

## LITERATURE REVIEW

English Version

OPEN ACCESS

# Nutritional Content and Benefits of Coconut Water for the Diabetes Metabolism: a Narrative Review

## Kandungan Gizi dan Manfaat Air Kelapa terhadap Metabolisme Diabetes: Kajian Naratif

Jeallyza Muthia Azra<sup>1,2</sup>, Budi Setiawan<sup>3\*</sup>, Zuraidah Nasution<sup>3</sup>, Ahmad Sulaeman<sup>3</sup>, Sri Estuningsih<sup>4</sup><sup>1</sup>Postgraduate Program in Nutrition Science, Department of Community Nutrition, Faculty of Human Ecology, IPB University, Bogor, Indonesia<sup>2</sup>Department of Nutrition, Faculty of Health Sciences, Universitas Esa Unggul, Jakarta, Indonesia<sup>3</sup>Department of Community Nutrition, Faculty of Human Ecology, IPB University, Bogor, Indonesia<sup>4</sup>Department of Veterinary Clinic Reproduction and Pathology, Faculty of Veterinary Medicine, IPB University, Bogor, Indonesia

### ARTICLE INFO

Received: 03-01-2022

Accepted: 30-09-2022

Published online: 09-06-2023

**\*Correspondent:**

Budi Setiawan

[bsetiawan@apps.ipb.ac.id](mailto:bsetiawan@apps.ipb.ac.id)DOI:  
10.20473/amnt.v7i2.2023.317-325**Available online at:**<https://e-journal.unair.ac.id/AMNT>**Keywords:**

Antioxidant, Arginine, Coconut water, Diabetes mellitus

### ABSTRACT

**Background:** Coconut water is one of the natural food products that is widely available around the world. This commodity provides nutritional content that could increase rehydration status and improve health. The application of coconut water to health, including improving type 2 diabetes metabolism, has gotten research interest in recent years.

**Objectives:** This narrative review paper aimed to summarize several articles about the nutritional content and the mechanism of the potential bioactive component in coconut water to improve type 2 diabetes metabolism.

**Methods:** This study design was a narrative review of several articles from five databases search: PubMed/MEDLINE, Scielo, PsycINFO, Microsoft Academic, and Google Scholar.

**Discussion:** Coconut water includes several biologically active components such as protein, amino acid, fatty acid, mineral, vitamin, and phenolic compounds. The recent discovery of nutrient content, especially antioxidant properties, and arginine in coconut water, signifies a good potential in improving type 2 diabetes mellitus. Antioxidant and arginine altered blood glucose, glycated hemoglobin, serum creatinine, blood urea, albumin, albumin/globulin ratio, liver function enzyme, lipid profile, antioxidant status, and lipid peroxidation without any significant hepatocellular damage. Arginine enhanced the nitric oxide synthase activity in the liver and arginine levels in the plasma. In mammals, the arginine-nitric oxide system, which includes AMPK, cGMP, PGC-1 $\alpha$ , and PI3K, can maintain blood glucose homeostasis, increase insulin sensitivity, and prevent diabetes-induced oxidative stress.

**Conclusions:** Coconut water can help to improve metabolism in type 2 diabetes mellitus conditions through antioxidant activity and arginine content.

### INTRODUCTION

Coconut water is the clear liquid inside the endosperm (kernel), which is usually consumed locally as fresh in tropical environments since it deteriorates easily when exposed to heat and water. There are three categories of coconut water based on maturity age: young or immature coconut (IMC) with 5-6 months of age had even less coconut flesh (jelly-like), mature coconut (MC) with 8-9 months of age had a soft thin (2-4 mm) layer of coconut flesh, and overly mature coconut (OMC) with > 12 months of age had a firm thick ( $\pm$  10 mm) layer of coconut flesh<sup>1</sup>. Young coconut water is popularly consumed across the world as a pleasant beverage as well as its health benefits, which are primarily due to its composition. However, in the early days of the coconut business, mature coconut water was considered a waste by-product.

Coconut water is becoming increasingly popular in the beverage business due to its delicious flavor and excellent nutritional content. Moreover, recent studies have shown that coconut water provides health benefits due to its content of macro and micro nutrients. Coconut water contains sugars, vitamins, minerals, protein, amino acids, and fatty acids. It is also rich in arginine, magnesium, potassium, vitamin C, and polyphenols<sup>2-4</sup>. Many of these nutrients are essential for improving health status.

