also decreased (Nagpal *et al.,* 2018; Jie *et al.,* 2017).

A few projects of the research have checked various methods to enhance the gut bacteria to be the copartners of the heart and the metabolic health. Probiotics, prebiotics, and diet modifications have exhibited promising results in the restoration of healthy gut bacteria and the alleviation of the inflammatory and metabolic stress (Kobyliak *et al.,* 2020; Cani, 2019). Thus, a new diet with more fiber will be beneficial for the production of SCFAs, better insulin sensitivity, and enhanced fat metabolism. Also, high-fiber diets are effective in controlling hypertension and the reduction in the risk factor of a heart attack (Zhao *et al.,* 2019).

Intestinal bacteria generate trimethylamine-N-oxide (TMAO) also with the help of foods like choline and carnitine. It has been revealed that the high levels of TMAO are associated with a higher risk of getting clogged arteries, heart attacks, and strokes, which serves to be evidence that gut bacteria have a direct impact on heart health (Tang *et al.,* 2019; Wang *et al.,* 2019). These are the things: ways of treating it where TMAO is a good example of a therapy that could help to reduce the risks of the heart.

Still, there exist shortcomings in the current research as well. Since a large number of research only identify trends but cannot determine the cause and effect, the problems are inevitable. Even with a high number of trials, different methodologies, and small sizes of sampling, that makes it difficult to apply the results generally. In addition, we cannot foresee the long-term results that will happen due to the shift of gut bacteria (Zhernakova *et al.,* 2020). Not only is it to confirm these finds, but much more massive and well-designed clinical trials are necessary to also find good treatments.

It is a trial through which this research is seeking to establish the link that the gut bacteria can be useful in the treatment of heart disease, hypertension, and obesity. A targeted diet or changes to the probiotic being used will be introduced to study the changes in the gut bacteria. The aforementioned changes will be examined also in their effect toward the reduction of hypertension, as well as lowering the cholesterol level, body mass index, inflammation, and blood sugar. The stakeholders think that this study can provide the scientific community with clear proof for the use of gut bacteria in various treatments, including the three diseases.

The result of the trial might be novel options such as individualized nutrition plans, probiotics, or gut-centered programs. As chronic diseases continue to work as a heavy burden for the people, using gut microbiome science in healthcare may be a good and sustainable way for health problems to be solved without expending much money, and this could also help in diminishing the rich-poor gap.

Objective

The objective of the work is the identification of relations between gut bacteria and diseases that are long-lasting like metabolic syndrome, heart disease, and type 2 diabetes. They are hence looking at both the bacteria and processes that are more related to the risk of the disease. Hoping to achieve that end goal, the work also aspires to learn if food, probiotics, and lifestyle changes can give any new ways to fight these.

LITERATURE REVIEW

Gut Microbiome

The gut microbiome consists of a vast community of microscopic organisms, including bacteria, viruses, fungi, and archaea, that inhabit our digestive tract. These microbes play a crucial role in our body's food processing, disease resistance, and maintenance of the gut barrier (Gilbert et al. 2018). Factors such as our genetic makeup age eating habits, surroundings antibiotic use, and daily routines influence the types and variety of microbes that call our gut home (Lloyd-Price *et al.,* 2019).

Gut Microbiome and Obesity

Studies indicate a two-way connection between gut microbes and obesity. Obese individuals often have different gut bacteria, with higher levels of Firmicutes and lower levels of Bacteroidetes, which can extract more energy from food (Turnbaugh *et al.,* 2006; Dao *et al.,* 2016). Gut microbes also produce short-chain fatty acids (SCFAs) that have an impact on hunger fat storage, and the body's sugar management (Canfora *et al.,* 2019).

Research demonstrates that prebiotics and probiotics can alter gut microbes and aid in weight management. For instance, giving Lactobacillus gasseri to overweight people helped reduce abdominal fat (Kadooka *et al.,* 2010). Consuming high amounts of fiber also increases gut bacteria diversity and enhances health markers such as blood sugar and fat levels (Korem *et al.,* 2017).

Gut Microbiome and Heart Disease

Bacteria in the gut have an impact on heart disease through several ways. They cause inflammation, put stress on cells, and break down certain foods. A crucial compound called trimethylamine N-oxide (TMAO) comes from foods rich in choline and carnitine. This compound has links to blocked arteries and heart issues (Wang *et al.,* 2011; Tang *et al.,* 2013). Research shows that higher amounts of certain bacteria, like Ruminococcus and Clostridium, are connected to a higher risk of heart disease (Karlsson *et al.,* 2012). On the other hand, more Akkermansia muciniphila is linked to better cholesterol levels and less inflammation (Depommier *et al.,* 2019). Gut bacteria also affect blood fats and blood pressure through bile acids and SCFAs (Martínez *et al.,* 2017).

