

# Effects of Yogurt Containing *Lactobacillus gasseri* OLL2716 on Autonomic Nerve Activities and Physiological Functions

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## Abstract

The purpose of this study was to investigate the effects of yogurt containing *Lactobacillus gasseri* OLL2716 (LG21) on autonomic nerve activities, peripheral blood flow, skin condition (skin pigmentations and moisture), saliva s-IgA and examination of quality of life (QOL). 20 healthy female volunteers (yogurt containing LG21 group: 10 people, yogurt containing Bifidobacterium (Bif) group: 10 people) were examined. The subjects ingested 100 g of yogurt twice daily for 4 weeks. Analysis was before and after 4 weeks dosage. By the effects for the autonomic nervous activity, parasympathetic increase was observed in the LG21 yogurt group, but was not significant increase. The LG21 yogurt was significantly increased on the peripheral blood flow. The LG21 yogurt was significantly increased on saliva s-IgA. The LG21 yogurt and Bif yogurt were significantly decrease on skin pigmentation. Also, LG21 yogurt was significantly increased on skin moisture. As a result of QOL questionnaire, incomplete evacuation, lower abdominal fullness, cold extremities and pimply or rough skin improved in LG21 yogurt and Bif yogurt after the administration period. These results suggest that the improvement effects of LG21 yogurt may be related to the activity of the parasympathetic nervous system.

## Keywords

Yogurt, *Lactobacillus gasseri* OLL2716 (LG21), Autonomic Nerve Activities, Blood Flow, Skin Condition

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## 1. Introduction

In recent years, society has become more stressful due to changes in the social environments. We are troubled with constipation and diarrhea from the stress that it is a healthy subject, and is constant, irregular life. Therefore, various functional foods, such as blood pressure lowering food and blood glucose lowering food, have been developed and marketed. It is thought to be important to health, keeping a bowel movement well, and fixing the intestinal environment. The live microbial feeds added to improve the intestinal microbial balance are now known as probiotics [1]. Probiotics are defined as “Live microorganisms which when administered in adequate amounts confer a health benefit on the host” [2]. Lactobacilli and bifidobacterium are the most commonly used probiotics while yogurt and freeze-dried cultures are popular foods containing probiotics. Probiotics have been used to manage diarrhea, enhance the immune response, enteric infection, prevent food poisoning and prevent colonic cancer.

The yogurt has been taken in as the food which is good for health and beauty from experience for a long time. Recently, there have been an increasing number of reports on the health-promoting effects of lactobacilli in yogurt. In the previous study reported that yogurt containing *Lactobacillus gasseri* OLL2716 (LG21) is effective against *Helicobacter pylori* (*H. pylori*), improved the pepsinogen I/II ratio in *H. pylori* positive healthy volunteers and patients with *H. pylori* infection, inhibits the formation of HCL-induced acute gastric lesions through the generation of prostaglandin E2 and healing of acetic acid-induced chronic gastric ulcer [3]-[6]. Moreover, the tablet containing *Lactobacillus gasseri* OLL2809 is effective on endometriosis, especially against menstrual pain and dysmenorrhea [7].

It has been experienced that persistent constipation worsens dermal characteristics and aggravates comedones as the intestinal environment deteriorates. We may expect a beauty effect if we improve constipation and intestinal environment by intake of the yogurt.

In the present study, we evaluated for the effects of yogurt containing *Lactobacillus gasseri* OLL2716 (LG21) on autonomic nerve activities, peripheral blood flow, skin condition (skin pigmentations and moisture), saliva s-IgA and examination of quality of life (QOL).

## 2. Materials and Methods

### 2.1. Subjects

The subjects were 20 healthy female volunteers obtained consent by a purpose of this study at the Kobayashi Medical Clinic Tokyo. The subjects were divided a randomized into two groups. In the yogurt containing LG21 group assumed 10 people (age;  $31.8 \pm 1.6$  years old). For the control, yogurt containing Bifidobacterium (Bif.) group assumed 10 people (age;  $27.6 \pm 0.9$  years old). All subjects provided informed consent for participation.