Coconut water is a natural, nutrient-dense beverage that may be classified as a functional food since it contains several biologically active components and has potential therapeutic properties. This natural drink is thought to help prevent and treat various health issues, including hypolipidemic, cardioprotective, hepatoprotective, antioxidant, and antithrombotic

effect<sup>5</sup>, lowering heart rate and blood pressure<sup>6</sup>, improve hydration status and physical performance<sup>7</sup>, reduce obesity and inflammatory gene expression<sup>8</sup>, and improve DM conditions<sup>2,9,10</sup>. Previous studies reported that the arginine content in coconut water has anti-diabetic activity<sup>2,9</sup>. As a result, regular consumption of coconut water is thought to have some anti-diabetic properties.

This narrative review summarizes coconut water's nutritional content and benefits to provide information for future preclinical and clinical studies using this commodity since it presents nutritional content and the mechanism of the potential bioactive component to improve metabolism in people with type 2 diabetes mellitus.

## METHODS

This study design is a narrative review of coconut water's nutrition and health benefits in diabetes mellitus from several articles. Five databases were used: PubMed, MEDLINE, Scielo, PsycINFO, Microsoft Academic, and Google Scholar. Several keywords were applied, such as coconut water AND (nutrient OR nutrition OR composition) AND (diabetes OR diabetes mellitus) AND the effect of coconut water on diabetes mellitus. The inclusion criteria are the article that reported about nutrients in coconut water and its effect on diabetes mellitus conditions, clinical studies using human subjects, pre-clinical studies using experimental animals, and published in peer-reviewed journals or edited academic books. Only articles written in the English language were considered in this review. The complete text of the articles that were chosen was then retrieved. The remaining studies were screened for eligibility after duplicates were deleted. The articles about the nutrients of the other parts of coconut, virgin coconut oil, and the benefits of the other health concentrations were excluded. Due to the low number of published papers on this topic, this study did not limit the year of publication and added several articles from sources other than those five databases to support this review. The search strategy for the articles can be found in Figure 1.

## DISCUSSION

### Nutrient Profile of Coconut Water and Diabetes Mellitus

Coconut water provides a variety of nutrients that are beneficial for the body. Young and old coconut water has a variety of contents, including water, protein, carbohydrates, fat, fiber, mineral nutrients, fatty acids, amino acids, and vitamins<sup>11-13</sup>. These compounds in coconut water affect health benefits, including diabetes mellitus type 2.

Table 1 shows the nutrient content of coconut water. All coconut water includes a trace quantity of protein. Even though coconut water has a low protein level, the presence of protein should not be overlooked<sup>1</sup>. Reducing sugars like fructose and glucose are also present in coconut water, leading to the Maillard reaction (nonenzymatic browning) that may occur during the heat treatment of ready-to-drink coconut water, resulting in

yellow or brown discoloration<sup>1</sup>. However, fructose and glucose are the primary energy sources in the human body's metabolism.

Minerals are one of the minor components of coconut water. Coconut water collected at various stages of maturity has a high K level but a low Na content (Table 1). Furthermore, the K level of old coconut water was higher than that of young coconut water<sup>1</sup>. Other minerals found in coconut water were Ca, Mg, and Na, although in smaller amounts. Since of such minerals, coconut water is an excellent alternative to the existing sports beverages because it can efficiently replenish electrolytes lost through epidermal and urine routes during exercise<sup>7</sup>. K and Mg are two nutrients proven to help lower blood pressure. Coconut water has been shown in animal tests to be a rich source of both minerals, making it beneficial in lowering blood pressure and improving circulation<sup>2,6</sup>. Moreover, Mg could improve insulin resistance, oxidative stress, and systemic inflammation while often reduced in older patients with diabetes<sup>14</sup>.

Coconut water also contains vitamins necessary for the proper functioning of the body. In coconut water, vitamins B1, B6, and C (Table 1). Vitamins B are water-soluble coenzymes necessary for cellular function and enzymatic processes<sup>15</sup>. Vitamin B1 (thiamine) is a vitamin that aids in producing energy from carbohydrates as a cofactor for  $\alpha$ -ketoglutarate dehydrogenase and pyruvate dehydrogenase and may boost insulin action by reducing glucotoxicity<sup>16</sup>. Vitamin B6 has been shown to have direct antioxidant activity (prevention of oxidative stress), indirect effects through chelating activity (prevention of mitochondrial toxicity), and anti-diabetic antioxidant properties<sup>15</sup>. Moreover, vitamin C is an antioxidizing nutrient that helps to reduce blood glucose and improves glycosylated hemoglobin (HbA1c)<sup>17</sup>.