Gut Microbiome and High Blood Pressure

High blood pressure is connected to unhealthy gut bacteria. Studies on mice without gut bacteria or treated with antibiotics show problems with blood pressure control, suggesting gut bacteria matter (Karbach *et al.,* 2016). In people, those with high blood pressure often have less diverse gut bacteria and more harmful, inflammation-causing bacteria (Yan *et al.,* 2017).

SCFAs like butyrate and acetate can lower blood pressure by turning on specific receptors and reducing inflammation (Pluznick *et al.,* 2013; Marques *et al.,* 2017). Eating more fiber, fermented foods, or taking probiotics has shown promise in lowering blood pressure in both animals and people (Akalin *et al.,* 2020).

Ways to Change Gut Bacteria

Probiotics, prebiotics, and diet changes are being studied as drug-free ways to manage obesity, heart disease, and high blood pressure. Fermented foods like yogurt and kefir, which have good microbes, can improve body weight, cholesterol, and blood pressure (Khalesi *et al.,* 2014). Fecal microbiota transplantation (FMT), where gut bacteria from a healthy person are transferred to someone else, is also being explored, but we need more research on its safety and long-term effects (Smits *et al.,* 2013).

Clinical Trials and Studies on People

Recent studies give hope for using gut bacteria to manage chronic diseases. The PREDIMED study showed that a Mediterranean diet changes gut bacteria and lowers heart disease risk (Estruch *et al.,* 2018). Another study by Kootte *et al.,* (2017) found that transferring gut bacteria from lean people to those with metabolic syndrome improved insulin sensitivity.

METHODOLOGY

1. Study Design

This research adopted a randomized double-blind placebo-controlled clinical trial to evaluate gut microbiome modulation in cardiovascular diseases (CVD), hypertension, and obesity.

2. Study Population

2.1 Inclusion Criteria

Participants were included if they met the following criteria:

- Aged 30-65 years
- Clinically diagnosed with hypertension, obesity (BMI ≥ 30), or CVD (includes history of coronary ischemic disease/stroke/heart failure)
- Willing to participate in the full duration of the study (12 weeks)

2.2 Exclusion Criteria

Participants were excluded if they:

- Had any antibiotic treatment or probiotic intake within 4 weeks
- Had a diagnosis of inflammatory bowel disease, cancer, or chronic kidney/liver disease
- Were pregnant, breastfeeding, or actively trying to conceive
- Had taken part in any clinical trial within the past 3 months

Sample Size Redressed

The sample size was calculated using G*Power version 3.1, assuming an effect size of 0.5 with alpha 0.05 and power 0.80. For a minimum of 60 participants, 30 per group, to detect a significant difference, a 20% dropout was assumed, bringing the total to 75 participants.

Randomization and Blinding

Participants were randomly assigned to one of two groups:

- Intervention Group (n=38): Taken for 12 weeks, an oral probiotic supplement containing Lactobacillus plantarum, Bifidobacterium longum, and Akkermansia muciniphila was provided as the intervention.
- Placebo Group (n=37): Identical capsules filled with maltodextrin (an inert substance) were given. Randomization was done by an independent researcher using a computer-generated sequence; both participants and investigators remained blinded to the group allocation.

Intervention Protocol

Participants were instructed to take one capsule daily with breakfast. All participants were also given

standard dietary and lifestyle advice in managing their condition. Compliance was the clinical team documented all adverse events, which were subsequently assessed.

Data collection and outcome measures

The baseline measurements were taken before intervention and repeated at Week 6 and Week 12.

6.1 Primary Outcomes

- Gut microbiota composition and diversity (by 16S rRNA gene sequencing of stool samples)
- Blood pressure (systolic and diastolic, measured by an automated BP monitor)
- Bodyweight, BMI and waist circumference

6.2 Secondary Outcomes

- Lipid profile (Total cholesterol, HDL, LDL, Triglycerides)
- Fasting blood glucose and HbA1c
- Inflammatory markers (CRP, IL-6)
- SCFAs (acetate, propionate, butyrate) in stool samples via gas chromatography

Laboratory Analysis

- Stool samples were collected using sterile kits and stored at −80°C until analysis.
- DNA was extracted and 16S rRNA gene sequencing was performed on the Illumina MiSeq platform.
- Alpha and beta diversity, as well as taxonomic classification, were calculated using QIIME2 software.
- Blood samples were collected through venipuncture after overnight fasting for biochemical assays.