### 2.2. Experimental Food

The yogurt containing LG21 ( $\geq 10^9$  c.f.u./g) was obtained from Meiji Dairies Corporation (Tokyo, Japan). The composition of 100 g of experimental food is energy: 89 kcal, protein: 3.8 g, lipids: 3.4 g, carbohydrates: 10.9 g, sodium: 49 mg, calcium: 134 mg. The yogurt containing *Bifidobacterium animalis* subsp. lactis (Bif) of the control used a commercial product. The subjects ingested 100 g of yogurt twice daily for 4 weeks.

### 2.3. Measurements of Autonomic Nervous Activities

Autonomic nervous activities were assessed using Pulse Analyzer Plus TAS9 (YKC Corporation, Tokyo). For the measuring finger tip pulse, HRV (the autonomic nerve balance) analysis program was used. Heart rate was measured by conducted on it. A frequency level from 0.04 to 0.15 Hz was classified as Low Frequency (LF), and a frequency level from 0.15 to 0.40 Hz was classified as High Frequency (HF). HF was considered as an indicator for parasympathetic nerve activity. The ratio between LF and HF (LF/HF) showed the overall balance of sympathetic and/or parasympathetic nerve, it is proportional to the degree of sympathetic nerve activity and inversely proportional to parasympathetic nerve activity.

### 2.4. Measurements of Peripheral Blood Flow

The peripheral blood flow measured the blood flow of the finger (the second, three or four fingers) of the non-

handedness side using a full-field laser perfusion imager (Moor FLPI, Moor Instruments, Essex, UK) [8] [9]. The measurement was performed before the start of the study and 4-week after the administration. We analyzed mean blood flow of one minute and showed the increase and decrease of the blood flow after the 4-week for 100 with the blood flow before the start.

## 2.5. Measurements of Salivary Components

Saliva samples were collected using the tasteless and odorless oral swabs (Salimetrics, USA) retained in the mouth for 5 min in a seated position, and the collected saliva was centrifuged at 1500 rpm for 40 min at 4°C. The s-IgA levels were measured with the Salivary Secretory IgA Indirect Enzyme Immunoassay Kit (Salimetrics, USA). The data showed the increase and decrease of the s-IgA after the 4-week for 100 with before the start.

## 2.6. Measurements of Skin Condition

VISIA (CanfieldScientific, USA) was used for the evaluation of skin conditions. Inside of the box on taking images kept highly uniformed brightness with six fluorescent lamps. The front, left, and right sides of the face were photographed to evaluate skin pigmentations. Skin moisture content was measured the right cheek of a face by the SKIN DIAGNOSTIC SD27 SD27 (Courage + Khazaka Electronic GmbH, Germany). The data showed the increase and decrease of the pigmentation and moisture after the 4 week for 100 with before the start.

## 2.7. Examination of Quality of Life (QOL) by Questionnaire

The quality of life (QOL) by questionnaire was assessed **Table 1**. All assessments were conducted by a researcher before the intervention and every week treatment period.

**Table 1.** Examination of QOL by questionnaire.

In the Past Week	Not Suffered at All	Hardly Suffered	Slightly Suffered	Moderately Suffered	Very Suffered	Extremely Suffered	Insufferable
1) Have you suffered from stomach pain?	1	2	3	4	5	6	7
2) Heartburn	1	2	3	4	5	6	7
3) Acid reflux from the stomach	1	2	3	4	5	6	7
4) Stomach pain on an empty stomach	1	2	3	4	5	6	7
5) Nausea	1	2	3	4	5	6	7
6) Stomach making noise	1	2	3	4	5	6	7
7) Fullness in the stomach	1	2	3	4	5	6	7
8) Burp	1	2	3	4	5	6	7
9) Fart	1	2	3	4	5	6	7
10) Constipation	1	2	3	4	5	6	7
11) Diarrhea	1	2	3	4	5	6	7
12) Loose stool	1	2	3	4	5	6	7
13) Hard stool (having difficulty to stool)	1	2	3	4	5	6	7
14) An urgency to defecate	1	2	3	4	5	6	7
15) Incomplete evacuation	1	2	3	4	5	6	7
16) Lower abdominal fullness	1	2	3	4	5	6	7
17) Impatience	1	2	3	4	5	6	7
18) Light sleep	1	2	3	4	5	6	7
19) Cold extremities	1	2	3	4	5	6	7
20) Pimply or rough skin	1	2	3	4	5	6	7