Several studies recently reported the presence of fatty acid content in coconut water. According to the<sup>4</sup>and<sup>18</sup>, young and old coconut water has saturated fatty acids (SFA) and unsaturated fatty acids (USFA). The SFA in coconut water includes lauric, myristic, palmitic, caprylic, and capric fatty acids. These fatty acids have been reported as antiviral, antioxidant, and antistress<sup>19</sup>. USFA, also contained in coconut water, is oleic and linoleic fatty acids. Linoleic acid is an essential fatty acid precursor of the omega-6 fatty acid pathway.

Conversely, oleic acid has a cholesterol-lowering impact, which could reduce the risk of stroke and high blood pressure in certain populations<sup>20</sup>. The fatty acid content of coconut water is higher in old than young coconut water. The fatty acid content in young coconut and old coconut water is present in Table 2.

Several amino acids are present in coconut water (Table 2). Amino acid is crucial not only as a basis for the animal body but also as an energy source and helps produce lymphocytes related to the immune system. Furthermore, amino acids show anti-diabetic properties in human visceral adipocyte cells under a high glucose environment<sup>21</sup>. Branched-chain amino acids (BCAA), including leucine, isoleucine, and valine, have indicated potential advantages for DM in clinical study<sup>22</sup>.

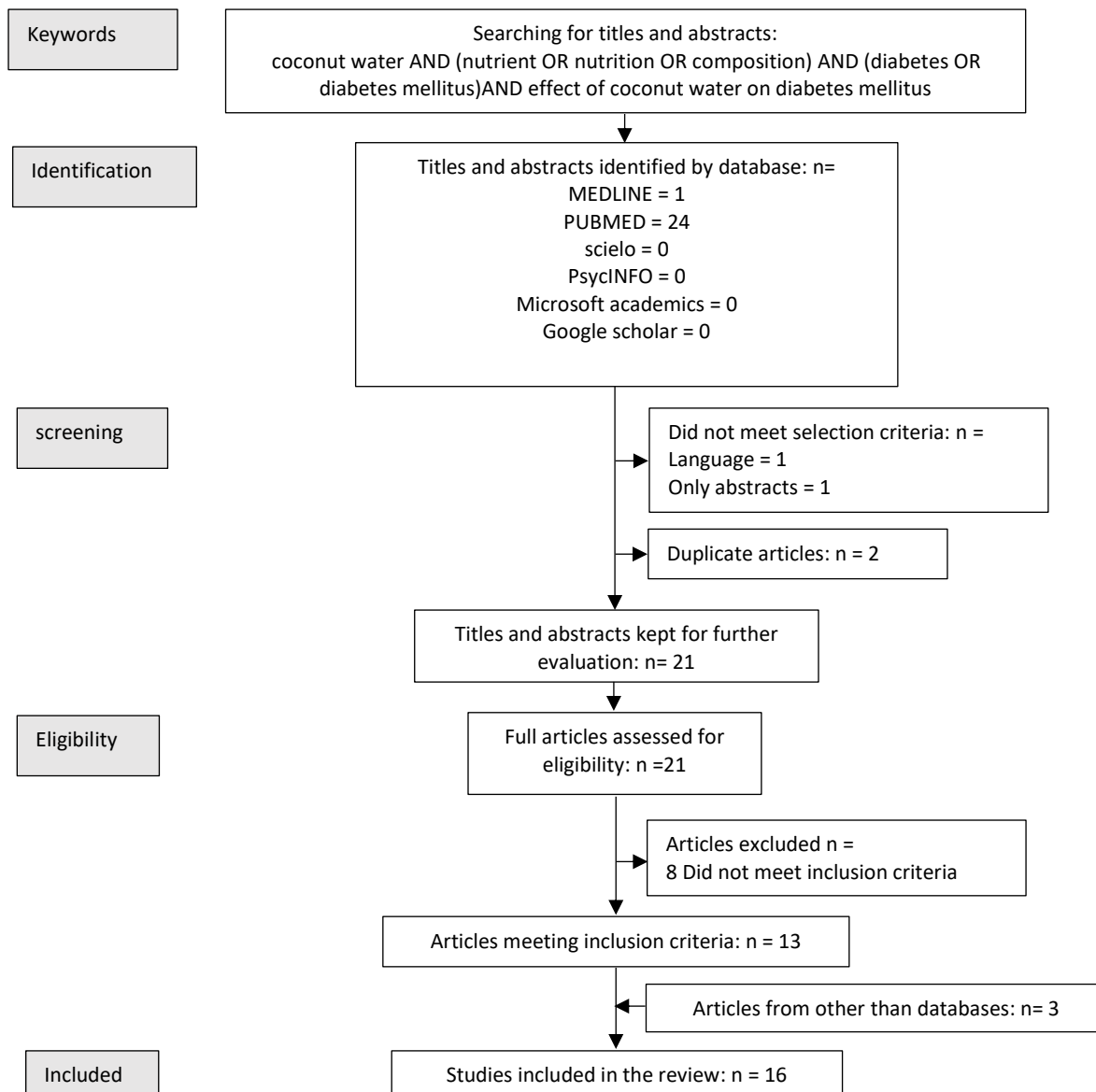


Figure 1. Search strategy for articles

Table 1. Nutrient content of coconut water, according to several publications in the reference list

Nutrient content	Young coconut water			Old coconut water		
