ผลการเปลี่ยนแปลงเมตาบอไลต์ในร่างกายมนุษย์จากการบริโภคอาหารอินทรีย์ เป็นระยะเวลา 7 และ 30 วัน : การศึกษาแบบนำร่อง

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บทคัดย่อ

การบริโภคอาหารอินทรีย์กำลังเป็นที่นิยมอย่างมากในปัจจุบัน การศึกษาวิจัยนี้จึงมุ่งศึกษาการเปลี่ยนแปลงของเมตาบอไลต์ในร่างกายที่เกิดขึ้นจากการบริโภคอาหารอินทรีย์ในช่วงระยะเวลาที่ต่างกัน โดยศึกษาจากกลุ่มอาสาสมัครที่เป็นคนไทยในวัยผู้ใหญ่ และแบ่งการศึกษาวิจัยออกเป็นสองกลุ่ม คือ กลุ่มอาสาสมัครที่มีผลสุขภาพอยู่ในเกณฑ์ปกติ และกลุ่มอาสาสมัครที่มีผลสุขภาพอยู่ในกลุ่มเสี่ยง โดยให้อาสาสมัครทั้ง 2 กลุ่ม บริโภคอาหารอินทรีย์เป็นระยะเวลา 7 วัน และ 30 วัน และประเมินผลทางสุขภาพจากการเจาะเลือดและเก็บตัวอย่างปัสสาวะ โดยเก็บตัวอย่างเลือดและปัสสาวะของอาสาสมัครในวันแรกก่อนเริ่มบริโภคอาหารอินทรีย์ (วันที่ 0) และเก็บตัวอย่างเลือดและปัสสาวะของอาสาสมัคร หลังจากการบริโภคอาหารอินทรีย์เป็นระยะเวลา 0, 7 วัน และ 30 วัน ผลจากการศึกษาพบว่า กลุ่มอาสาสมัครทั้ง 2 กลุ่ม มีน้ำหนักตัว ดัชนีมวลกาย อัตราการเผาผลาญ และปริมาณของธาตุสังกะสี เปลี่ยนแปลงอย่างมีนัยสำคัญหลังจากบริโภคอาหารอินทรีย์เป็นระยะเวลา 30 วัน และผลจากการศึกษาเมตาบอไลต์ในปัสสาวะ พบว่ามีการเปลี่ยนแปลงของสารเมตาบอไลต์ที่มีความสัมพันธ์เชื่อมโยงกับกลไกของระบบเมตาบอลิซึม โดยพบว่าสารเมตาบอไลต์ nicotinamide-beta-riboside, biliverdin, octadecanoic acid, 2-methyl-1-hydroxybutyl-ThPP, s-adenosyl-l-homocysteine, 2,3-diketo-5-methylthiopentyl-1-phosphate, fumarate และ pyridoxal phosphate มีระดับเพิ่มสูงขึ้น และสารเมตาบอไลต์ allopregnanolone, dolichyl beta-d-glucosyl phosphate, corticosterone, dehydroepiandrosterone sulfate, n-carbamoyl-l-aspartate และ leukotriene C4 มีระดับลดลง ซึ่งการเปลี่ยนแปลงของระดับเมตาบอไลต์ข้างต้นจะสามารถบ่งบอกถึงผลที่มาจากการบริโภคอาหารอินทรีย์ที่ส่งเสริมสุขภาวะที่ดีได้

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Human metabolite profiling changes with organic food consumption for 7 and 30 days: A pilot study

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Abstract

Organic food consumption is a growing interest worldwide. The aim of this study is to assess overall metabolite changes that occur during organic food consumption. The Thai adult participants were classified into two groups, with a normal or at-risk health status, and then provided with a diet containing organic foods for 7 and 30 days. Health checkups,including blood and urine sampling, were performed at 0, 7 and 30 days. The effects on body weight, body mass index, the basal metabolic rate and zinc concentrations showed significantdifferences after 30 days. Urine metabolite profiling showed some changes related to human metabolic pathways. Organic food consumption was associated with higher levels of nicotinamidebeta-riboside, biliverdin, octadecanoic acid, 2-methyl-1-hydroxybutyl-ThPP, s-adenosyll-homocysteine, 2,3-diketo-5-methylthiopentyl-1-phosphate, fumarate and pyridoxal phosphate and lower levels of allopregnanolone, dolichyl beta-d-glucosyl phosphate, corticosterone, dehydroepiandrosterone sulfate, n-carbamoyl-l-aspartate and leukotriene C4. The observed metabolite changes might indicate the health-related impact of organic food consumption.

