Effect of *Portulaca Oleracea* L. extract on functional constipation: A randomized, double-blind, placebo-controlled trial

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**Abstract**

**Background:** This study aimed to investigate the efficacy of *P. oleracea* in the management of patients with functional constipation.

**Methods:** A total of 60 patients with functional constipation as defined by the Rome IV criteria were enrolled in this randomized, double-blind, placebo-controlled study; 70% ethanol extracts of the aerial parts of *P. oleracea* were used for the intervention. Patients were randomly assigned to the *P. oleracea* or placebo groups. Treatment response, quality of life, and changes in colonic transit time (CTT) were evaluated.

**Results:** Complete spontaneous bowel movement (CSBM) improved significantly in the *P. oleracea* group compared with that in the placebo group over 8 weeks of treatment (\(P = 0.003\)). Overall Patient Assessment of Constipation Quality of Life (PAC-QOL) and Patient Assessment of Constipation Symptoms (PAC-SYM) score improvements were observed in the *P. oleracea* group (\(P < 0.05\)). Moreover, CTT decreased from 44.5 ± 22.0 h to 33.7 ± 22.7 h in the *P. oleracea* group after 7 weeks of treatment (\(P = 0.04\)). There were no significant differences in the Bristol Stool Form Scale (BSFS) or adverse events between the groups.

**Conclusions:** Compared to placebo, the use of *P. oleracea* in patients with functional constipation significantly improved CSBM, severity of symptoms, and quality of life. Further large studies are required to assess the benefits of *P. oleracea* in the treatment of functional constipation.

**Keywords:** Bowel movement, colon transit time, functional constipation, *Portulaca oleracea*

**INTRODUCTION**

Constipation is a heterogeneous, multifactorial disorder. Patients with constipation present with a varying set of symptoms, including infrequent bowel movements, defecatory disorders, and hard stool consistency. The prevalence of constipation is approximately 16%, with female predominance, and increases with age. Although it is not fatal in most cases, chronic constipation can result in...
Guidelines recommend a stepwise approach for the management of constipation. After initial lifestyle modifications, bulking agents and osmotic laxatives are recommended as first-line pharmacologic treatments. However, more than half of patients are not sufficiently satisfied with their treatment. Patient satisfaction with treatment varies, and alternative conservative management is widely used by patients with constipation.

*P. oleracea* is an annual grassy plant with succulent leaves that are widely spread worldwide. It is known as purslane and is used in herbal medicine. It is known to display diuretic, antipyretic, antiseptic, antispasmodic, analgesic, and anti-inflammatory effects. Recently, *P. oleracea* has been suggested to be effective for fecal evacuation in an experimental animal model. However, the efficacy of *P. oleracea* for the management of patients with constipation has not yet been reported. Thus, we conducted the current study to identify the effect of *P. oleracea* in patients with functional constipation, as defined by the Rome IV criteria.

**PATIENTS AND METHODS**

**Study design**

A single-center, double-blind, randomized, placebo-controlled study was conducted to evaluate the efficacy of *P. oleracea* in patients with functional constipation. The study was conducted in accordance with good clinical practice guidelines and the Declaration of Helsinki. This study was approved by the institutional review board (IRB No. DKUH 2018-04-015, approved date 20-06-2018), and written informed consent was obtained before enrollment.

Data were collected between June 2018 and December 2018 at the Dankook University Hospital in Korea. Screening for functional constipation was conducted within 4 weeks prior to enrollment. After screening, the baseline colon transit time (CTT) was measured using radiopaque markers. Demographic data such as age, sex, height, weight, body mass index (BMI), and laboratory data were obtained.

Eligible patients were sequentially randomized to either *P. oleracea* (480 mg) once daily or placebo (480 mg) once daily for an 8-week treatment period. Computer-generated random numbers were used to allocate the patients. A randomization sequence was created with a random block size of four. The allocation was concealed by a pharmacist, and blinding of allocation was maintained except in emergency situations or for analysis after completion of the study. The placebo and the active drug were identical in shape and color with similar flavors and scents to ensure that blinding was maintained. The placebo was composed of microcrystalline cellulose (480 mg). Further, 480 mg dose of *P. oleracea* extract was determined based on the previous study with 5000 mg/kg/day (486.22 mg/60 kg/day in humans) of no observed adverse effect level in rats.

