



## Brief report

## Effect of dietary fatty acid and micronutrient intake/energy ratio on serum diamine oxidase activity in healthy women



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## ABSTRACT

**Objective:** Serum diamine oxidase (DAO) activity varies to a greater extent in women than in men. DAO activity during the luteal phase was higher than that during the follicular phase in healthy women. Recent reports have indicated that duodenal lipid infusion increased DAO activity in the intestinal lymph in rats. The aim of this study was to elucidate the effect of dietary nutrient intake on serum DAO activity in healthy women.

**Methods:** Thirty-four healthy Japanese women were recruited. Food surveys were performed using dietary records for 3 d during both the follicular and luteal phases. Nutrient intake was calculated and expressed as the energy intake ratio. The correlation between DAO activity and nutrient intake was analyzed.

**Results:** Serum DAO activity in both phases was positively correlated with intake of long-chain fatty acids, saturated fatty acids, and monounsaturated fatty acids ( $P < 0.05$ ). Intake of phosphorus, calcium, zinc, magnesium, iron, and vitamin B<sub>12</sub> during the luteal phase was positively correlated with serum DAO activity ( $P < 0.05$ ).

**Conclusion:** In healthy women, serum DAO activity was influenced by dietary fatty acid and micronutrient intake.

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## Introduction

Diamine oxidase (DAO) metabolizes polyamines and histamine and is abundant in the small intestine, kidney, and placenta [1]. Serum DAO activity has been used as a marker of intestinal mucosal integrity in intestinal diseases and after chemotherapy [2,3]. Recent reports have indicated that bolus administration of

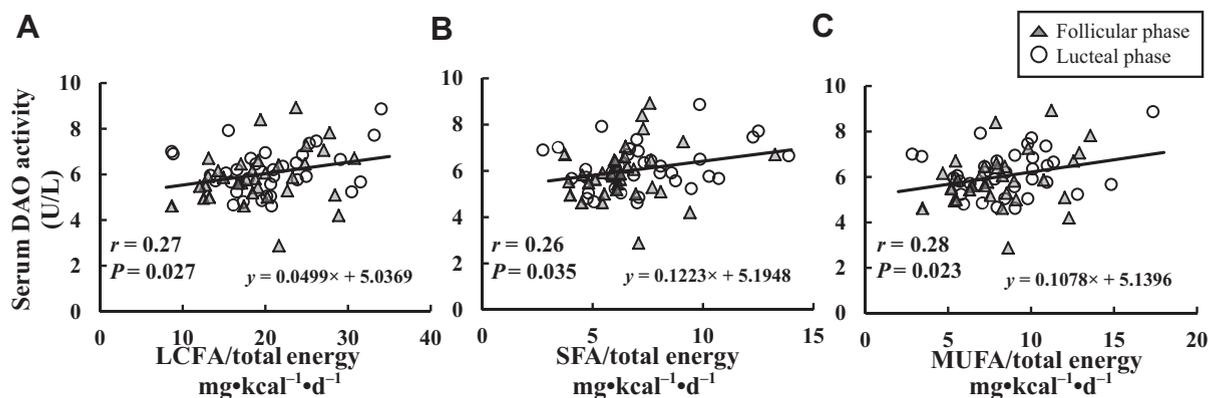
lipid emulsion or olive oil into the duodenum increased intestinal lymph DAO activity dose-dependently in rats [4]. As for micronutrients, several rat and pig studies have indicated that dietary magnesium or copper deficiency decreased blood DAO activity [5,6] but dietary zinc intake decreased serum DAO activity [7]. However, it is unclear whether dietary fatty acid and micronutrient intake are related to serum DAO activity in humans.

Serum DAO activity varies to a greater extent in women than in men. Additionally, DAO activity is high during pregnancy [2,8,9]. We have demonstrated that serum DAO activity is influenced by the menstrual cycle. Specifically, activity is higher during the luteal phase than during the follicular phase in healthy young women [8]. Ovarian steroid hormones, which indicate cyclical fluctuations and affect food intake, peak during the luteal phase of the menstrual cycle in women [10].

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**Fig. 1.** Scatter plot of serum diamine oxidase activity and dietary fatty acid intake/energy ratio. (A) Long-chain fatty acids; (B) saturated fatty acids; (C) monounsaturated fatty acids. *r* is the correlation coefficient; *P* value by Pearson product-moment correlation test. DAO, diamine oxidase; LCFA, long-chain fatty acid; MUFA, monounsaturated fatty acid; SFA, saturated fatty acid.