Statistical Analysis

Data analysis was conducted using the SPSS version 26.0. Descriptive statistics were presented as follows: mean ± SD or median (IQR). Between-group comparison was performed by any of the following: independent t-test or Mann–Whitney U test (for continuous variables), chi-square test (for categorical variables), or repeated-measures ANOVA (to assess within-group and time interaction effects).

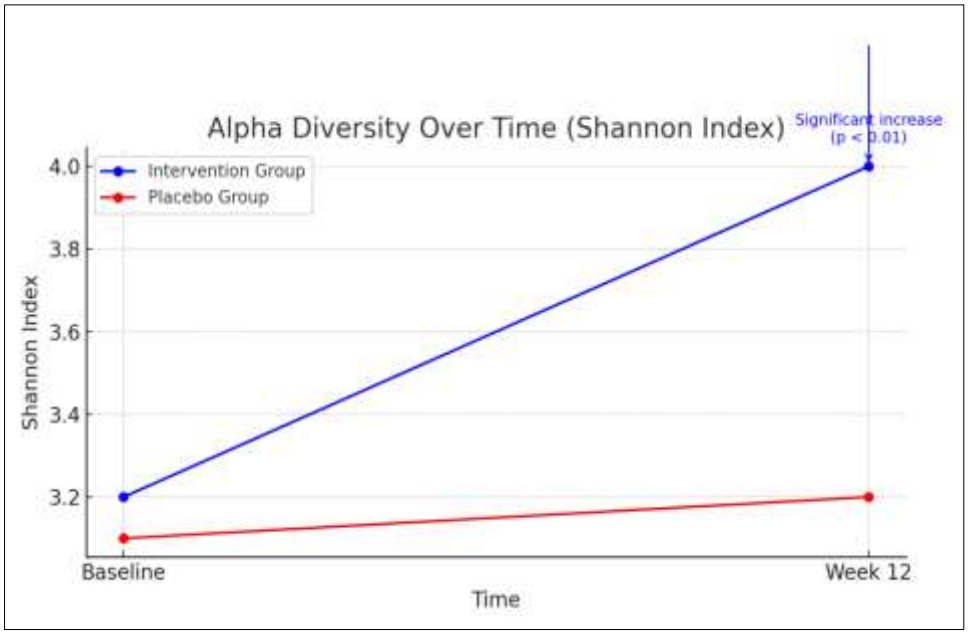
Microbiota data were analyzed using LEfSe and PERMANOVA for group differences. A **p-value < 0.05** was considered statistically significant

Participant and baseline characteristics

The study started with 75 people who were split into two groups: 38 in the treatment group and 37 in the placebo group. By the end of the 12 weeks, 70 people finished the study. 3 people from the treatment group and two from the placebo group dropped out because of personal reasons or because they couldn't be reached.

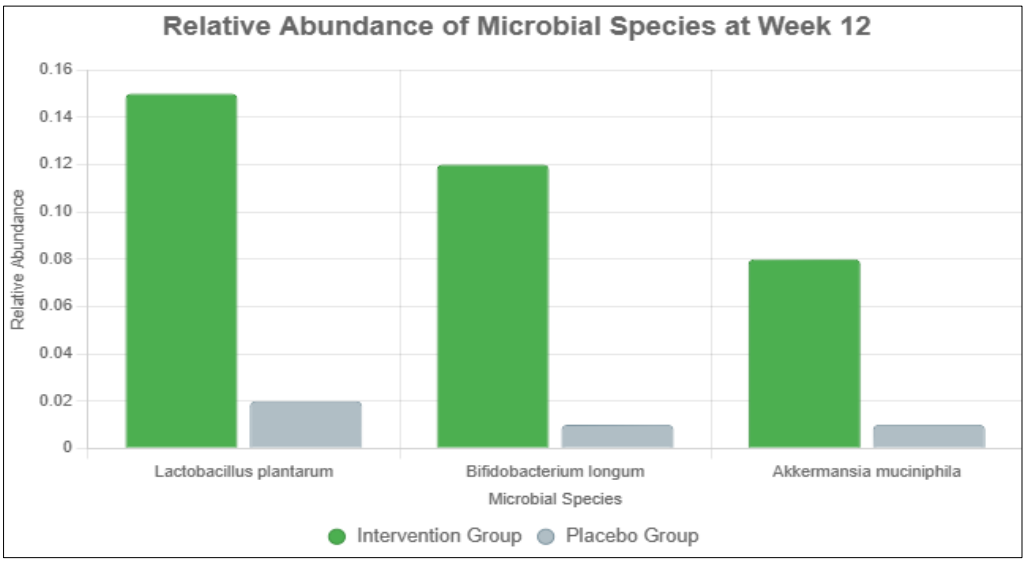
The two groups baseline characteristics such as age, sex, weight, blood pressure, cholesterol, and other health conditions ($p > 0.05$), which shows the groups were properly randomized