## 2.8. Statistical Analysis

All the data are presented as mean  $\pm$  SEM. The statistical analysis was evaluated by T-test before the start of the study and 4 week after the administration. Statistical comparison of experimental Food was analyzed using the Wilcoxon test. The quality of life (QOL) by questionnaire was evaluated test in consideration of a variable effect. P values of  $<0.05$  were defined as statistically significant.

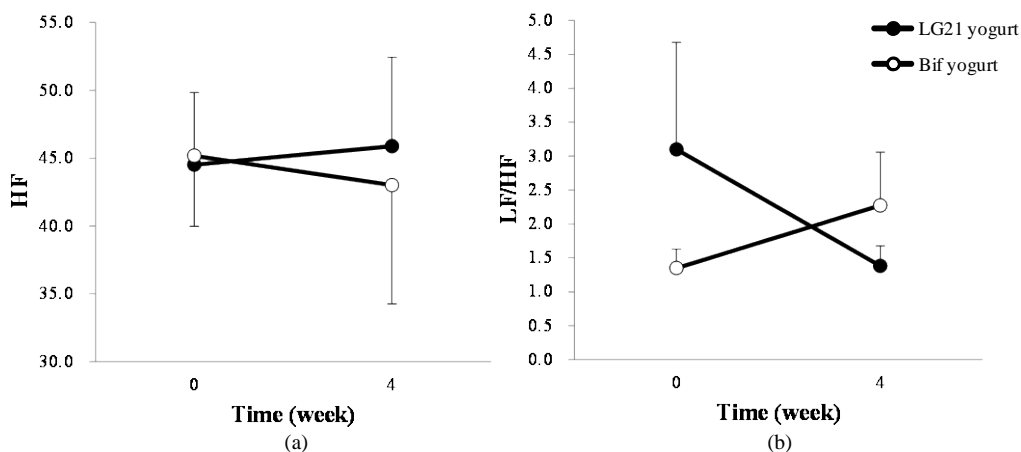
## 3. Results

### 3.1. The Autonomic Nervous Activities

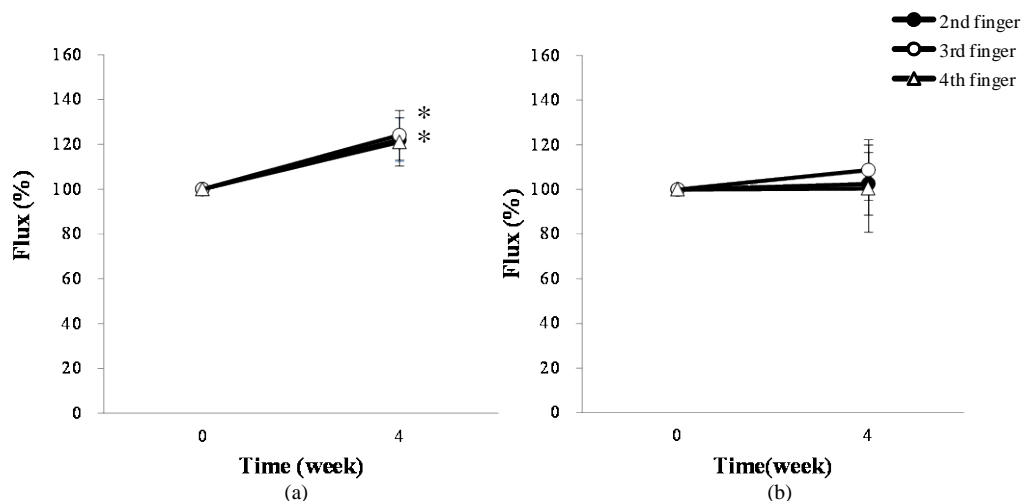
The result of the autonomic nervous activities was shown in **Figure 1**. The LG21 yogurt group slightly increased the parasympathetic nerve activity (**Figure 1(a)**). The LG21 yogurt group was decreased the LF/HF ratio. The Bif yogurt group increased the LF/HF ratio (**Figure 1(b)**). Both in the LG21 yogurt group and Bif yogurt group, significant changes were not observed on the change of autonomic nervous activities after 4 week.

