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### Probiotics and Blood Pressure: A Literature Review

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#### ABSTRACT

##### Background

Hypertension is a noncommunicable disease that can effect many complication for health, therefore we need effective blood pressure management. Effective management can be combined and non-pharmacological therapy through probiotics.

##### Objectives

The aims of this paper was to analyze the effectiveness of probiotics to reduce blood pressure.

##### Research methods

Literature review was based on the search of Google Scholar, Science Direct and Pubmed published from 2010 to 2019. The keywords used are probiotics, blood pressure, probiotics for blood pressure, and hypertension. Articles used using inclusion and exclusion criteria.

##### Result

The literature review in accordance with the search strategy in getting as many as 285 articles published ten years related to the effect of probiotic on blood pressure. 95 were deleted because it has the same title. A total of 162 articles are not relevant to the article, after using the inclusion and exclusion criteria obtained 8 articles that are eligible for this literature review. As results, probiotics can be used to reduce blood pressure consuming a variety of species and over 6 weeks in duration. It can inhibit the Angiotensin Converting Enzyme (ACE), and reduce the production of angiotensin-I to angiotensin-II.

##### Conclusion

Probiotics therapy can be used for reduce blood pressure.

**Keywords:** Probiotic, Blood pressure, Probiotic for blood pressure, Hypertension

#### INTRODUCTION

Hypertension is one of the non communicable diseases which has become a major problem in

Indonesia and several countries in Indonesia. Based on hypertension data from 45 countries in the world, estimated prevalence of hypertension is around 32.3% (CI 29.4-35.3) with the most cases

in Latin America and Caribbean Based countries. [1] Based on WHO data in 2017, the prevalence of hypertension in the world population aged over 18 years is 24% in men and 20.5% in women. The prevalence of hypertension in Indonesia based on Riskesdas 2018 is 34.1% of the population over the age of 18 who suffer from hypertension. [2]

Hypertension is characterized by an increase in systolic and diastolic blood pressure more than normal. In addition, it is caused by damage to the endothelium so that blood pressure becomes increased. The causes of hypertension are various, ranging from lifestyle, heredity, dietary factors, stress and others. [3]

Treatment of hypertension that has been done with pharmacological and non pharmacological therapy. Pharmacological therapy will be given according to the grade of hypertension. [4] The use of drugs in the long run can leave waste or residue in the body that can affect health. Therefore, companion therapy is needed in addition to the main therapy. Non-pharmacological treatment of hypertension has little side effects. Some non-pharmacological therapies for hypertension such as consumption of vegetable, fruits, and whole grains is recommended to lower pressure, physical activity three or four times per week (average of 40 minutes per session), relaxation techniques, dietary supplements, and others. [5] Other non-pharmacological therapy for hypertension is one of them with probiotics.

Some studies use probiotics as a therapy in reducing blood pressure. Probiotic capsules (lactobacillus acidophilus, lactobacillus delbrueckii bulgarius, bifidobacterium, streptococcus thermophilus  $4 \times 10^9$  CFU) given to 64 pregnant women with Diabetes Gestational Mellitus (GDM) for 8 weeks are significant for systolic ( $106 \pm 1.85$ ,  $p=0.002$ , effect size 4.5) and diastolic blood pressure ( $60.69 \pm 1.54$ ,  $p<0.001$ , effect size 6.75). The group given probiotics decreased systolic blood pressure by 2.4 mmHg and diastolic by 8.1 mmHg. [6] Soya milk probiotics (lactobacillus plantarum  $2 \times 10^7$  CFU) given for 8 weeks in diabetics aged 35-68 years showed a significant effect on systolic blood pressure ( $p = 0.002$ , effect size 4.5) and diastolic ( $p < 0.001$ , effect size 1.96). [7] Several other studies have shown that probiotics have not

significantly influenced systolic and diastolic blood pressure. [8, 9]