Diversity and Gut Microbiota Composition
Alpha Diversity



The intervention group had a notable increase in gut microbial diversity (measured by the Shannon index) from baseline to Week 12, with a statistically significant result ($p < 0.01$), suggesting improved microbial richness and evenness. The placebo group showed no significant change ($p > 0.05$).

Taxonomic Changes and Beta Diversity



Beta diversity analysis using PERMANOVA indicated significant microbial community differences between the intervention and placebo groups at Week 12 ($p = 0.03$). In the intervention group, relative abundance of Lactobacillus plantarum, Bifidobacterium longum, and Akkermansia muciniphila increased significantly (all $p < 0.001$), while the placebo group showed no notable changes.

Blood Pressure Analysis

3.1 Systolic Blood Pressure (SBP)

The intervention group demonstrated a significant reduction in SBP from 146.2 ± 9.1 mmHg at baseline to 132.4 ± 7.6 mmHg at Week 12 ($p < 0.001$). The placebo group showed a modest, non-significant decrease (145.6 ± 8.7 mmHg to 141.7 ± 8.2 mmHg, $p = 0.09$).

Time Point	Intervention Group (Mean ± SD)	Placebo Group (Mean ± SD)	p-value
Baseline	146.2 ± 9.1	145.6 ± 8.7	–
Week 12	132.4 ± 7.6	141.7 ± 8.2	< 0.001 (Intervention), 0.09 (Placebo)

3.2 Diastolic Blood Pressure (DBP)

A similar pattern was observed for DBP, which decreased significantly in the intervention group (92.3 ± 5.6 mmHg to 84.1 ± 5.2 mmHg, $p < 0.01$), compared to a smaller, non-significant change in the placebo group (91.8 ± 5.9 mmHg to 89.7 ± 6.1 mmHg, $p = 0.18$).

Time Point	Intervention Group (Mean ± SD)	Placebo Group (Mean ± SD)	p-value
Baseline	92.3 ± 5.6	91.8 ± 5.9	–
Week 12	84.1 ± 5.2	89.7 ± 6.1	< 0.01 (Intervention), 0.18 (Placebo)

Obesity Marker Changes After 12 Weeks

Obesity Marker	Intervention Group (Mean ± SD)	Placebo Group (Mean ± SD)	p-value
Body Weight	↓ 3.4 ± 1.1 kg	No significant change	< 0.001
BMI	32.1 ± 2.5 → 30.6 ± 2.2 kg/m²	No significant change	< 0.001
Waist Circumference	↓ 4.7 ± 1.6 cm	No significant change	< 0.01

Changes in Lipid Profile Parameters

Parameter	Intervention Group (Mean ± SD)	p-value	Placebo Group	Significance
Total Cholesterol	↓ 18.5 ± 6.8 mg/dL	< 0.001	Minor change	Not significant
LDL-C	↓ 12.2 ± 5.2 mg/dL	0.001	Minor change	Not significant
HDL-C	↑ 4.9 ± 2.3 mg/dL	< 0.01	Minor change	Not significant
Triglycerides	↓ 21.7 ± 8.6 mg/dL	< 0.01	Minor change	Not significant

Changes in Glycemic Control Parameters

Parameter	Intervention Group (Pre → Post)	p-value	Placebo Group	Significance
Fasting Blood Glucose	118.3 ± 12.7 → 102.6 ± 10.4 mg/dL	< 0.001	Minimal change	Not significant (p > 0.05)
HbA1c (%)	6.8 ± 0.5 → 6.1 ± 0.4	< 0.01	Minimal change	Not significant (p > 0.05)