Patients were instructed to report their constipation-related symptoms, complete spontaneous bowel movement (CSBM), spontaneous bowel movement (SBM), adverse events, and need for rescue medication at each visit (baseline, week 4, and week 8). Laboratory tests, electrocardiography, patient assessment of constipation quality of life (PAC-QOL), and patient assessment of constipation symptoms (PAC-SYM) were obtained at baseline and after 8 weeks of treatment. CTT was assessed during the screening period and repeated at week 7 during the intervention. In the absence of defecation for more than 4 consecutive days, bisacodyl (10 mg) was permitted to be used as rescue therapy and was requested not to be used after symptom relief.

**Preparation of the extract**

The intervention medicine consisted of KDC16-2, a 70% ethanol extract of *P. oleracea*. The aerial parts of *P. oleracea* were used to produce the product. The plant was collected and identified by Dr. Rho MC and manufactured. A voucher specimen (KRI-BKR2016-003) was deposited. Dry *P. oleracea* (100 kg) was extracted using 70% ethanol at a 1:12–13 ratio at 70°C for 4 h. After removing the solid substance by using a 10-μm filter, the extract was concentrated and mixed with dextrin (1:1 ratio); 25 kg of the final product (KDC16-2) was produced after filtering sterilized mixture and drying under 180°C–200°C conditions. The purified product contained bioactive compounds such as portulacanone C, trans-n-feruloyltyramine, and cis-n-feruloyl-3’-methoxytyramine identified by high-performance liquid chromatography (HPLC), nuclear magnetic resonance, and electrospray ionization-mass spectrometry.

**Participants**

Outpatients between the ages of 20 and 65 years who had symptoms of functional constipation as defined by the Rome IV classification were enrolled. Patients were included if they had symptoms during the last 3 months, with symptom onset at least 6 months before diagnosis, and reported at least two of the following symptoms with more than 25% of defecations: straining, lumpy or hard stool, a sensation of incomplete evacuation, a sensation of anorectal obstruction blockage, use of a manual maneuver,
or <3 spontaneous bowel movements per week.\textsuperscript{[10]} Colonoscopy was performed in patients aged >50 years to exclude organic causes of constipation. Patients with irritable bowel syndrome defined by the Rome IV criteria were not included in this study.

Patients were excluded if they had undergone gastrointestinal surgery, except for cholecystectomy. Patients were also excluded if they had a history of inflammatory bowel disease, liver cirrhosis, heart failure (NYHA grade III or IV), renal disease (creatinine clearance <30 mL/min), uncontrolled diabetes mellitus, hypothyroidism, neurologic disorder, or allergic reaction to \textit{P. oleracea}. Patients taking probiotics were excluded from the study. Pregnant or breastfeeding women were also excluded.

\textbf{Measurements}

Patients were requested to report SBM, CSBM, and stool consistency by using the 7-point BSFS (1 = “separate hard lumps, like nuts (hard to pass)” to 7 = “watery, no solid pieces, entirely liquid”).\textsuperscript{[11]} Patients were asked to rate the severity of constipation-related symptoms, such as flatulence, gas, bloating, a sensation of incomplete evacuation, and straining, on a 0–10-point visual analog scale, where a higher score indicated greater severity.

The PAC-SYM questionnaire consists of 12 items scored by patients on a 5-point scale ranging from 0 (absence) to 4 (very severe). The PAC-SYM contains three domains: abdominal symptoms, rectal symptoms, and stool symptoms.\textsuperscript{[12]} Patients were also requested to score the PAC-QOL questionnaire. The PAC-QOL consists of 28 items and four subscales that include physical discomfort, psychosocial discomfort, worries and concerns, and satisfaction with bowel habits on a 5-point scale.\textsuperscript{[13]}

The CTT test was performed at baseline and at week 7. Patients were requested to ingest 20 radiopaque markers for 3 consecutive days. The numbers of markers in the right colon, left colon, and rectosigmoid were counted on day 4. CTT was calculated by multiplying 1.2 by the number of radio-opaque markers in each segment and summed to yield the whole CTT.\textsuperscript{[14]} Additional X-ray evaluation was performed on day 7 to assess CTT in the case of slow transit with a cutoff value of 59 h.\textsuperscript{[14]} All adverse events were requested to be reported and recorded during the study period.

\textbf{Primary and secondary efficacy outcomes}

The primary outcome was the improvement in the frequency of CSBM per week after 8 weeks of treatment.