Keywords: organic food, healthy food, body mass index, metabolite compounds

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Introduction

Organic food is produced through agricultural methods that do not use fertilizers, herbicides and insecticides. Due to their quality and safety, organic foods are becoming mainstream for healthy-conscious consumers. Thailand's organic food market has grown rapidly in recent decades and such foods have long been recognized as a safe. Consumption of organic foods contributes to maintaining human health while being environmentally friendly and has been shown to lower the likelihood of developing chronic degenerative noncommunicable diseases (CDNCDs)[1]. In addition to improving quality of life, healthy foods may be beneficial by enhancing physiological homeostasis. For example, organic foods are linked to health advantages such as higher antioxidant activity[2] and a lower risk of developing cancer[3]. The total antioxidant capacity in human plasma has been reported to change with Mediterranean-style organic food consumption[4].

Biologically active substances in organic foods are of interest to health conscious consumers. Organic foods have been reported to induce higher antioxidant activity, vitamin C and minerals (magnesium and phosphorus) levels and lower nitrates and pesticide residues[5]. Research has explored phytonutrients in organic foods, including carotenoids, flavonoids and other polyphenols. Endogenous antioxidative systems interact with diverse reactive oxygen species to protect against oxidative damage to biological systems.

Emerging technologies have enhanced metabolite identification in diverse biological specimens including cerebrospinal fluid, saliva, serum and urine. Metabolites in urine can be collected passively, noninvasively and longitudinally, allowing detection and monitoring of metabolic abnormalities[6]. Urine is a rich source of cellular metabolites including urea, inorganic salts, creatinine, ammonia, organic acids, water-soluble toxins and urobilin. These metabolites have been measured by high-resolution nuclear magnetic resolution (NMR) spectroscopy and several mass spectrometry (MS)-based techniques. The application of liquid chromatography-mass spectrometry (LC-MS) for identification and quantification allows metabolic profiling. This technique is a routine diagnostic method in the clinical laboratory that assesses all metabolites in biological samples with high levels of sensitivity and specificity[7].

In recent years the higher concentration of bioactive agents in organic foods has been appreciated and studies on their consumption have increased[8-10]. However, few studies have assessed urinary metabolites. We investigated and compared the effects of organic food consumption on the metabolism of healthy and at-risk participants.

Materials and Methods

Study design and participants

The participants for the present study were identified and recruited through Suan Sampran company. The inclusion criteria were to include 1) healthy subjects with no recent

history of infectious and noninfectious diseases and 2) subject with at-risk health with no recent history of infectious and noninfectious diseases. All subjects were nonsmoker and normally active. People with psychiatric disorders were excluded from the study. The day before the beginning of the intervention, the subjects fasted overnight (no food after 20:00 hours the previous evening, only water permitted). The participants first provided blood and urine samples as described below. Then, the participants consumed organic food daily for each meal for 7 and 30 days, and blood and urine were collected on Days 8 and 31. The organic foods were prepared and cooked by Suan Sampran company and then provided to the participants 3 times a day for 7 and 30 days. Dietary record data were used to assess food intake.

Ethical approval and participants' content consent

The Institutitional Review Board of Mahidol University, Thailand approved the design of the study and provided ethical approval number MU-CIRB 2018/127.2706. Participants were recruited through the Department of Human Resources at Suan Sampran. The study was conducted according to the criteria set by the Declaration of Helsinki, and each subject signed an informed consent form before participating in the study. The participants were free to withdraw their participation during the intervention or to withdraw themselves from the intervention for any reason.

Chemicals

HPLC- or LCMS- grade acetonitrile, methanol and water were purchased from Merck (USA). Formic acid of analytical grade was purchased from Merck (USA).