	Bhagya et al. 2012 <sup>2</sup>	Santoso et al. 1996 <sup>11</sup>	Jayakumar et al. 2015 <sup>12</sup>	USDA 2019 <sup>4</sup>	Preetha et al. 2012 <sup>10</sup>	Kailaku et al. 2015 <sup>13</sup>
water	N/A	553 mL	N/A	95/100 gr	N/A	330ml
energy	N/A	N/A	N/A	19kcal/100g	N/A	N/A
Proteins	150 mg/dL	2.10%	0.01%	0.72g/100g	13.60%	N/A
fat	N/A	1.26%	0.01%	0.2g/100g	N/A	N/A
Ash	N/A	14.89%	N/A	0.39g/100g	N/A	N/A
Carbohydrates	N/A	81.8%	N/A	3.71g/100g	N/A	N/A
total fiber	N/A	N/A	N/A	1.1g/100g	N/A	N/A
<i>Sugar</i>						
Total sugars	4.8%	N/A	N/A	2.61g/100g	N/A	5.04%
Sucrose	N/A	N/A	N/A	N/A	N/A	0.85%
Fructose	N/A	N/A	N/A	N/A	N/A	2.07%
Glucose	N/A	N/A	N/A	N/A	N/A	2.12%
Reducing sugar	4%	N/A	4.40%	N/A	N/A	N/A
Total solids	N/A	N/A	6.50%	N/A	N/A	5.50 <sup>9</sup> Brix
<i>Mineral</i>						

Nutrient content	Young coconut water			Old coconut water		
	Bhagya et al. 2012 <sup>2</sup>	Santoso et al. 1996 <sup>11</sup>	Jayakumar et al. 2015 <sup>12</sup>	USDA 2019 <sup>4</sup>	Preetha et al. 2012 <sup>10</sup>	Kailaku et al. 2015 <sup>13</sup>
Zn	N/A	N/A	N/A	0.1mg/100g	N/A	N/A
Ca	40 mg/dL	0.47%	44 mg/100 mL	24 mg/100 g	1.32%	N/A
Fe	N/A	4.06 ppm	106 mg/100 mL	0.29mg/100/g	N/A	N/A
Mg	16 mg/dL	0.11 %	10mg/100mL	25mg/100/g	0.42%	24.30mg/kg
P	N/A	0.08%	9.20 mg/100 mL	20mg/100g	N/A	N/A
K	220 mg/dL	3.5%	290 mg/100 mL	250mg/100g	7.71%	1504.00mg/kg
Na	40 mg/dL	0.03%	42 mg/100 mL	105mg/100g	N/A	23.82mg/kg
Cu	N/A	0.96 ppm	26 mg/100 mL	0.04 mg/100 g	N/A	N/A
M N	N/A	N/A	N/A	0.142 mg/100 g	0.08%	N/A
Se	0.01mg/dL	N/A	N/A	1 µg/100 g	N/A	N/A
<b>Vitamin</b>						
B1	N/A	N/A	N/A	N/A	N/A	6.65
B6	N/A	N/A	N/A	N/A	N/A	0.04
C	N/A	N/A	N/A	N/A	N/A	16.65

**Table 2.** Fatty acid and amino acid content of coconut water, according to several publications presented in the reference list