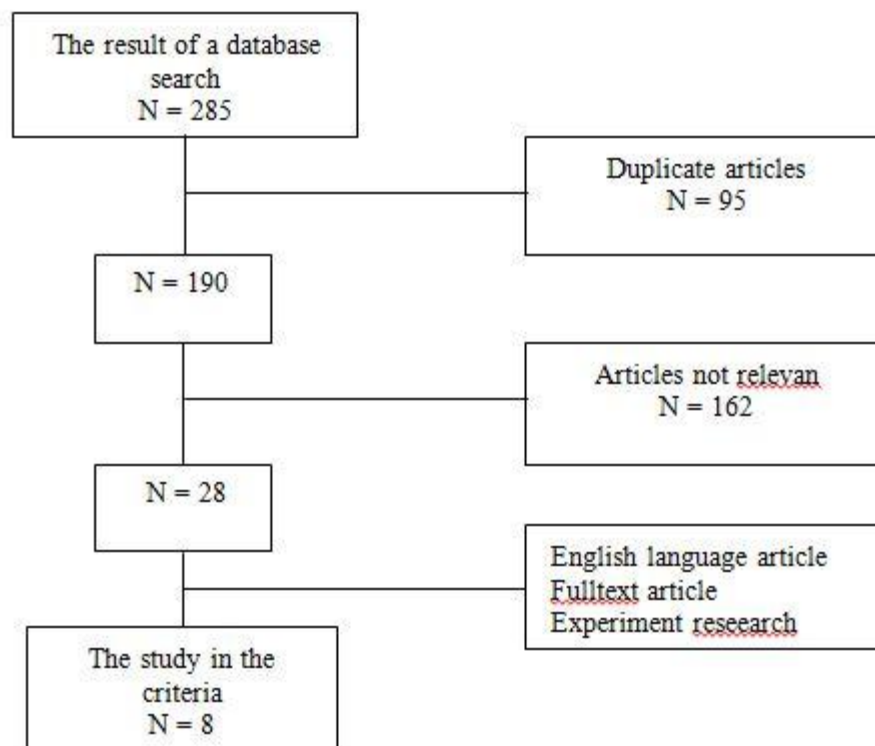
A meta-analysis of 9 studies showed that probiotics are more effective in lowering blood pressure if they consume a variety of species, the duration of administration is more than 8 weeks and the daily dose is  $\geq 10^{11}$  CFU. [8] Probiotics can work as Angiotensin Converting Enzyme (ACE) inhibitors. This enzyme plays a role in the process of angiotensin I to angiotensin II. Lactobacillus probiotics that can have high potential as ACE inhibitors include lactobacillus reuteri, lactobacillus bulgarius, lactobacillus rhamnosus, and lactobacillus helveticus. [10] This study aims to analyze the role of probiotics on blood pressure.

## MATERIALS AND METHODS

This literature review used articles from Google Scholar, Science Direct, Pubmed, DOAJ published from 2010 to 2019. The inclusion criteria are full text articles, using English language, experimental research, including dosage, type of bacteria and duration of administration of probiotics. The exclusion criteria are articles was non English language, incomplete articles, case study. The keywords used were probiotics, blood pressure, probiotics for blood pressure, hypertension.

## RESULTS AND DISCUSSION

The results of a research database are 285 articles. as many as 95 articles have similarities or similarities to the title, 162 articles are not relevant. After using the inclusion and exclusion criteria 8 articles were found that are suitable for this literature.



**Figure 1. Flowchart of the exclusion process and final selection**

**Table 1. The research of probiotic on blood pressure**

Author	Respondents	Contains	Dossage (CFU), Source	Duration (Week)	Result (Mean post±SD) Intervension vs control	Range of mean pre-post Intervension vs control	Effect size
Hajifaraji 2016[6]	64 respondent with gestational diabetes mellitus (GDM) (18-45 years) 32 intervension 32 control	<i>L. achidophilus</i> <i>L. delbrueckii</i> <i>bulgarius</i> <i>Bifidobacterium</i> <i>S. thermophilus</i>	>4x10 <sup>9</sup> Capsule	8	SBP 106,5±1,85 vs 115,2±1,93 p=0,002 DBP 60,69±1,54 vs 71,30±1,60 p<0,001	Δ↓ 2,4 vs ↑ 9,6 mmHg Δ↓ 8,1 vs ↑ 6,3 mmHg	4,5 6,75
Hariri 2014[7]	40 diabetes people (35-68 year): 20 intervension 20 control	<i>L. plantarum</i>	2x10 <sup>7</sup> Milk soya probiotic	8	SBP 13,05±0,16 vs 14,40±0,23 p=0,002 DBP 9,10±1,00 vs 10,50±0,12 p<0,001	-	4,55 1,96