Blood sample collection

Samples of approximately 4 mL of venous blood were collected by an experienced medical technologist on Days 0, 7 and 30. Blood samples were collected in serum- separating tubes and ethylenediaminetetraacetic acid BD Vacutainers (Becton Dickinson (Pty) Ltd., Franklin lakes, NJ) for and serum and plasma acquisition, respectively, according to standardized procedures.

Fasting blood glucose concentrations in serum were determined by the hexokinase method. Creatinine, cholesterol, high-density lipoprotein cholesterol (HDL-C), thyroid stimulating hormone (TSH), zinc and gamma-glutamyltransferase (GGT) in serum were analyzed with an automatic biochemical analyzer- the Siemens ADVIAII400 model (Tarrytown, NY). Cortisol was determined by an electrochemiluminescence method [Beckman Coulter's DxI 800 Immunoassay System, Beckman Coulter, Inc. 250 S. Kraemer Blvd. Brea, CA 92821 U.S.A.]. The serum samples were centrifuged for 10 minutes at a speed of 3,000 rpm before the analysis.

Sample preparation

Urine samples were collected from 94 participants after waking up in the morning

on Days 0, 7 and 30, aliquoted into four 1.5 mL microcentrifuge tubes and stored at -80 °C until analysis. Urine samples were thawed at 4 °C prior to analysis. Methanol (500 µl) was add to every 500 µl of urine. Then, the mixture was vortexed for 1 min, incubated at -20 °C for overnight and centrifuged at 13,000 rpm for 15 min at 4 °C to precipitate the protein. Five hundred microliters of supernatant was transferred to a sterile tube and dried under a vacuum centrifuge concentrator at room temperature. The dried samples were reconstituted in 200 µl of 0.1% formic acid. After vortexing for 1 min, the mixture was centrifuged at 13,000 rpm for 5 min at 4 °C to remove fine particulates. The clear supernatant was transferred to a vial and maintained at 4 °C.

Metabolite profile analysis and data processing

Then, 150 µl of sample was transferred to a vial and analyzed by liquid chromatography mass spectrometry. Liquid chromatography separation was performed using a Thermo Scientific HPLC Utimate 3,000 system equipped with a Dionex Utimate 3,000 quaternary pump delivery system (UHPLC+focused) and an Acclaim Polar Adventage II C18 column (3 µm, 2.1 X 100 mm, Thermo, USA). The column temperature was set at 40 °C. Mass spectrometry was performed using a Bruker Compact Mass Quadrupole Time-of-Flight (Q-TOF) mass spectrometer (Bruker, Germany), operating in both positive and negative ion modes. The mass range was set at 50-1,000 m/z. The nebulizing gas pressure was set at 2 bar, the drying gas flow rate was 8 L/min, and the drying gas temperature was 220 °C. Before each run, a calibrant solution of 10 mM sodium formate was injected. The control of the instrument and data processing were performed using OToFcontrol 4.0 and Data Analysis 4.3 (Bruker Daltonics) software. The mobile phases were used 0.1% formic acid in water (A) and acetonitrile modified with 0.1% formic acid (B). The flow rate was set at 0.4 ml/min. The gradient elution program started with 1% B to 99% B, with a linear gradient from 0 to 20 min, followed by isocratic separation at 99% B for 5 min, reestablishment of the initial conditions for 25 min, and then further isocratic separation at 1% B for 5 min.

The raw LC-MS data were imported to the Profile Analysis software (Bruker, Daltonics) for processing by the Find Molecular Features (FMF) peak detection algorithm. After the data were analyzed with MetaboAnalyst 4.0 software (free access to https://www.metaboanalyst.ca/) for normalization by using total ion intensity, a list of interesting features including the retention time, m/z value, and normalized peak intensity were taken for volcano plot construction to identify discriminatory metabolites before and after organic food consumption. Statistically significant differences in mean values were tested using independent sample t tests, and $p<0.05$ was considered statistically significant.

Metabolite identification

Significantly changed metabolites were identified using the Human Metabolome Database (HMDB) (http://www.hmdb.ca/)[11].