### 3.2. The Peripheral Blood Flow

The result of the peripheral blood flow was shown in **Figure 2**. The LG21 yogurt group significantly increased



**Figure 1.** Effects of the yogurt on the autonomic nervous activities. (a) HF; (b) LF/HF ratio (Mean  $\pm$  SE. n = 10).



**Figure 2.** Effects of the yogurt on the peripheral blood flow. (a) LG21 yogurt; (b) Bif yogurt (Mean  $\pm$  SE. n = 10), \*: p < 0.05 vs 0.

the peripheral blood flow of second and third finger at 115.6%, 119.3%, respectively. The Bif yogurt group did not change in the peripheral blood flow.

### 3.3. The Salivary Components

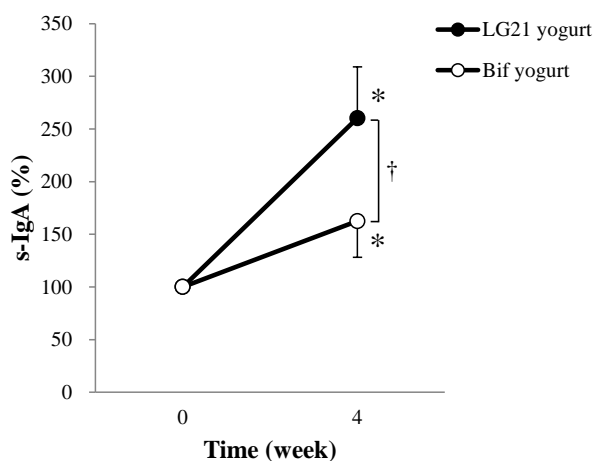
The result of the saliva s-IgA level was shown in **Figure 3**. The LG21 yogurt group and the Bif yogurt group significantly increased the s-IgA levels. A significant difference was observed between the LG21 yogurt group and the Bif yogurt group.

### 3.4. The Skin Condition

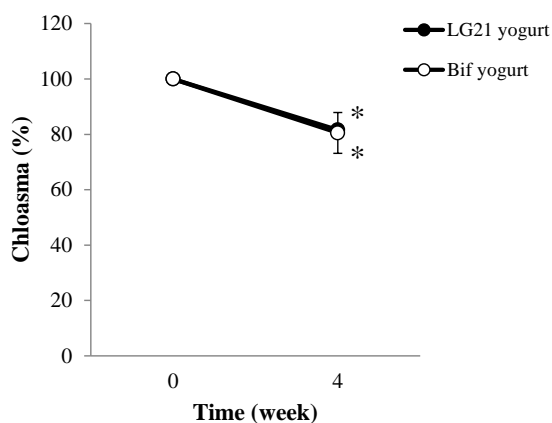
The result of the skin pigmentation was shown in **Figure 4**. The LG21 yogurt and Bif yogurt significantly decreased on skin pigmentation at 85.7%, 80.5%, respectively. The result of the skin moisture was shown in **Figure 5**. The LG21 yogurt significantly increased on skin moisture at 114.1%. The Bif yogurt group did not change in the skin moisture. A significant difference was observed between the LG21 yogurt group and the Bif yogurt group.