Sharaveftino v 2013[11]	40 hypertension people (30-69 years): 25 intervention 15 control	<i>L. plantarum</i> <i>TENSIA</i>	7,5 x 10 <sup>12</sup> Cheese probiotic	3	Morning SBP 121,8±1,5 vs 120,0±1,8 p=0,078 Afternoon SBP 120,6±1,2 vs 119,3±1,6 p=0,716  Morning DBP 78,4±0,9 vs 78,6±1,0 p=0,240 Afternoon DBP 78,0±1,2 vs 76,4±1,3 p=0,026	Δ↓ 9,2 vs 1,08 ↓11,1 mmHg  Δ↓ 8,8 vs 0,91 ↓10,7 mmHg  Δ↓ 4 vs ↓3,5 0,21 mmHg  Δ↓ 1,6 vs 1,2 ↓3,2 mmHg
Chang 2011[8]	Healthy people (20-60 year): 53 intervention 48 placebo	<i>L. acidophilus</i> <i>S. thermophilus</i> <i>Bifidobacteria infantis</i>	4,8x10 <sup>12</sup> Yogurt	8	SBP p=0,276 DBP p=0,825	Δ↓ 1,07 vs - ↑0,91 mmHg Δ↓ 0,32 vs ↓ 0,43 mmHg
Ivey 2014[12]	156 overweight people, > 55 year Group 1: yogurt probiotic yogurt and capsule probiotic Group 2: yogurt probiotic yogurt and placebo capsule Group 3: milk and probiotic capsule Group 4: milk and placebo capsule	Capsule contains: <i>L acidophillus La5</i> <i>Bifidobacterium animalis subsp lactis Bb12</i>	3x10 <sup>9</sup> Yogurt and capsule	6	Group 1 and 2 SBP 131±14 vs 129±11 P=0,548 DBP 74±10 vs 75±7 p=0,422  Group 3 and 4 SBP 130±12 vs 129±13 P=0,601 DBP 75±9 vs 73±8 P=0,543	Δ 0 vs ↓ 1 0,15 mmHg Δ 0 vs ↑ 1 0,11 mmHg  Δ↓ 2 vs ↓ 1 0,07 mmHg Δ↓ 2 vs ↓ 1 0,22 mmHg
Jones 2012[13]	People 20-75 year: 62 intervention 62 placebo	<i>L. Reuteri</i>	2,9 x 10 <sup>9</sup> Capsule	9	SBP 130,74±11,84 vs 129,69±11,41 p=0,615 DBP 77,15±4,57 vs 77,89±5,16 p=0,452	Δ↑ 0,18 vs ↓ 0,09 1,18 mmHg  Δ↓ 7,46 vs ↓ 0,15 0,19 mmHg
Jones 2012[9]	People 18-74 year: 59 intervention 61 placebo	<i>L. Reuteri</i>	5,8 x 10 <sup>10</sup> Yogurt	6	SBP 133,13±11,58 vs 124,45±12,39 p=0,452 DBP 77,9±7,06 vs 73±7,51 p=0,593	Δ↓ 1,19 vs ↓ 0,72 3,07 mmHg  Δ↓ 0,98 vs ↓ 0,72 1,18 mmHg
Savard 2011[14]	People 18-54 year	Group 2: <i>Bifidoanimalis</i>	Yogurt	4	Group 1 vs 2 vs 3 SBP 103,0±8,4 vs 102,1±10,3	Group 1 vs 2 - vs 3