Results

Participant Characteristics

The study included 18 participants (9 males and 9 females) ranging in age from 30 to 58 years. Most participants had a body mass index in the overweight range, whereas 44% were in the normal range, and none were underweight. The basic characteristics of the participants are summarized in Table 1.

Table 1 Demographic data for each group in the study

Variable	Healthy group (n = 10)	Risk group (n = 8)
Age	38.90 ± 10.50	41.88 ± 9.26
Male	5 (50)	4 (50)
Female	5 (50)	4 (50)
Systolic blood pressure (mmHg)	116.60 ± 8.66	115.60 ± 10.88
Diastolic blood pressure (mmHg)	68.00 ± 8.34	76.50 ± 11.94

Results were expressed as the mean ± S.D.

Effects of Organic Food Consumption on Health Status

The body composition variables showed significant reductions in body weight, the percentage of body fat, excess body fat, the basal metabolic rate, belly fat and BMI among the healthy group after both 7 and 30 days compared to baseline data. However, significant differences in body weight, the basal metabolic rate (BMR) and BMI were found in the at-risk group after both 7 and 30 days compared to baseline data. Changes in body age from 31.80±8.02 to 31.30±8.20 (7 days) and 30.90±8.80 (30 days) were significant (Table 2). These changes did not reflect significant differences in waist circumference.

Interestingly, the cholesterol level decreased significantly in the at risk-group over the 30 days of the intervention (214.90±24.22 to 206.30±26.97 mg/dL, $p<0.001$). No significant difference in cholesterol was observed in the healthy group. Organic food consumption had no significant effects on serum HDL in either group. Compared with baseline data, serum zinc concentrations were significantly higher at 7 days in both groups and at 30 days in the healthy group. The mean serum zinc concentrations in the healthy group at 7 and 30 days were 78.90±14.53 and 80.60±5.81 µg/dL, respectively, compared to the baseline mean of 63.10±16.02 µg/dL (Table 2).

Table 2 Characteristics of participants (healthy group and risk group) with health checkup at baseline, 7 days and 30 days

Parameter	Healthy group (n=10)			Risk group (n=8)		
	Day 0	Day 7	Day 30	Day 0	Day 7	Day 30
Weight (kg)	64.49±9.97	63.34±9.80[c]	63.27±9.78[b]	64.69±12.02	64.26±12.11[a]	63.93±12.58[a]
Body Fat (%)	24.78±6.05	24.35±6.07[a]	24.07±6.66[b]	30.20±12.13	30.54±11.56	30.53±11.44
Excess Body Fat (kg)	2.56±2.99	2.26±2.95[a]	2.10±3.41[b]	6.89±9.53	7.05±9.07	7.18±9.29
BMR	1,396±239.4	1,376±232.4[b]	1,379±231.9[a]	1,296±163.4	1,282±161.2[a]	1,274±165.3[a]
Body Age	31.80±8.02	31.30±8.2	30.90±8.80[a]	41.25±16.55	42.13±16.05	42.00±15.77
Belly Fat	7.30±3.06	7.00±2.83[a]	6.90±2.81[a]	8.37±3.81	8.62±3.89	8.50±4.11
BMI (kg/m^2)	22.96±1.83	22.56±1.84[c]	22.55±1.91[b]	25.84±5.93	25.65±5.94[a]	25.53±6.13[a]
Waist Circumference (cm)	81.05±6.67	81.25±6.73	81.15±6.56	81.31±10.85	81.63±11.08	81.50±11.45
Glucose (mg/dL)	87.00±6.05	91.20±9.53	90.80±8.53[a]	94.25±19.94	94.63±16.30	101.4±17.85[b]
Cholesterol (mg/dL)	181.5±20.21	189.3±21.11	183.4±23.72	214.9±24.22	211.8±35.85	206.3±26.97[c]
HDL (mg/dL)	52.23±14.13	54.91±12.55	53.55±11.98	58.79±16.85	59.69±16.81	56.39±18.54
Creatinine (mg/dL)	0.95±0.24	0.95±0.24	0.91±0.25[a]	0.75±0.13	0.73±0.14	0.72±0.13
TSH (uIU/mL)	1.75±0.93	1.92±0.89	1.95±0.74	1.85±0.78	2.30±0.84[a]	2.11±0.93
Zinc (µg/dL)	63.10±16.02	78.90±14.53[b]	80.60±5.81[b]	71.25±7.48	83.00±12.96[a]	80.63±11.26
Cortisol (µg/dL)	10.24±2.93	11.37±3.80	11.81±5.34	8.69±2.24	9.03±3.35	9.09±3.19
GGT (U/L)	24.00±15.25	21.30±11.20	17.50±7.32[a]	26.00±12.35	23.25±12.27[a]	21.25±10.54
Cholinesterase	8,701±2,154	8,833±2,029	8,502±1,950	8,850±1,823	8,898±1,917	8,908±1,498