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The patients were requested to report bowel movements for the previous 1 week at each visit (baseline, week 4, and week 8) without using any laxatives. The secondary outcomes were the effects of \textit{P. oleracea} on other variables. The responder rate, defined as the proportion of patients with an increase of ≥1 CSBM per week from the baseline, was calculated. The proportion of patients who had ≥3 CSBMs per week assessed at week 8 among those with ≤2 CSBMs at baseline was also calculated. Because bowel movements alone cannot reflect subjective symptom relief or patient satisfaction, other patient assessment parameters were evaluated. Changing scores of patients’ assessment for constipation-related symptoms, PAC-QOL, PAC-SYM, BSFS, and CTT were compared for each group to determine the efficacy of \textit{P. oleracea}.

\textbf{Sample size}

Considering that there was no relevant data about the efficacy of \textit{P. oleracea} on functional constipation, it was assumed that there was a 7.3% improvement in the intervention group and 1.6% improvement in the control group after 8 weeks of treatment. The standard deviation was assumed to be 8%. A sample size of 30 subjects in each group was assigned to detect a difference of 5.7% in improvement between patients who received \textit{P. oleracea} and placebo. Further, 80% statistical power, a two-sided significance level of 5%, and a 20% dropout rate were considered.

\textbf{Statistical analysis}

Patient demographics were summarized using descriptive statistics. Data are expressed as mean ± standard deviation or median with interquartile range for continuous variables and as percentages of the total number for categorical variables. The primary efficacy analysis was performed using the intention-to-treat (ITT) population. Multiple imputations were used to handle the missing data. Per-protocol (PP) analysis was conducted in patients who had follow-up outcome measurements at least once after treatment. Comparisons between the intervention and placebo groups were assessed using the Chi-square ($\chi^2$) test for categorical variables and \textit{t} tests or Wilcoxon–Mann–Whitney test for continuous variables. Repeated measures ANOVA was used to evaluate the effect of \textit{P. oleracea} on improvement in stool frequency, constipation-related symptoms, PAC-QOL, PAC-SYM, and CTT during the study period. Two-sided \textit{P} values <0.05 were considered statistically significant. Statistical analyses were conducted using R software (version 3.4.4).

\textbf{RESULTS}

\textbf{Participant characteristics}

A total of 60 patients were randomized and equally
distributed to the treatment and placebo groups. Twelve patients dropped out due to the following reasons: consumption of antibiotics (n = 1), drug compliance (<80%, n = 3), loss to follow-up (n = 2), and medication use possibly affecting study outcomes (n = 6). Finally, 48 participants completed the study protocol and were used to analyze the efficacy of *P. oleracea* on functional constipation [Figure 1].

In the current study, 50 patients (83%) were women. Females were more prevalent in both groups, although the proportion of males was higher in the placebo group than in the *P. oleracea* group (30% vs. 3.3%). The enrolled participants were relatively young and metabolically competent. There were no significant clinical differences between the two groups in terms of age, BMI, blood pressure, bowel movement, or laboratory tests [Table 1]. Baseline CSBM and SBM were similar between the groups. Of the 60 patients, 57 (95%) reported <3 CSBMs per week, and 36 patients (60%) reported <3 SBMs per week at baseline. The degree of constipation-specific quality of life and symptoms were moderate in both groups at baseline. However, patients with functional constipation in the *P. oleracea* group reported more difficulties with PAC-QOL and PAC-SYM than those in the placebo group.

### Efficacy of portulaca extract supplementation on stool frequency

After 4 weeks of treatment, a mean 1.2 increase in CSBM per week was achieved in the *P. oleracea* group compared with 0.5 increments in the placebo group (*P* = 0.028). The effect of *P. oleracea* on stool frequency was maintained for 8 weeks [Table 2]. The mean CSBM at week 8 was 2.1/week in the *P. oleracea* group and 1.2/week in the placebo group, and the mean difference from baseline was 1.1/week and 0.1/week in each group, respectively. In the PP population, the response rate was higher in the *P. oleracea* group. The proportion of patients with a ≥1/week increase in CSBM was 68% in the *P. oleracea* group and 30% in the placebo group (*P* = 0.02) [Figure 2a]. Additionally, of the 45 participants whose CSBM was <3/week at baseline, 37.5% of patients treated with *P. oleracea* achieved ≥3/week CSBM compared with 9.5% in placebo after 8 weeks of treatment (*P* = 0.04) [Figure 2b]. There were no statistically significant changes in SBM between the groups.