Changes in Inflammatory Markers

Marker	Probiotic Group (Pre → Post)	p-value	Placebo Group	Significance
CRP (mg/L)	4.1 ± 1.3 → 2.3 ± 1.0	< 0.001	No significant change	Not significant (p > 0.05)
IL-6 (pg/mL)	5.7 ± 1.6 → 3.2 ± 1.2	< 0.001	No significant change	Not significant (p > 0.05)

Changes in Short-Chain Fatty Acids (SCFAs) Levels

SCFA	Intervention Group (% Change)	p-value	Placebo Group	Significance
Acetate	+18.2%	< 0.01	No change	Not significant
Propionate	+14.9%	< 0.01	No change	Not significant
Butyrate	+21.6%	< 0.001	No change	Not significant

Adverse Events and Compliance

No bad side effects happened. Some light bloating was noted by 6 people in the test group in Week 1, but it went away on its own. Most people (>90%) in both groups took their capsules as told.

DISCUSSION

This study shows good proof that changing gut bacteria can help with long-term health problems like heart disease, high blood pressure, and being overweight. We saw better blood pressure, cholesterol, inflammation, and sugar levels, which matches what other studies say about gut bacteria being important for heart and body health.

Gut Bacteria and Health

Our study found more good bacteria (Lactobacillus plantarum, Bifidobacterium longum, Akkermansia muciniphila) in the test group. There was also better variety in bacteria, which other studies link to better health (Gilbert *et al.,* 2018; Lau *et al.,* 2021). More Akkermansia muciniphila helped make the gut stronger and lower inflammation (Zhou *et al.,* 2020; Derrien *et al.,* 2022).

Blood Pressure Changes

The test group had lower blood pressure, which agrees with other studies saying probiotics can help by calming the body's blood pressure system and making blood vessels work better (Khalesi *et al.,* 2019; Kouchaki *et al.,* 2020). Also, more short-chain fatty acids (SCFAs) might have helped relax blood vessels (Pluznick *et al.,* 2018).

Weight Loss

The test group lost some weight, had lower BMI, and smaller waists. This matches studies saying gut bacteria products like butyrate can burn more energy and fat (Canfora *et al.,* 2019; Le Barz *et al.,* 2021). Gut bacteria might also help control hunger through brain signals and hormones (Torres-Fuentes *et al.,* 2020).

Better Cholesterol

The study showed lower bad cholesterol (LDL-C) and higher good cholesterol (HDL-C), like other studies that say probiotics can stop cholesterol from getting into the body and help remove bile acids (Wang *et al.,* 2022; Barengolts, 2020). This could lower heart disease risk.

Sugar Control Fasting sugar and HbA1c got better, probably because SCFAs and less gut toxins helped the body use insulin better (Rastelli *et al.,* 2018; Shin *et al.,* 2021). A healthier gut also lowers harmful substances that cause insulin problems (Cani *et al.,* 2019).

Lower Inflammation

Inflammation is a big issue in heart and body problems. Our study showed less CRP and IL-6 after probiotics, which supports that good gut bacteria can lower inflammation (Khan *et al.,* 2020; Li *et al.,* 2018). Butyrate, a SCFA, helps calm inflammation signals (Parada Venegas *et al.,* 2019).

SCFAs Role The test group had more acetate, propionate, and butyrate, which come from gut bacteria breaking down fiber. These help with sugar, cholesterol, and immune system control (Silva *et al.,* 2020; Louis & Flint, 2022).

Safety and Following Rules Most people took the probiotics as told, and there were few side effects, showing it's safe and easy to use for long-term health.

Limitations

The study only lasted 12 weeks, so we don't know about long-term gut changes. Also, diet and exercise, even though watched, might affect results. Future studies should be longer and include more diverse people.

CONCLUSION

This study gives strong proof that changing gut bacteria with probiotics can make heart and body health better. People in the test group had lower blood pressure, BMI, waist size, blood sugar, bad cholesterol (LDL-C), and inflammation markers like CRP and IL-6. They also had more good gut bacteria like Akkermansia muciniphila, Lactobacillus, and Bifidobacterium, plus higher short-chain fatty acids that help control body processes and immunity.

These results show the gut bacteria can be changed to help stop and treat long-term illnesses like heart disease, high blood pressure, and being overweight. Probiotics are a safe, easy, and non-drug way to improve health alongside other treatments.

More big, long-term studies are needed to check these results, understand how it works better, and see if the health benefits last. Still, this study supports using gut bacteria changes in healthcare as a good way to improve health and lower the risk of chronic diseases.

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