Results were expressed as the mean ± S.D. Significance was assessed by paired t-test using the scientific software GraphPad Prism. Probability (P) values of less than 0.05 were considered significant. ([a]<0.05, [b]<0.01 and [c]<0.001).

Effect of Organic Food Consumption on Metabolite Profiles

The effects of organic food consumption on the urine metabolite profiles of healthy participants and at-risk participants at 7 and 30 days showed included significant metabolite changes in both positive and negative MS modes in each study group. Notably, the metabolites showed log2-fold changes > 1 or < -1 in the volcano plots (Figure 1). In the volcano plots, the pink dots indicate 2-fold or greater decreases and increases in metabolite concentrations after consumption of the diet containing organic foods.

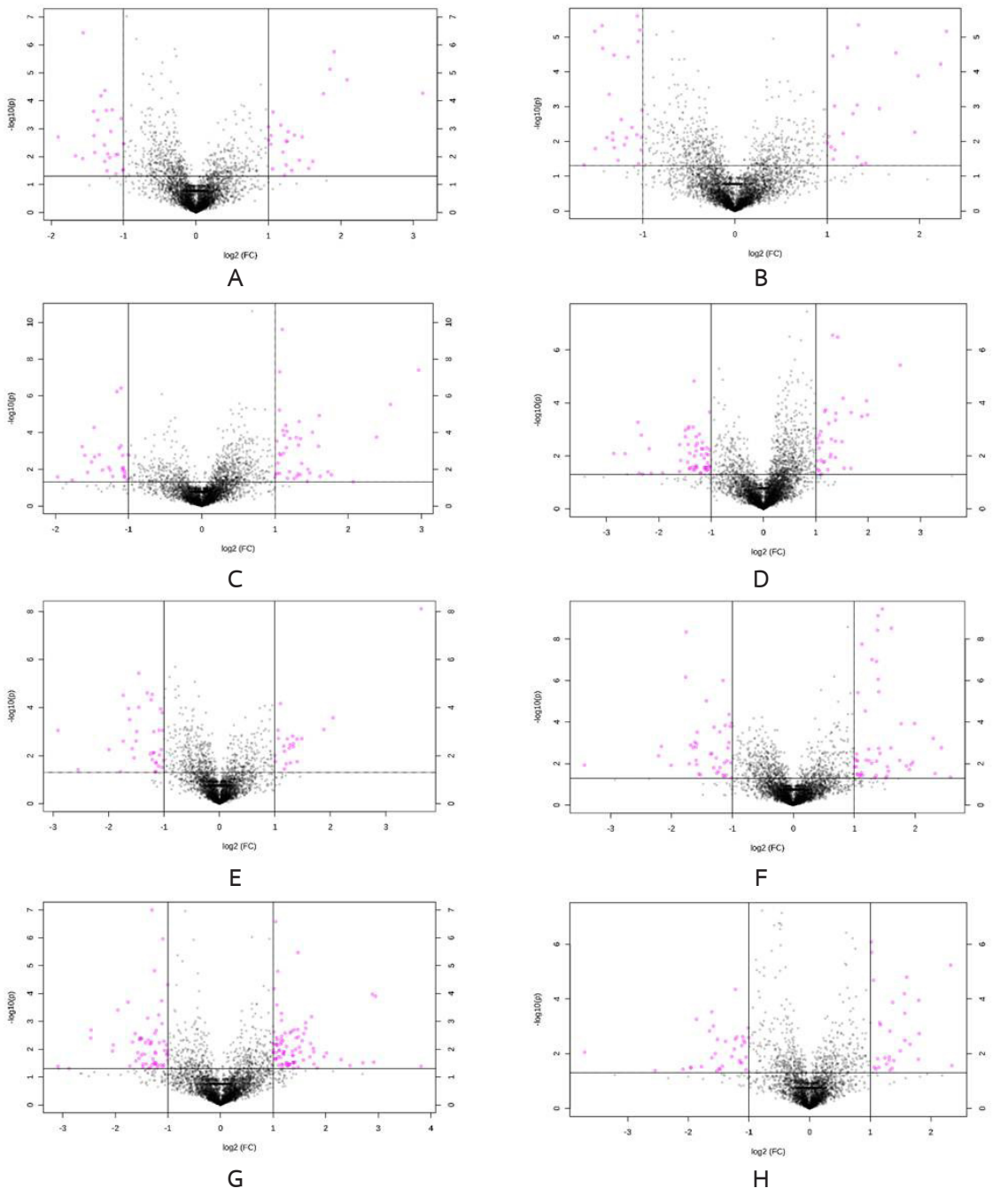

Figure 1 Metabolites abundance changes between day 0, day 7 and day 30. A - B represent group of intervention healthy in negative and positive mode between day 0 and day 7. C - D represent group of intervention at risk in negative and positive mode between day 0 and day 7. E - F represent group of intervention healthy in negative and positive mode between day 0 and day 30. G - H represent group of intervention at risk in negative and positive mode between day 0 and day 30.

To identify the metabolites, which are shown in the supplemental tables (Tables S1-S8), we used the Human Metabolome Database (HMDB). Interestingly, we found that some of the metabolites that changed after 7 and 30 days of organic food consumption were related to the metabolic