### Improvement in constipation-related symptoms, PAC-QOL scores, and PAC-SYM scores

At baseline, the *P. oleracea* group suffered significantly more from constipation than the placebo group. However, patients treated with *P. oleracea* showed improvement in constipation-related symptoms and quality of life throughout the study period. Compared with placebo, *P. oleracea* treatment was significantly associated with sustained symptom relief in flatulence, gas, bloating, a sensation of incomplete evacuation, straining, and hard stool, during 4–8 weeks period (all *P* < 0.01; PP analysis) [Figure 3]. Regarding PAC-QOL, only patients treated with P. oleracea reported statistically significant improvement in all aspects of PAC-QOL, including the overall scores and subscores [Table 3]. Significant improvement in PAC-SYM was also reported in the P. oleracea group [Table 4].

**P. oleracea** extract supplementation is associated with a decrease in CTT

There was no difference in CTT between the *P. oleracea* and
placebo groups at baseline ($P = 0.408$). The mean CTT was 40.63 ± 32.11 h in this study population. After 7 weeks of treatment, a significant improvement in CTT was observed in the *P. oleracea* group. There was a significant difference in CTT between the groups during the course of treatment ($P = 0.04$). An average 10.8-h decrease in CTT was achieved in the *P. oleracea* group, whereas an increase of 5.2 h in CTT was observed in the placebo group [Table 5]. A major improvement in CTT was accomplished in the left colon ($P = 0.02$), and the rectosigmoid colon showed a non-significant decreasing trend in CTT ($P = 0.25$) in the *P. oleracea* group.

### Stool consistency

There was no significant difference in stool consistency between the groups (2.9 ± 1.3 vs. 3.3 ± 1.5, $P = 0.68$). Improvements in stool consistency on the BSFS were observed in both groups of patients. However, the BSFS was not different between the *P. oleracea* and placebo groups at week 8 (4.0 ± 1.2 vs. 4.0 ± 1.5, $P = 0.48$).

### DISCUSSION

In the current study, *P. oleracea* was found to be an effective treatment for functional constipation. The use of *P. oleracea* was associated with improvement in bowel movement, including CSBM and SBM, constipation-related symptoms, and quality of life, over the 8-week trial. Significantly increased CSBM per week from baseline was observed in the *P. oleracea* group compared to that in the placebo group ($P = 0.003$). Moreover, *P. oleracea* was effective in reducing the CTT during the study period. Sustained symptom relief and enhanced quality of life can be achieved in patients treated with *P. oleracea*. However, there was no significant difference in stool consistency between the groups.

To the best of our knowledge, this is the first clinical trial to demonstrate the efficacy of *P. oleracea* in treating functional constipation. *P. oleracea* has been suggested to have many clinical effects, such as neuroprotective, muscle relaxant,
anti-inflammatory, analgesic, antiulcerogenic, antimicrobial, and lipid-lowering activities. Although it has been known that unroasted seeds of *P. oleracea* have a laxative effect in Unani medicine, its role in functional constipation remains to be evaluated. In a previous experimental animal study, *P. oleracea* treatment significantly improved fecal evacuation, which was facilitated by an increase in fecal weight, fecal water content, and intestinal transit compared with placebo. This result suggests that the improvement in the bowel movement of the *P. oleracea* group was derived from fecal bulking combined with increased bowel motility.

In the current study, an average 1.2 increase in CSBM/week was achieved in the *P. oleracea* group, and responder rates were significantly higher in the *P. oleracea* group (68% vs. 30%, *P* = 0.02). These results were supported by changes in CTT due to a significant decrease in CTT observed in the *P. oleracea* group (*P* = 0.04). Interestingly, accelerated CTT in the distal colon was prominent after *P. oleracea* supplementation. In this study, the left colon was the most time-consuming segment (18.40 ± 18.77), followed by the rectosigmoid (13.53 ± 13.94), and finally the right colon (8.70 ± 8.97) at baseline. After 7 weeks of treatment with *P. oleracea*, a significant decrease in CTT was observed in the left colon, and CTT tended to decrease in the rectosigmoid colon.