We hypothesized that serum DAO activity is correlated with intake of dietary nutrients, particularly long-chain fatty acids (LCFA) and micronutrients, in humans. In this study, the relationships between DAO activity and nutrient components, including carbohydrates, proteins, lipids, micronutrients, and dietary fiber, were evaluated in healthy young women with typical dietary habits of the younger generation. Additionally, we evaluated the effect of the menstrual cycle on serum DAO activity and dietary nutrient intake.

## Materials and methods

### Participants

This study involved 34 Japanese women (20–29 y of age) who were students or staff at Kobe University Graduate School of Health Sciences and Kobe University Hospital. All participants were healthy, had regular menstrual cycles, and lacked any exclusion criteria, including marriage, pregnancy, vaginal infection, use of antibiotics or hormonal contraceptive pills, and history of any disease or abnormal findings through medical examination. This study was approved by the Ethics Committee of Kobe University School of Medicine. All participants were included in this study after informed consent.

Food surveys and blood samples were collected during the follicular and luteal phases. For food surveys, dietitians performed individual interviews with participants using self-administered 3-d dietary records and a food frequency questionnaire validated by national registered dietitians of Japan. During the study, the women did not have any food or fiber restrictions and were asked to maintain their typical dietary habits and physical activity levels. Energy and nutrient contents of each diet were calculated using Healthy Maker Pro 501 R5 software (Mushroom Soft Co., Ltd., Okayama, Japan).

### Serum DAO activity

Blood samples were centrifuged at 3000g for 10 min at 4°C and stored at –80°C until analysis. Serum DAO activity was measured by Macrophi Inc. (Takamatsu, Japan) using a colorimetric assay [11]. The relationship between DAO activity and the ratio of dietary nutrient intake to energy was analyzed.

### Statistical analysis

Statistical analyses were conducted using Statcel2 software (OMS Publishing Inc., Saitama, Japan). Pearson product-moment correlation or Spearman's rank correlation was performed. Data are expressed as mean  $\pm$  SD, and *P* < 0.05 was considered statistically significant.

## Results

### Participant characteristics

All participants were healthy, unmarried Japanese women. Their mean age was  $23.3 \pm 2.5$  y, height was  $157.9 \pm 4.6$  cm,

weight was  $49.7 \pm 4.7$  kg, and body mass index was  $20 \pm 2.5$  kg/m<sup>2</sup>, all of which were within the normal range.

### Dietary nutrient intake

Daily energy and nutrient contents of each diet did not indicate any difference between the follicular and luteal phases (data not shown). These dietary nutrient intakes were within the range of average intake of women ages 20 to 29 in the 2014 National Health and Nutrition Survey conducted by the Ministry of Health, Labor and Welfare of Japan [12].

To eliminate the influence of total energy intake, nutrient intake was adjusted by energy intake ratio. The energy-adjusted amount of macro- and micronutrients is one of the most commonly used methods [13]. The energy intake/body weight ratios were  $35.6 \pm 7.4$  and  $35.0 \pm 7.1$  kcal/kg, the carbohydrate intake/energy ratios were  $53.4 \pm 5.8$  and  $53.7 \pm 5.5\%$ , the protein intake/energy ratios were  $13.9 \pm 1.9$  and  $14.2 \pm 1.9\%$ , and the lipid intake/energy ratios were  $30.4 \pm 5.2$  and  $30.0 \pm 5.8\%$ , in the follicular and luteal phases, respectively. In comparison of follicular and luteal phase in each participant, the carbohydrate, protein, and lipid intake/energy ratios varied widely, ranging from 0.5 to 2.5. Additionally, we previously reported differences in serum DAO activity between the follicular and luteal phases [8]. Thus, we evaluated the relationship between serum DAO