pathways shown in Table 3. Participants who consumed organic food consumption for 7 days displayed higher concentrations of nicotinamide-beta-riboside, biliverdin, octadecanoic acid and 2-methyl-L-hydroxybutyl-ThPP but lower concentrations of allopregnanolone, dolichyl beta-D-glucosyl phosphate and corticosterone. Higher levels of S-adenosyl-L-homocysteine, 2,3-diketo-5-methylthiopentyl-1-phosphate, fumarate and pyridoxal phosphate, and lower levels of dehydroepiandrosterone sulfate, N-carbamoyl-L-aspartate and leukotriene C4 were observed with organic food consumption for 30 days.

Table 3 Metabolites related to metabolic pathways identification based on UHPLC-QTOF-MS in 7 and 30 days after organic food consumption

Compound	Pathway Name	Healthy	At-risk
7 Days			
Nicotinamide-beta-riboside	Nicotinate and nicotinamide metabolism	↑	
Biliverdin	Porphyrin and chlorophyll metabolism	↑	
Allopregnanolone	Steroid hormone biosynthesis	↓	
Octadecanoic acid	Biosynthesis of unsaturated fatty acids		↑
2-Methyl-1-hydroxybutyl-ThPP	Valine, leucine and isoleucine degradation		↑
Dolichyl beta-D-glucosyl phosphate	N-Glycan biosynthesis		↓
Corticosterone	Steroid hormone biosynthesis		↓
30 Days			
S-Adenosyl-L-homocysteine	Cysteine and methionine metabolism	↑	
2,3-Diketo-5-methylthiopentyl-1-phosphate	Cysteine and methionine metabolism	↑	
Fumarate	Pyruvate metabolism, Citrate cycle (TCA cycle)	↑	
Dehydroepiandrosterone sulfate	Steroid hormone biosynthesis		↓
N-Carbamoyl-L-aspartate	Pyrimidine metabolism		↓
Pyridoxal phosphate	Vitamin B6 metabolism		↑
Leukotriene C4	Arachidonic acid metabolism		↓