In addition, prominent symptom improvement was achieved in patients treated with *P. oleracea* in the present study. The analgesic, anti-inflammatory, and antimicrobial properties of *P. oleracea* may have a potential effect on relieving constipation symptoms. It has been hypothesized that functional dysbiosis of the gut microbiota can induce

### Table 4: Changes in PAC-SYM

| PAC-SYM          | Portulaca (n=25) | Placebo (n=23) | *P*  |
|------------------|------------------|----------------|------|
| Global score     | 1.8±0.5          | 1.4±0.6        | <0.001|
| Abdominal symptoms | 0.7±0.6          | 1.1±0.4        |      |
| Baseline         | 1.6±0.6          | 1.2±0.7        | <0.001|
| Week 8           | 0.7±0.6          | 1.1±0.6        |      |
| Rectal symptoms  | 1.3±0.9          | 0.8±0.7        | 0.006 |
| Baseline         | 0.5±0.5          | 0.6±0.6        |      |
| Week 8           | 2.3±0.7          | 1.9±0.7        | 0.001 |

Data are presented as the mean±standard deviation. A repeated-measures ANOVA was conducted to calculate *P* values in per-protocol population.

### Table 5: Changes in colon transit time

|          | Portulaca (n=25) | Placebo (n=23) | *P*  |
|----------|------------------|----------------|------|
| Total colon | 44.45±22.0       | 36.5±40.5      | 0.04 |
| Baseline  | 33.7±22.7        | 41.6±34.8      |      |
| Week 7    | 9.1±6.9          | 8.2±11.0       | 0.67 |
| Right colon | 11.0±9.4        | 8.9±8.2        |      |
| Baseline  | 13.2±12.2        | 21.2±22.4      | 0.02 |
| Week 7    | 20.6±15.0        | 15.9±22.3      |      |
| Left colon | 14.7±13.1        | 12.26±15.0     | 0.25 |
| Baseline  | 8.8±9.1          | 11.4±17.4      |      |
| Week 7    |                  |                |      |

Data are presented as the mean (h) ± standard deviation. A repeated-measures ANOVA was conducted to calculate *P* values in per-protocol population.
visceral hypersensitivity,\textsuperscript{10} and significant symptom relief induced by fecal microbiota transplantation was reported in patients with irritable bowel syndrome.\textsuperscript{13} In addition, symbiotics appeared to be more effective than a placebo in chronic constipation.\textsuperscript{18} Although there is a lack of data about \textit{P. oleracea} on the human gut microbiome, a broad spectrum of antimicrobial activity against Gram (+) and (−) strains was reported, especially in \textit{S. aureus} and \textit{Shigella dysenteriae}.\textsuperscript{19} These results suggest that \textit{P. oleracea} extract is effective for functional constipation through its direct biological activity and alteration of dysbiosis of the gut microbiota.

Our study shows that \textit{P. oleracea} is effective in terms of bowel movement, symptom control, and quality of life in patients with functional constipation. However, there are several limitations to the current study, and caution should be exercised when interpreting these results. First, the sample size was relatively small, and there was an imbalance in the sex ratio between the groups. The proportion of men was higher in the placebo group. However, patients were randomly assigned, and there was no intention to have sex ratio differences between the groups. Although 20\% of the participants dropped out in the present study, the dropout rate in each group was balanced. Moreover, other demographic factors, including age and BMI, did not differ between the two groups. Second, an imbalance in PAC-QOL and PAC-SYM scores was observed at baseline. These results might be influenced by the female predominance in the active treatment group. However, this score difference at baseline did not attenuate the effect of \textit{P. oleracea} on functional constipation. Despite lower PAC-QOL and PAC-SYM scores in the \textit{P. oleracea} group than in the placebo group, a statistically significant improvement was observed in the \textit{P. oleracea} group after 8 weeks of treatment. Third, a relatively young population was included in the current study. However, the relatively young characteristics of this population might result in a more homogeneous study population, and there were relatively low chances of including other defaecatory evacuation disorders. Fourth, this study did not include patients who were pregnant or lactating, leaving the potential role of herbal medicine on functional constipation in this population. Lastly, this study does not provide knowledge related to toxicity from long-term use of this product and the active ingredients for constipation. Thus, caution is needed when applying these results to the general population.

In conclusion, our randomized controlled study indicated that treatment with \textit{P. oleracea} is effective for treating functional constipation. It improves bowel motility and is superior to placebo in terms of constipation-related symptom relief and quality of life.

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**Conflicts of interest**

There are no conflicts of interest.