Fatty acid and amino acid content	Young coconut water			Old coconut water	
	Bhagya et al. 2012 <sup>2</sup>	Santoso et al. 1996 <sup>11</sup>	USDA 2019 <sup>4</sup>	Preetha et al. 2013 <sup>9</sup>	Nasution et al. 2018 <sup>18</sup>
<b>Saturated Fatty acids</b>					
Lauric acid (C12:0)	N/A	N/A	0.088g/100g	N/A	20.9 ± 4.0 g/L
Myristic acid (14:0)	N/A	N/A	0.035g/100g	N/A	8.4 ± 0.0 g/L
Palmitic acid (18:0)	N/A	N/A	0.017g/100g	N/A	12.0 ± 0.4 g/L
Caprylic acid (C8:0)	N/A	N/A	0.014g/100g	N/A	5.5 ± 1.2 g/L
Capric acid (C10:0)	N/A	N/A	0.011g/100g	N/A	3.6 ± 0.8g/L
<b>Unsaturated</b>					
Oleic acid (C18:1n-9)	N/A	N/A	0.008g/100g	N/A	10.2 ± 1.2 g/L
Linoleic acid (C18:1)	N/A	N/A	0.002g/100g	N/A	12.5 ± 1.6 g/L
Stearic acid (C18:0)	N/A	N/A	0.01g/100g	N/A	7.2 ± 2.2 g/L
<b>Amino acids</b>					
L-arginine	30 mg/dL	16.8mg/g	0.118g/100g	5.85%	N/A
Alanine	N/A	9.18mg/g	0.037g/100g	N/A	N/A
Glutamic acid	N/A	19.9mg/g	0.165g/100g	N/A	N/A
Leucine	N/A	6.74mg/g	0.053g/100g	N/A	N/A
Lysine	N/A	5.28mg/g	0.032g/100g	N/A	N/A
Tryptophan	N/A	1.74mg/g	0.008g/100g	N/A	N/A
threonine	N/A	3.43mg/g	0.026g/100g	N/A	N/A
Isoleucine	N/A	3.30mg/g	0.028g/100g	N/A	N/A
Methionine	N/A	1.65mg/g	0.013g/100g	N/A	N/A
Cystine	N/A	0.82mg/g	0.014g/100g	N/A	N/A
Phenylalanine	N/A	4.01mg/g	0.037g/100g	N/A	N/A
Tyrosine	N/A	1.74mg/g	0.022g/100g	N/A	N/A
Valine	N/A	4.75mg/g	0.044g/100g	N/A	N/A
histidine	N/A	3.08mg/g	0.017g/100g	N/A	N/A
Aspartic acid	N/A	8.96mg/g	0.07g/100g	N/A	N/A
Glycine	N/A	4.61mg/g	0.034g/100g	N/A	N/A
Proline	N/A	3.93mg/g	0.03g/100g	N/A	N/A
Serine	N/A	5.72mg/g	0.037g/100g	N/A	N/A

Among the amino acid ingredients in coconut water, L-arginine is the primary bioactive substance (Table 2). It is reportedly beneficial against DM or hypoglycemic effects and reduces oxidative stress in rats<sup>10,23</sup>. Previous studies found that coconut water which contains arginine improves DM conditions without causing any damage to the liver and kidneys. It affects several biomarkers, including increased insulin levels; decreased blood glucose levels; improved lipid profile, liver profile (glutamate oxaloacetate transaminase

(SGOT), glutamate pyruvate transaminase (SGPT), and alkaline phosphatase (ALP), albumin, and protein), and kidney profile (urea, creatinine, and nitrite) in rats with DM<sup>2,9,10,23</sup>. Additionally, including arginine in coconut water might have a cardio-protective impact due to nitric oxide synthesis, promoting vasorelaxation<sup>5</sup>. In rats fed a high fat/cholesterol diet, the hypolipidemic effect of arginine in coconut water was also observed<sup>24</sup>.

Treatment with coconut water was effective in lowering tissue lipid peroxides (malonaldehyde (MDA),

hydroperoxides (HD), and conjugated dienes (CD)) in the kidney, liver, aorta, and heart, proving that coconut water contains antioxidant properties. Furthermore, coconut water lowers lipid deposition, causing no hepatic injury or inflammatory infiltration<sup>2</sup>. Coconut water not only has the potential to reduce blood sugar but also can reduce diabetic retinal damage. It is speculated due to the antioxidant activities in coconut water, serving as a potential medication or nutrient for managing diabetes and its complications<sup>25</sup>.