Discussion

The aim of this study was to investigate the short-term effect of an organic food diet on the health status of Thai adults. Improved health is an important benefit of organic food consumption[12]. A positive dietary pattern emphasizes the consumption of foods with higher antioxidants, low pesticide levels, low levels of toxic metabolites, and reduced exposure to antibiotic-resistant bacteria. This study is one of the first to explore the effects of an organic diet on human health. Accordingly, we observed health status parameters, such as glucose, cholesterol, HDL, creatinine, TSH, zinc, cortisol, GGT and cholinesterase before and after organic food consumption. The study participants were from Suan Sampran company, 55% of whom had a normal BMI. This study demonstrated that organic food consumption led to significant changes in weight, the basal metabolic rate and BMI in both the healthy and at-risk groups. Similarly, a previous study showed weight loss and a change in body composition with a Mediterranean (Italian) organic diet[13]. We found no studies reporting that an organic food diet is associated with reductions in overweight status and the risk of obesity or with a reduced incidence of metabolic syndrome[14]. However, our at-risk group showed significantly lower total cholesterol levels after consuming the organic diet, which is consistent with a previous report indicating that organic food consumption is associated with reducing total cholesterol[15]. Similarly, multiple studies have reported evidence that organic food consumption is associated with a low risk of cancer[14,16]. The impact of organic food consumption on reducing the risk of various diseases may be greater in health-conscious consumers. A recent review of the health benefits of organic diets concluded that organic food consumption significantly reduces the frequency of infertility, birth defects, allergic sensitization, otitis media, preeclampsia, metabolic syndrome, high BMI and non-Hodgkin lymphoma[1].

One of the major benefits of organic food consumption is increased antioxidant concentrations. Consumption of organic foods for 7 and 30 days resulted in increased zinc levels. The effects of zinc include maintaining the homeostasis of biological processes such as metabolic pathways, cell proliferation, cognitive functions and immune responses. Zinc also prevents oxidative stress by inhibiting free radical formation[17]. Although few studies have compared healthy and at risk-groups in terms of organic food consumption, some findings have been demonstrated, including higher zinc concentrations after organic food intake and significant improvement of nutrient levels in at-risk groups.

We prospectively investigated the association between organic food consumption and human metabolite profiling at 7 and 30 days. Healthy participants had higher concentrations of nicotinamide-beta-riboside and biliverdin after consuming the study diet. The increased nicotinamide-beta-riboside concentration is interesting because higher levels are related to energy metabolism and neuroprotection[18]. Nicotinamide riboside is a

precursor of nicotinamide adenine dinucleotide (NAD+) in metabolic pathways such as glycolysis, the citric acid cycle and mitochondrial electron transport. Notably, nicotinamide riboside upregulates SIRT1 and SIRT3 expression, which may contribute to its role in neurotherapy in Alzheimer's and Parkinson's diseases[19]. In addition, nicotinamide riboside has been shown to prevent hearing loss through activation of SIRT3[20]. Biliverdin has anti-inflammatory effects through suppression of Toll-like receptor 4 (TLR4) and NF-κB. Others have shown that biliverdin induces phosphatidylinositol 3-kinase and AKT (PI3K/AKT) and increases adipocyte size. Studies by McDonnell and Mohiuddin elegantly demonstrated that biliverdin upregulates the activity of biliverdin reductase with direct effects on the immune system[21]. In addition, allopregnanolone, which is an active metabolite of progesterone, possesses neuroactive properties. In the present study, organic food consumption was associated with a reduction in allopregnanolone levels. No report in the published literature is available on the effect of organic food intake on allopregnanolone levels. However, allopregnanolone levels might be related to the pathophysiology of psychiatric disorders and cognitive impairment[22]. The low levels of allopregnanolone in organic foods consumed by the healthy participant group can be hypothesized to be correlated with serotonin levels. In a previous clinical trial, Poroma and colleagues demonstrated that allopregnanolone is associated with the serotonin system in healthy women[23]. Additionally, allopregnanolone binding to GABA receptor A (GABAA) leads to enhanced GABA action as well as changes in the hypothalamic-pituitary-adrenal (HPA) axis response to IL-1β in stressor processing[24].