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## SUPPORTING INFORMATION

### Table S1: Changes in laboratory test after intervention

| Group          | Baseline       | Week 8       | \( P \)  |
|----------------|----------------|--------------|--------|
| **WBC**       |                |              |        |
| placebo       | 5.89±1.74      | 5.94±1.11    | 0.374 |
| \( P. oleracea \) | 6.56±1.90      | 7.00±2.92    | 0.938 |
| **RBC**       |                |              |        |
| placebo       | 4.55±0.38      | 4.57±0.39    | 0.956 |
| \( P. oleracea \) | 4.48±0.36      | 4.47±0.35    | 0.892 |
| **Hemoglobin**|                |              |        |
| placebo       | 13.79±1.28     | 13.85±1.33   | 0.956 |
| \( P. oleracea \) | 12.98±1.36     | 12.99±1.26   | 0.892 |
| **Platelets** |                |              |        |
| placebo       | 243.04±51.73   | 255.26±54.03 | 0.410 |
| \( P. oleracea \) | 281.80±44.67   | 284.76±50.73 | 0.992 |
| **Creatinine**|                |              |        |
| placebo       | 0.74±0.18      | 0.75±0.15    | 0.750 |
| \( P. oleracea \) | 0.64±0.12      | 0.66±0.11    | 0.455 |
| **Uric acid** |                |              |        |
| placebo       | 4.48±1.58      | 4.41±1.22    | 0.965 |
| \( P. oleracea \) | 4.79±0.90      | 4.56±1.00    | 0.509 |
| **Cholesterol**|                |              |        |
| placebo       | 173.30±36.02   | 165.49±47.38 | 0.668 |
| \( P. oleracea \) | 178.02±42.72   | 181.60±28.75 | 0.823 |
| **Protein**   |                |              |        |
| placebo       | 7.37±0.41      | 7.38±0.34    | 0.981 |
| \( P. oleracea \) | 7.48±0.36      | 7.39±0.30    | 0.242 |
| **Albumin**   |                |              |        |
| placebo       | 4.92±0.23      | 4.88±0.22    | 0.306 |
| \( P. oleracea \) | 4.90±0.23      | 4.78±0.22    | 0.058 |
| **AST**       |                |              |        |
| placebo       | 18.78±5.08     | 20.91±9.80   | 0.225 |
| \( P. oleracea \) | 17.56±4.60     | 19.52±4.95   | 0.066 |
| **ALT**       |                |              |        |
| placebo       | 18.43±13.85    | 19.96±14.42  | 1.000 |
| \( P. oleracea \) | 15.24±8.40     | 16.72±8.32   | 0.490 |
| **Total bilirubin** |            |              |        |
| placebo       | 0.59±0.29      | 0.68±0.33    | 0.391 |
| \( P. oleracea \) | 0.56±0.64      | 0.41±0.14    | 0.923 |
| **BUN**       |                |              |        |
| placebo       | 19.39±25.92    | 16.78±21.21  | 0.392 |
| \( P. oleracea \) | 11.83±3.48     | 11.04±2.02   | 0.771 |
| **Sodium**    |                |              |        |
| placebo       | 141.48±1.88    | 140.04±1.64  | 0.005**|
| \( P. oleracea \) | 140.68±1.31    | 139.56±1.58  | 0.009**|
| **Potassium** |                |              |        |
| placebo       | 4.25±0.35      | 4.15±0.28    | 0.264 |
| \( P. oleracea \) | 4.22±0.43      | 4.19±0.42    | 0.899 |
| **Chloride**  |                |              |        |
| placebo       | 103.78±4.52    | 101.74±1.71  | 0.069 |
| \( P. oleracea \) | 102.52±2.42    | 102.00±2.43  | 0.357 |
| **Ca**        |                |              |        |
| placebo       | 9.76±0.39      | 9.65±0.32    | 0.466 |
| \( P. oleracea \) | 9.58±0.28      | 9.51±0.34    | 0.291 |
| **P**         |                |              |        |
| placebo       | 3.91±0.43      | 3.91±0.54    | 0.877 |
| \( P. oleracea \) | 3.64±0.46      | 3.68±0.43    | 0.640 |
| **TSH**       |                |              |        |
| placebo       | 2.49±1.81      | 2.66±1.41    | 0.334 |
| \( P. oleracea \) | 1.71±0.58      | 1.70±0.64    | 0.691 |
| **Free T4**   |                |              |        |
| placebo       | 1.20±0.15      | 1.27±0.15    | 0.109 |
| \( P. oleracea \) | 1.22±0.10      | 1.27±0.13    | 0.116 |