Group 1: Plasebo (20)	<i>lactis</i> 10 <sup>9</sup> + <i>L.achidophilus</i> +	vs 107,2±10,6 P=0,20	Δ↓ 0,8 vs ↓2,5 vs ↑ 1 mmHg
Group 2 (20)	green tea extract		
Group 3 (28)	Group 3: <i>Bifidoanimalis</i> <i>lactis</i> 10 <sup>10</sup> + <i>L.achidophilus</i> + green tea extract	DBP70,3±6,5 vs 69,3±6,1 vs 71,9±7,3 p=0,29	Δ↑ 1,3 vs ↓0,9 vs ↑0,6 mmHg

Previous research (9 studies) intervened by administering probiotics to blood pressure. Of the 9 studies, there were 3 studies on probiotics that had statistically significant results in reducing blood pressure, while other studies had not had a significant effect.

Hajifaraji's study using a 180 mg probiotic capsule consisting of 4 bacterial strains (*lactobacillus achidophilus*, *lactobacillus delbrueckii bulgarius*, *bifidobacterium*, *streptococcus thermophilus*,) given to pregnant women with GDM for 8 weeks with doses > 4x10<sup>9</sup> CFU showed differences in blood pressure sata (p = 0.02) and diastolic (p <0.001, 95% CI) in the intervention group and the placebo group. These four bacteria can have an influence on blood pressure. [6]

Research by Hariri using the probiotic *lactobacillus plantarum* 2x10<sup>7</sup> given to diabetics aged 35-68 years has shown significant results on systolic blood pressure (p = 0.002, effect size 4.55), and diastolic (p <0.001, effect size 1, 96), but did not provide information on how much decreased systolic blood pressure before and after the intervention. [7]

The Sharaveftinov study using the probiotic *lactobacillus plantarum* TENSIA 7.5x10<sup>12</sup> for 3 weeks given to 40 adults with hypertension showed significant differences in the intervention and control groups in the afternoon diastolic blood pressure (78.0 ± 1.2, p = 0.026, effect size 1.2, Δ ↓ 1.6 mmHg). This study has not shown a significant effect on morning diastolic blood pressure (78.6± 0.9, p = 0.240, effect size 0.21), but shows a positive trend towards a decrease in morning diastolic blood pressure (78.4 ± 0, 9, p = 0.040, Δ ↓ 4 mmHg)

This study showed no significant effect on systolic blood pressure in the intervention and control groups (morning systolic blood pressure p

= 0.078, effect size 1.08, Δ ↓ 9.2 mmHg, and afternoon systolic blood pressure p = 0.716, effect size 0, 91, Δ ↓ 8.8 mmHg). [11]

Research by Chang with the use of probiotic *lactobacillus achidophilus*, *streptococcus thermophilus*, and *bifidobacteria infantis* (4x8x10<sup>12</sup> CFU) for 8 weeks in healthy people aged 20-60 years showed no significant association of probiotics and systolic blood pressure (p = 0.276, effect size -0, 04, Δ ↓ 1.07 mmHg) and diastolic (p = 0.825, Δ ↓ 0.32 mmHg). [8]

Research by Chang with the use of probiotic *lactobacillus achidophilus*, *streptococcus thermophilus*, and *bifidobacteria infantis* (4x8x10<sup>12</sup> CFU) for 8 weeks in healthy people aged 20-60 years showed no significant association of probiotics and systolic blood pressure (p = 0.276, effect size -0, 04, Δ ↓ 1.07 mmHg) and diastolic (p = 0.825, Δ ↓ 0.32 mmHg). [12]

Jones's study in adults (20-75 years) using probiotic capsules (*lactobacillus reuteri* 2.9 x 10<sup>9</sup>) for 9 weeks resulted in no difference in blood pressure in the intervention and control groups (systolic: p= 0.615, effect size 0.09 , Δ ↑ 0.18 mmHg, diastolic: p = 0.452, effect size 0.15, Δ ↓ 7.46 mmHg). [13]