As a result of organic food consumption for 30 days in the healthy group, human urine metabolites, including S-adenosyl-L-homocysteine, 2,3-diketo-5-methylthiopentyl-1-phosphate, fumarate, and dehydroepiandrosterone sulfate, were found to be significantly different in our study. S-Adenosyl-L-homocysteine and 2,3-diketo-5-methylthiopentyl-1-phosphate are involved in the cysteine and methionine metabolism pathways. Alterations in cysteine and methionine metabolism have been linked to maintenance of the equilibrium of free radicals in the human body[25]. Interestingly, fumarate is a tricarboxylic acid metabolite associated with the citric cycle. Fumarate is found with high levels of succination protein ann high glucose concentrations during mitochondrial stress[26]. However, elevated levels of fumarate metabolites are associated with oxidative stress and suppression of the anti-inflammatory cytokine IL-13 in adipocytes[27]. Dehydroepiandrosterone sulfate (DHEA) has been reported to have a protective action on the cardiovascular[28] and neuronal signaling[29] pathways and to improve physiological and psychological well-being in elderly individuals.

In accordance with the urine metabolite results in the at-risk participant group, octadecanoic acid, 2-methyl-1-hydroxybutyl-ThPP, dolichyl beta-D-glucosyl phosphate, and

corticosterone may be targets of organic food consumption. Octadecanoic, or stearic, acid are mainly derived from the biosynthesis of unsaturated fatty acids. The stearic acid sources used include shea butter, cocoa butter, and hydrogenated soybean oil. Although little research has been conducted on organic food consumption, stearic acids are known to be involved in cardiovascular disease[30]. The present study also found that 2-methyl-1-hydroxybutyl-ThPP increased after organic food consumption, which is an intermediate in the valine, leucine and isoleucine degradation pathways. These metabolic pathways of branched-chain amino acids, specifically valine, leucine and isoleucine, have been studied in various physiological and pathological conditions[31]. Dolichyl beta-D-glucosyl phosphate is an intermediate for oligosaccharide-lipid synthesis in the processing of glycoproteins that acts as an efficient donor of D-glucose residues to lipid-bound oligosaccharides[32]. Dolichyl beta-D-glucosyl phosphate decreases the development of CDNCDs by lowering plasma cholesterol levels. Mannan oligosaccharides (MOSs) can be derived from plant cell wall polysaccharides and recalcitrant starch. MOSs supplementation results in amelioration of plasma cholesterol levels and progression of atherosclerosis[33]. In a study by Bouhnik and colleagues, 12 healthy elderly volunteers were given a diet intended to change cholesterol metabolism through consumption of short-chain fructo-oligosaccharides[34]. To our knowledge, this was the first study to demonstrate that low corticosterone metabolite concentrations during organic food intake enhanced immune responses. Together, these results clearly indicated that organic food consumption did not significantly increase plasma cortisol levels in either group. On the other hand, elevated corticosterone can directly alter immune activity via genomic and nongenomic mechanisms[35]. Supporting this result, Mediterranean diets including olive oil are suggested to have several active ingredients for neuroprotection[36]. Organic food consumption for 30 days generated pyridoxal phosphate in the at-risk group, which is a vitamin B6 metabolite and cofactor in neuronal processes[37]. Dietary intake of organic foods for 30 days caused pyridoxal phosphate metabolite changes in the at-risk group. This metabolite is known to decrease inflammatory reactions in various diseases[38]. Leukotriene C4 (LTC4), a trigger of oxidative stress and DNA damage under ER stress, is implicated in metabolic diseases and neurodegeneration[39]. The finding that organic foods suppress LTC4 production may result in the design of antioxidative therapies.

In conclusion, organic food consumption has a substantially impact on human health and on the environment. Consuming organic food for 7 days and 30 days has improved physical health, with changes in some metabolite-related metabolic pathways. Organic food consumption as part of a healthy diet might help prevent chronic diseases. Additional prospective studies are required to ascertain the relationship between organic food consumption and metabolic signaling pathways.

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