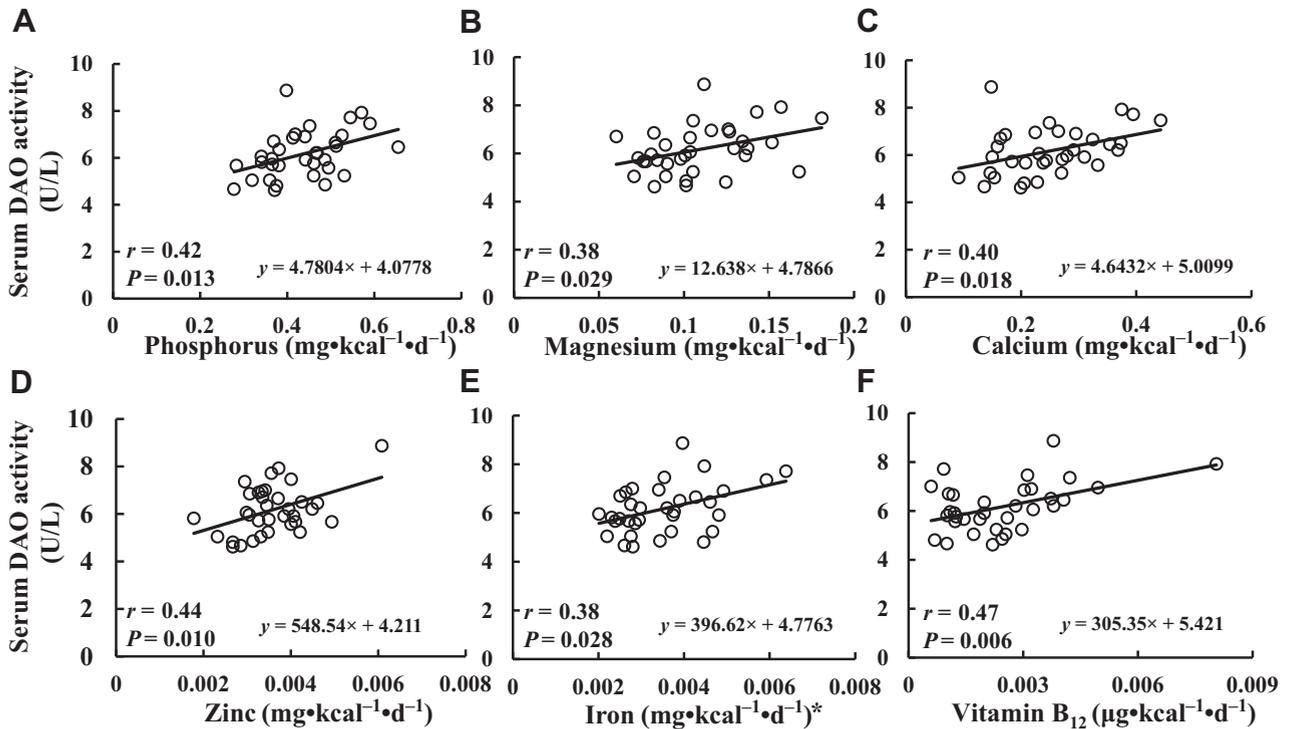
**Table 1**

Correlations between serum diamine oxidase activity and dietary nutrient intake/energy ratio

Dietary nutrients	R	P
Carbohydrates	–0.219	0.073
Proteins*	0.094	0.443
Lipids	0.186	0.129
SCFA (butyric acid)*	0.135	0.269
MCFA*	0.143	0.241
PUFA	0.168	0.172
$\omega$ -6 PUFA	0.145	0.237
$\omega$ -3 PUFA	0.207	0.090
EPA*	0.029	0.809
DHA*	0.008	0.948
Soluble dietary fiber*	0.118	0.332
Insoluble dietary fiber	–0.055	0.654

DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; MCFA, medium-chain fatty acids; PUFA, polyunsaturated fatty acids; SCFA, short-chain fatty acids  
R is correlation coefficient; *P* value is determined by Pearson product-moment correlation or

\* Spearman's rank correlation test.



**Fig. 2.** Scatter plot of serum diamine oxidase activity and dietary micronutrient intake/energy ratio during the luteal phase. (A) Phosphorus; (B) magnesium; (C) calcium; (D) zinc; (E) iron; (F) vitamin B<sub>12</sub>. *r* is correlation coefficient; *P* value by Pearson product-moment correlation or \*Spearman's rank correlation test. DAO, diamine oxidase.

activity and the dietary nutrient intake/energy ratio in different phases of the menstrual cycle.