#### Phytochemicals in Coconut Water and Diabetes

Phenolic compounds are phytochemicals with various biological characteristics, including antioxidant activity. Several studies have reported quantifying and identifying phenolic components in various stages of

coconut water maturity. Natural young coconut water contains various phenolic acid compounds that can counteract free radicals and protect DNA due to antioxidant characteristics such as gallic acid, ferulic acid, protoca teuchic acid, p-coumaric acid, caffeic acid, and vanillic acid<sup>3</sup>. Thus, natural young coconut water can be used as a ready-to-eat beverage product that has nutrients with natural health benefits. However, old coconut water contains various nutrients, including antioxidants and phenolics. The main phenolic found in old coconut water were catechins, salicylic acid, and other phenolics such as p-hydroxybenzoic acid, syringic acid, m-coumaric acid, p-coumaric acid, gallic acid, dan caffeic acid<sup>26</sup>. The phenolic chemicals identified in coconut water are presented in Table 3.

**Table 3.** The phenolic acid content of coconut water, according to different authors presented in the reference list

Phenolic acid	Value		Molecular weight (g/mol) *
	Young coconut water	Old coconut water	
	Gheeta et al. 2019 <sup>3</sup>	Mahayothee et al. 2016 <sup>26</sup>	
Polyphenols	3.75 mg/dL	N/A	N/A
gallic acid	38.94 µg/mg	exist	170,12
Protoca teuchic acid	15.59 µg/mg	N/A	154,121
Caffeic acid	4.2µg/mg	exist	180,159
Ferulic acid	24.35 µg/mg	N/A	194,186
Vanilic acid	2.65 µg/mg	N/A	168,148
p-coumaric acid	5.8µg/mg	exist	164,16
Catechins	N/A	4.02 mg/100 g day 190 4.32 mg/ 100 g day 225	290,271
Salicylic acid	N/A	1.12 mg/100 g day 190 1.01 mg/100 g day 225	138,122
p-hydroxybenzoic acid	N/A	exist	138,122
syringic acid	N/A	exist	198,174
m-coumaric acid	N/A		164,16

Source: \*<https://pubchem.ncbi.nlm.nih.gov>

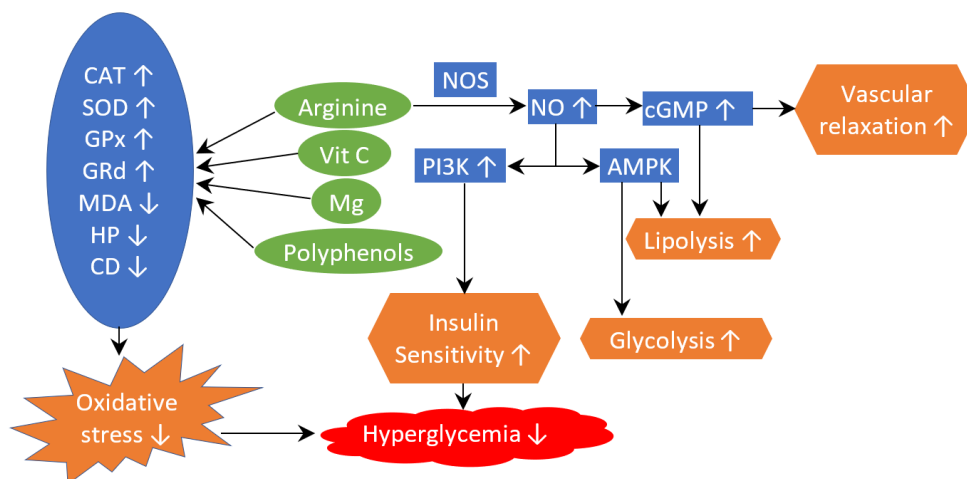
Coconut water contains several popular functional food ingredients such as oleic acid and phenolic compounds<sup>3,4,26</sup>. Phenolic chemicals are powerful free radical scavengers with substantial antioxidant properties, reducing oxidative stress. It inhibits the pathophysiology of myocardial infarction by scavenging free radicals and reducing oxidative stress<sup>5</sup>. Polyphenol, one of the compounds in coconut water, effectively controlled hyperglycemia in streptozotocin-diabetic rats<sup>27</sup>.

