

# The Effect of Oral Probiotic on the Interleukin-10 Serum Levels of Acne Vulgaris

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## Abstract

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**BACKGROUND:** Acne vulgaris is a chronic inflammatory skin disorder that commonly found in pilosebaceous units which can have an impact on the patient's psychological burden. The relationship between dermatology and mental health is increasingly understood by the evidence shows that functional integrity and microbes in the gastrointestinal tract may play a role in mediating skin inflammation and emotional behaviour. The gut-brain-skin theory was first described in 1930 by Stokes and Pillsbury, became the basis of many current studies that look for clinical implications of the relationship between the gastrointestinal tract, brain and skin in acne vulgaris. Probiotics are live microorganisms which can provide a healthy effect to the hosts when consumed in adequate amounts.

**AIM:** To determine the effect of oral probiotic on the interleukin-10 serum levels in acne vulgaris and also to determine the side effect of oral probiotic on acne vulgaris.

**METHODS:** This is a pre-experimental clinical study with a pretest-posttest design involving 33 subjects with acne vulgaris. The subjects in this study were measured for IL-10 serum levels before and after oral probiotic was given for 30 days. This research has been approved by the Health Research Ethics Commission of the Faculty of Medicine, Universitas Sumatera Utara.

**RESULTS:** This study found an increase in serum IL-10 levels after oral probiotic in acne vulgaris. The value of serum IL-10 levels before oral probiotic administration was  $5.27 \pm 1.49$  pg/ml, while the value of serum IL-10 levels after oral probiotic administration was  $6.19 \pm 1.68$  pg/ml) with p values obtained through Wilcoxon test was 0,0001 ( $p < 0.05$ ). The side effect of oral probiotic found in this study is bloating that was found in 2 subjects within the first week using oral probiotic.

**CONCLUSION:** Oral probiotic trigger elevated IL-10 serum levels of acne vulgaris. This study supports previous studies that suggested oral probiotic can be considered as adjuvant acne vulgaris therapy and its side effect is quite safe and tolerable.

## Introduction

Acne vulgaris is a chronic inflammatory skin condition which has an impact on the psychological burden. The relationship between dermatology and mental health is increasingly understood by the evidence that functional integrity and microbes in the gastrointestinal tract may play a role in mediating skin inflammation and emotional behaviour [1]. The intestinal microbiota consists of trillions of microbes

that affect normal physiology and alter host susceptibility to disease [2], [3]. Intestinal microbiota is important for immune system maturation, normal intestinal development as a natural barrier to foreign matter and bacteria, and also the synthesis of vitamin K and B12 [4]. Changes in the intestinal microbiota or exposure to specific bacteria in the intestine can stimulate the central nervous system and peripheral nervous system in animals causes changes in brain function and shows the presence of intestinal microbiota and brain axis [3], [5], [6].

The gut-brain-skin theory was first described in 1930 by John H. Stokes and Donald M. Pillsbury, became the basis of many studies that look for clinical implications of the relationship between the gastrointestinal tract, brain and skin particularly in acne [1], [7], [8]. Based on evidence that as many as 40% of acne patients experience hypochloridia, namely a decrease in gastric acid; Stokes and Pillsbury elucidate the hypothesis that insufficient gastric acid might induce migration of colon bacteria to the distal portion of the small intestine and interfere with normal intestinal microflora. Furthermore, changes in stressed microbial flora can increase intestinal permeability which in turn, stimulates systemic inflammation and also local skin inflammation. They also recommend the direct introduction of acidophilic organisms in cultures such as *Bacillus acidophilus* to overcome stress-triggered cycles [1], [8].

Probiotic are living microorganisms that when consumed in adequate amounts can give a healthy effect on hosts [9]. Probiotic have been extensively investigated because of their effects on the gastrointestinal system and digestive function, but these microbes can be applied more broadly based on evidence of the gut-brain-skin theory which was stated for 80 years ago. The first report on probiotic originated in 1907 by Elie Metchnikoff which illustrates the relationship of consuming acid producing bacteria in yogurt with longevity [10]. Probiotic acts against pathogenic bacteria, support barrier functions and contribute to the regulation of natural and acquired immune responses [9], [10].

## Methods

This is a pre-experimental clinical study with a pretest-posttest design involving 33 subjects with acne vulgaris. The subjects in this study were measured for IL-10 serum levels before and after oral probiotic was given for 30 days. The oral probiotic that was given is L-Bio® and consumed by participants as much as 2 sachets per day mixed with 500 cc of water before breakfast in the morning. One L-Bio® sachet contains rice starch, malodextrin, *B. lactis* W51, *B. lactis* W52, *L. acidophilus* W55, *L. casei* W56, *L. salivarius* W57, *L. lactis* W58 with total bacterial cells  $> 10^8$  cfu (*colony forming unit*). The serum IL-10 levels were examined by Quantikine ELISA method, using the human IL-10 kit obtained from *R & D Systems catalog D1000B*. This research has been approved by the Health Research Ethics Commission of the Faculty of Medicine, Universitas Sumatera Utara.