#### Relationship between serum DAO activity and dietary nutrient intake/energy ratio

During both menstrual cycle phases, serum DAO activity was positively correlated with LCFA, saturated fatty acid (SFA), and monounsaturated fatty acid (MUFA) intake/energy ratios ( $r = 0.27, 0.26,$  and  $0.28,$  respectively;  $P < 0.05$ ; Fig. 1). The energy intake did not correlate with serum DAO activity; therefore, fatty acid intake had a specific relationship with serum DAO activity. There was no correlation between carbohydrates, proteins, lipids, short-chain fatty acids (SCFAs), medium-chain fatty acids (MCFAs), polyunsaturated fatty acids, dietary fiber, or micronutrient intake/energy ratios and serum DAO activity (Table 1).

During each menstrual cycle phase, carbohydrates, proteins, lipids, and dietary fiber were not correlated with serum DAO activity (data not shown). However, serum DAO activity was positively correlated with phosphorus, magnesium, calcium, zinc, iron, and vitamin B<sub>12</sub> intake/energy ratios during the luteal ( $P < 0.05$ ; Fig. 2), but not the follicular phase.

#### Discussion

Serum DAO activity was positively correlated with consumption of LCFA, particularly SFAs and MUFAs, in healthy women with typical dietary habits. However, SCFA, MCFA, lipids, carbohydrates, proteins, and dietary fiber intakes did not correlate with serum DAO activity. Dietary phosphorus, calcium, zinc, magnesium, iron, and vitamin B<sub>12</sub> intakes were positively correlated with DAO activity during the luteal phase. These

results suggest that serum DAO activity is influenced by food intake as well as the menstrual cycle.

Our findings were consistent with recent rat experimental data indicating that increased DAO release into the intestinal lymph was specific to LCFA feeding and was not affected by MCFA, carbohydrate, or protein consumption [14]. Our results also are consistent with a clinical study indicating that bile replacement increased serum DAO activity in biliary cancer patients with external biliary drainage [14]. LCFA and other lipids are emulsified by the detergent properties of bile acids and transported into the intestinal lymph as chylomicrons, whereas MCFA are directly transported to the portal blood flow. During LCFA absorption, histamine is released into the intestinal lymph and subsequently stimulates DAO release from the intestinal mucosal epithelium to the lymph [4]. However, the detailed mechanism underlying these observations is under investigation.

Dietary intakes of several micronutrients also were positively correlated with serum DAO activity in this study. As for zinc intake, this result of increased DAO activity with zinc in healthy women does not agree with the dose-dependent decrease in serum DAO activity followed by different dietary zinc intakes in weaned pigs [7]. The discrepancy suggests the diversity of relation between dietary zinc intake and DAO activity within specific experimental animal condition or normal human. As for the micronutrient intestinal absorption, dietary zinc intake interacts with calcium, iron, and vitamins absorption in human [15]. No correlation between dietary copper intake and DAO activity is consistent with the rat study indicating that copper intake did not increase DAO activity [6]. Positive correlation between magnesium intake and DAO activity is also consistent with the rat study that dietary magnesium deficiency decreased DAO activity in both the duodenum and plasma [5]. These reports

support that specific dietary micronutrient may affect blood DAO activity. Further detailed in vivo studies are required. Increased serum DAO activity can reduce the increased blood histamine levels suspected to accompany premenstrual syndrome (PMS). Magnesium and calcium levels are reduced during PMS, and oral administration of magnesium or calcium relieves PMS symptoms [16,17]. Findings from the present study suggest that healthy women may have the mechanisms to prevent PMS symptoms.

We also hypothesized that soluble fiber intake was correlated with increased serum DAO activity following a report indicating that 7 g/d galactomannan administration for 4 wk increased serum DAO activity in elderly patients [18]. However, we did not detect a correlation. This may be due to the fact that the participants in this study, including university students, consumed only a small amount of soluble dietary fiber ( $2.3 \pm 0.8$  g/d). This daily consumption was less than in the aforementioned study [18].

Future clinical research is required to clarify the relationship between serum DAO activity and dietary nutrient intake in healthy men, young and postmenopausal women, possibly as a randomized crossover clinical trial. Serum DAO activity is considered to be a blood marker indicating intestinal mucosal integrity during cancer chemotherapy but varies among individuals because of polymorphisms and food allergies. Additionally, our data suggest that nutrient intake affects serum DAO activity.

## Conclusion

Serum DAO activity was influenced by dietary fatty acid and micronutrient intake in healthy women. Therefore, it may be necessary to consider the influence of nutrients, particularly fatty acids, when serum DAO activity is evaluated as a measure of intestinal integrity.

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