A similar study by Jones using yogurt probiotics (*lactobacillus reuteri* 5.8 x 10<sup>10</sup>) for 6 weeks showed no effect on differences in systolic blood pressure (p = 0.462, effect size 0.72, Δ ↓ 1.19 mmHg) and diastolic (p = 0.593, effect size 0.72, Δ ↓ 0.98 mmHg) in the intervention and control groups. [9] Savard's study gave probiotics for 4 weeks to 68 respondents who were divided into the first group (placebo), the second group (*bifidoanimalis lactis* 10<sup>9</sup>, *lactobacillus achidophilus*, green tea extract), and the third group (*bifidoanimalis lactis* 10<sup>10</sup>, *lactobacillus achidophilus*, green tea extract). This study has not shown a significant difference in blood

pressure between groups (systolic:  $p = 0.20$ , diastolic:  $p = 0.29$ ), but the greatest decrease in blood pressure was found in the second group (systolic decrease  $\Delta \downarrow 2.5$  mmHg, diastolic decrease  $\Delta \downarrow 0.9$  mmHg). [14]

The effectiveness of probiotics on blood pressure can be influenced by various factors, one of which is the number of bacteria and the duration of intervention. Probiotics with diverse bacterial contents provide a significant effect in lowering blood pressure compared to probiotics with no bacterial content.

ACE is an enzyme that plays a role in regulating blood pressure. The basic structure of enzymes is the building of proteins. Protein building consists of several amino acids, which are derived from the results of a series of work cycles from groups of community bacteria. Enzyme work is influenced by the substrate, temperature, acidity, cofactors, and inhibitors. Inhibitors are molecules that can decrease enzyme activity. [15] Some studies mention the role of probiotics as ACE inhibitors, so that it can suppress angiotensin I to angiotensin II. Angiotensin I have mild

Research shows that consumption of probiotics can increase absorption of mineral absorption. [10] Food intake or prebiotics that enter the body can be useful substances in the presence of probiotics. The more variety of prebiotics eaten, the condition of bacterial microflora in the body will be better too so that the absorption of nutrients increases. [15] Bacteria in the large intestine produce molecules when digesting food, one of which produces short chain fatty acids. These short chain fatty acids are then absorbed by the blood. This fat helps regulate blood pressure. [15]

In the condition of hypertension can be caused by endothelial dysfunction factors. Endothelial plays an important role, one of which is in vascular homeostasis. Endothelial damage caused by damage to the cells making up these organs. Every 1 cell of the human body there are 1 to 9 families of bacteria that work for the survival and function of these cells. The mechanism of action of these probiotics pair up with each other, help each other,

vasoconstriction properties but is not strong enough to cause significant functional changes in the circulation process. After the formation of angiotensin I, there are two amino acids that break down the angiotensin to form angiotensin II, the amino acid peptide-8. This change occurs a few seconds while blood flows through small vessels in the lungs, which are catalyzed by enzymes (ACE). Angiotensin II is what can cause vasoconstriction of blood vessels. This vasoconstriction occurs mainly in arterioles and is slightly weak in veins. Arterial vasoconstriction will increase peripheral resistance, consequently increasing arterial pressure. Blood contains oxygen coming from the lungs, pumped out by the heart through the left ventricle to the aorta, then throughout the body through the arteries to reach the smallest blood vessels (capillaries). The presence of ACE inhibitors due to probiotics can suppress the occurrence of angiotensin II so that it can help reduce blood pressure. [16][17] Research on probiotics in goat milk, it was found that this probiotic has a strong enough effect as an angiotensin I inhibitor. [10]

protect each other, and form a community for their survival. In certain conditions can cause bacteria to lose their partners so that they become foreign agents, and in certain families the bacteria become dominant. Bacteria that are dominant in number can cause damage to a cell, organ, so that the clinical manifestations of certain diseases, one of which is hypertension. The existence of intake of probiotics which, if given in sufficient quantities can help maintain the balance of bacteria in the body. Balanced bacteria can help regenerate cells that have been damaged. The process of cell regeneration up to the RNA / DNA cell nucleus occurs in 3 cycles of cell regeneration, where each cycle takes about 3 months. [15]

## CONCLUSIONS

Probiotics can act as ACE inhibitors. Probiotics can help lower blood pressure by consuming a variety of species and over 6 weeks in duration.

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