### 3.5. The Examination of Quality of Life (QOL)

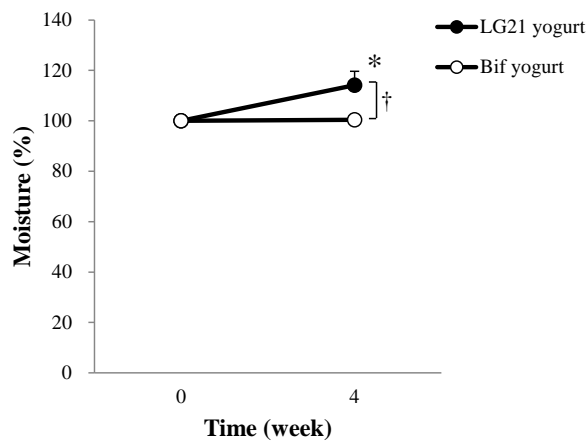
The result of QOL questionnaire was shown in **Table 2**, **Table 3**. A significant difference was observed between



**Figure 3.** Effects of the yogurt on the saliva s-IgA leve. (Mean  $\pm$  SE. n = 10). \*: p < 0.05 vs 0, †: p < 0.05 LG21 yogurt vs, Bif yogurt.



**Figure 4.** Effects of yogurt on skin pigmentation. (Mean  $\pm$  SE. n = 10), \*: p < 0.05 vs 0.



**Figure 5.** Effects of yogurt on skin moisture. (Mean ± SE. n = 10). \*: p < 0.05 vs 0, †: p < 0.05 LG21 yogurt vs. Bif yogurt.

**Table 2.** Effects of QOL by questionnaire on an intake period becomes long.

		Week course (P value)	Standard	P value
1)	Have you suffered from stomach pain?	0.286		
2)	Heartburn	0.079		
3)	Acid reflux from the stomach	0.153		
4)	Stomach pain on an empty stomach	0.761		
5)	Nausea	0.587		
			Before vs.2w	0.099
6)	Stomach making noise	0.049	Before vs.3w	0.062
			Before vs.4w	0.099
			Before vs.2w	0.093
7)	Fullness in the stomach	0.024	Before vs.3w	0.076
			Before vs.4w	0.020
8)	Burp	0.189		
9)	Fart	0.600		
10)	Constipation	0.999		
11)	Diarrhea	0.276		
12)	Loose stool	0.688		
13)	Hard stool (having difficulty to stool)	0.150		
14)	An urgency to defecate	0.229		
15)	Incomplete evacuation	0.019	Before vs.2w	0.021
16)	Lower abdominal fullness	0.043	Before vs.2w	0.039
17)	Impatience	0.214		
18)	Light sleep	0.385		
			Before vs.2w	0.038
19)	Cold extremities	0.018	Before vs.3w	0.023
			Before vs.3w	0.032
20)	Pimply or rough skin	0.031	Before vs.4w	0.046

**Table 3.** Effects of QOL by questionnaire between LG21 yogurt group and the Bif yogurt group.

		Pre vs. 4W (P value) Bif. vs. LG21
1)	Have you suffered from stomach pain?	0.579
2)	Heartburn	0.188
3)	Acid reflux from the stomach	0.034
4)	Stomach pain on an empty stomach	0.023
5)	Nausea	0.027
6)	Stomach making noise	0.896
7)	Fullness in the stomach	0.839
8)	Burp	0.793
9)	Fart	0.154
10)	Constipation	0.532
11)	Diarrhea	0.510
12)	Loose stool	0.086
13)	Hard stool (having difficulty to stool)	0.745
14)	An urgency to defecate	0.995
15)	Incomplete evacuation	0.602
16)	Lower abdominal fullness	0.948
17)	Impatience	0.780
18)	Light sleep	0.443
19)	Cold extremities	0.422
20)	Pimply or rough skin	0.231

the LG21 yogurt group and the Bif yogurt group. As a result of QOL questionnaire, acid reflux from the stomach, stomach pain on an empty stomach and nausea improved in LG21 yogurt group. In the generally, an index of various QOL was improved if an intake period becomes long. As a result of QOL questionnaire, incomplete evacuation, lower abdominal fullness, cold extremities and pimply or rough skin improved in LG21 yogurt group and Bif yogurt group after the administration period.