## Results

From a total of 33 subjects, female gender was 20 subjects (60.6%), more common than male gender 13 subjects (39.4%). The majority of the research subjects were 17-25 years old (90.9%). Based on the severity of acne vulgaris, we found the highest number of subjects was severe acne vulgaris, namely 12 subjects (36.4%), followed by mild acne vulgaris 11 subjects (33.3%) and moderate acne vulgaris 10 subjects (30.3%).

**Table 1: Characteristics of the research subject**

Characteristics	Number (n)	Percentage (%)
Gender		
Male	13	39.4
Female	20	60.6
Age		
17-25 years old	30	90.9
26-35 years old	3	9.1
Acne severity		
Mild	11	33.3
Moderate	10	30.3
Severe	12	36.4

In this study, we found the mean value of serum IL-10 levels before administration of oral probiotic was  $5.27 \pm 1.49$  pg/ml while the mean serum IL-10 level after administration of oral probiotic was  $6.19 \pm 1.68$  pg/ml. The *p* value obtained through the Wilcoxon test is 0.0001 ( $p < 0.05$ ). This shows a significant difference in serum IL-10 levels before and after administration of oral probiotic.

**Table 2: Comparison of serum IL-10 levels before and after probiotic administration**

Acne vulgaris	serum IL-10 (pg/ml) levels					<i>p</i>
	n	Mean	SD	Min	Max	
Before	33	5.27	1.49	3.41	11.30	0.0001
After	33	6.19	1.68	3.43	12.60	

The side effect of oral probiotic found in this study is bloating that was found in 2 subjects (6.1%) within the first week using oral probiotic.

**Table 3: The side effect of oral probiotic on clinical subjects**

Side effect	Cases	
	n	(%)
Bloating	2	6.1
No present	31	93.9

## Discussion

Probiotic are living microorganism that when consumed in adequate amounts can give a healthy effect on hosts [9]. Probiotic has been extensively investigated because of their effects on the gastrointestinal system and digestive function, but can be applied more broadly based on evidence of the gut-brain-skin theory by John H. Stokes & Donald M. Pillsbury which is the basis of the many studies

currently looking for clinical implications of the relationship between the gastrointestinal tract, brain and skin in acne vulgaris [1], [7], [8].

Evaluation of the effect of probiotic on serum IL-10 levels in patients with acne vulgaris has never been studied before. Previous studies evaluated the effect of probiotic on IL-10 levels on the immune cell supernatant by Livingstone et al., [11]. The study of Weid et al looked-for certain strains of lactic acid bacteria in inhibiting T-helper cell function in vitro and research by Hepburn et al aimed to examine the effect of daily probiotic supplementation on the cytokine profile of 20 healthy volunteers [12], [13].

Clinical trials that evaluating the effects of oral probiotic on acne are still limited. The first clinical trial was carried out by Siver in 1961 involved 300 patients where 80% of patients experienced improvement especially in inflammatory lesions [1], [8], [10]. Recent clinical trials by Jung et al., in 2013 showed that antibiotics and oral probiotic can provide a synergistic effect, especially in inflammatory acne. The study involved 45 patients aged 18-35 years who were randomly divided into 3 groups which are only probiotic supplement, minocycline group and probiotic plus minocycline groups. In this study, it was found that the group using probiotic and minocycline had a better reduction in the total number of lesions compared to the other two groups [14], [15]. The latest clinical trials were conducted in 2016 involved 57 patients with facial papulopustular lesions diagnosed with acne, seborrheic dermatitis and rosacea, which was randomly divided into 37 patients as the experimental group and 20 patients as a control group. The experimental group was given additional oral probiotic supplement *E. coli* Nissle every day for 1 month. The results of the study found 89% of the experimental group experienced significant improvement and complete recovery compared to the control group (56%) ( $p < 0.01$ ).

Probiotic are useful for acne because they can help inflammatory regulation by stimulating synthesis of regulatory cytokines (IL-10) which has been shown in many studies [10], [17], [18]. Interleukin-10 is the most important anti-inflammatory cytokines where the main function is to limit and eliminate the inflammatory response and regulation of differentiation and proliferation of many immune cells such as T cells, B cells, NK cells, APC cells, mast cells and granulocytes [19].

This study found that the mean serum IL-10 level before oral probiotic administration was  $5.27 \pm 1.49$  pg/ml while the mean serum IL-10 level after oral probiotic administration was  $6.19 \pm 1.68$  pg/ml ( $p = 0,0001$ ); showed that oral probiotic had an effect on increasing serum IL-10 levels. The side effect of oral probiotic found in this study is bloating that was found in 2 subjects (6.1%) within the first week using oral probiotic.

In conclusion, oral probiotic trigger elevated

IL-10 serum levels of acne vulgaris which is antiinflammatory cytokine. This study supports previous studies that suggested oral probiotic can be considered as adjuvant acne vulgaris therapy and its side effect is quite safe and tolerable.

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