#### 4. Discussion

The yogurt has been taken in as the food which was good for health and beauty from experience for a long time. The beneficial effects of yogurt have been extensively reviewed. As a result of QOL questionnaire, incomplete evacuation, lower abdominal fullness, cold extremities and pimply or rough skin significantly improved in yogurt after the administration period.

In the present study, LG21 yogurt slightly increased the parasympathetic nerve activity, decreased LF/HF ratio, although a significant difference was not observed. Moreover, LG21 yogurt increased peripheral blood flow. It is generally known that autonomic nerves comprising sympathetic and parasympathetic nerves regulate various body functions such as blood pressure, body temperature, glucose metabolism, energy metabolism and digestion. The peripheral blood flow reflects the sole regulation of blood vessels by the sympathetic nerves, sympathetic nervous activation results in peripheral vasoconstriction and consequent reduction in blood flow. By contrast, inhibition of sympathetic nerves results in peripheral vasodilation and resultant increased blood flow. In the previous studies reported that the probiotic strain *Lactobacillus johnsonii* strain La1 suppressed sympathetic nerves innervating the adrenal gland and kidney of urethane-anesthetized rats, lowering the blood glucose and blood pressure levels, and facilitated the gastric parasympathetic nerve elevating appetite and body weight [10] [11]. After ingesting on the LG21 yogurt, subjects had increased peripheral blood flow, which is suggestive

of the inhibition of sympathetic activity by the parasympathetic activation. Feeling of cold or a chilly sensation is called “Hie-sho” in Japanese, meaning cold syndrome. The factors responsible for chilly sensation are assumed to be poor peripheral blood flow and impaired metabolism. Therefore, the activity of sympathetic neurons may be important for chilly sensation [12]. Our result showed that LG21 yogurt fixed the autonomic nerve balance. These findings suggest that LG21 yogurt may be useful for the treatment of chilly sensation.

The LG21 yogurt and Bif yogurt significantly increased in the saliva s-IgA levels. IgA is the main immunoglobulin involved in mucosal defense. The increase in IgA has been attributed to the anti-infection properties of probiotics in diarrhea [13]. Recent findings have shown that secretion of IgA is critical in the regulation of the composition of the microbial community in the gut [14] [15]. In the present study, it is shown that yogurt may exert antitumour activity by a decrease in the inflammatory immune response mediated by IgA increase [16].

The LG21 yogurt and Bif yogurt significantly decreased on skin pigmentation. In addition, the LG21 yogurt significantly increased on skin moisture. It has been reported that the yogurt improved on the skin moisture [17]. For many years, it has been reported that persistent constipation worsens dermal characteristics and aggravates comedones as the intestinal environment deteriorates. Ara et al. reported that the analysis of the correlation between the defecation frequency and dermal characteristics, especially comedones, a significant increase in the number of comedones was noticed in the groups with a defecation frequency of 5 or 6 times and of 4 or fewer times per week, compared with the 7 or more-times group, confirming a correlation of worsening dermal characteristics with a greater tendency to constipation.

The improvement effect of yogurt on skin function may be related to the improvement of constipation [18].

Irritable bowel syndrome symptom includes abnormal motility, visceral hypersensitivity, inflammation, autonomic activity, and modulation of central nervous system. Brain-gut interactions play a prominent role in the modulation of gut function in health and disease. In the present study, the improvement effect of LG21 yogurt on skin function may be related to the improvement of constipation by autonomic activity and modulation of central nervous system. Moreover, the results that improvement was observed by a QOL questionnaire were confirmed in the objective evaluation.

In this study, we evaluated for the effects of the LG21 yogurt on autonomic nerve activities, peripheral blood flow, skin condition (skin pigmentations and moisture), saliva s-IgA and examination of QOL.

## 5. Conclusion

In conclusion, these results suggest that the improvement effects of LG21 yogurt may be related to the activity of the parasympathetic nervous system.

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