#### How Coconut Water Can Improve Metabolism in Diabetic Conditions

Hyperglycemia, or a rise in plasma glucose level, is a symptom of diabetes, and it is linked to hyperinsulinemia and impaired insulin action (insulin resistance). Hyperglycemia causes reactive oxygen species (ROS) and lipid peroxidation, which are well-

known adverse effects linked to forming free radicals and lead to insulin resistance<sup>28</sup>. Furthermore, insulin resistance can arise due to a deficiency in insulin binding induced by a reduction in receptor number or affinity or deficits in effector molecules, including glucose transporters and enzymes involved in glucose metabolism<sup>28</sup>. Insulin resistance is linked to high blood pressure, dyslipidemia, and coronary heart disease.

Coconut water, a healthy natural drink, includes several biologically active components that can improve DM metabolism. There are two main mechanisms for how coconut water can help improve metabolism in DM conditions. The first one is the antioxidant activity of phytochemicals and the Mg it contains in coconut water, and the second one is the action of the arginine content of coconut water (Table 2 and Table 3). The mechanism of coconut water improves metabolism in diabetic conditions is shown in Figure 2.



**Figure 2.** The mechanism of coconut water improves metabolism in diabetes conditions (modified from Hu et al. 2017<sup>29</sup>, Liang et al. 2018<sup>30</sup>)

Coconut water, both young and old, has been shown to protect diabetic rats from oxidative stress. The mechanisms including increased antioxidant enzyme activities (catalase (CAT), superoxide dismutase (SOD), glutathione peroxidase (GPx), and glutathione reductase (GRd) and decreased levels of the peroxidation product (malondialdehyde (MDA), hydroperoxides (HP), and conjugated dienes (CD))<sup>2,10</sup>. SOD catalyzes the dismutation of superoxide ions generating oxygen and H<sub>2</sub>O<sub>2</sub>. However, CAT lowers the concentration and breakdown of hydrogen peroxide, thus reducing oxidative stress. In diabetes mellitus, nonenzymatic glycosylation and oxidation are known to block these enzymes as the disease progresses<sup>23</sup>. In cells, GPx and GRd are required to maintain a steady ratio of reduced glutathione to oxidized glutathione. Including biologically active substances such as arginine, vitamin C, Mg, and polyphenols in coconut water contributes to its better benefits in decreasing oxidative stress<sup>2,31</sup>. Apart from being a key regulator of glucose metabolism and enhancer of insulin sensitivity, arginine may have a role in restoring GPx in diabetic rats<sup>10</sup>. Vitamin C may scavenge singlet oxygen, superoxide, and hydroxyl radicals directly while increasing tissue glutathione levels. Furthermore, Mg can reduce free radical generation. Moreover, polyphenols such as gallic and ferulic acids are excellent free radical scavengers and reduce oxidative stress.<sup>2</sup>

In animal studies, treatment with young and old coconut water has been shown to increase body weight, reduce plasma glucose and glycated hemoglobin (HbA1c) and increase plasma insulin level<sup>2,9,23</sup>. The hypoglycemic effect of coconut water is probably due to the upregulation of antioxidant status, inhibition of lipid peroxidation, and insulin sensitivity improvement<sup>2</sup>. It was reported that young coconut water treatment lowered the serum triglycerides, free fatty acids, and systolic blood pressure in fed high cholesterol diets and fructose-fed insulin-resistant hypertension rats<sup>2,24</sup>. Histopathological analysis showed that young coconut water reduced lipid deposition and inflammatory infiltration of the liver without causing substantial hepatocellular damage<sup>2</sup>.

Old coconut water elevated the level of liver function enzyme (alkaline phosphatase (ALP), serum glutamate oxaloacetate transaminase (SGOT), and serum glutamate pyruvate transaminase (SGPT)) in alloxan-induced diabetic rats. It also improved the albumin and albumin/globulin ratio levels and nephrotoxicities, such as blood urea and serum creatinine. Furthermore, it enhances nitric oxide synthase activity in the liver and arginine in plasma, suggesting that arginine in coconut water can help with nitric oxide production<sup>9,23</sup>. Arginine has significant effects as an antioxidant, hypolipidemic, vasodilator, and antiatherogenic<sup>32</sup>.

Coconut water also contains the amino acid arginine, which can improve DM metabolism. Several studies have been carried out to investigate the impact of L-arginine on body metabolism. L-arginine supplementation of about 0.25% for three weeks reduced fat accumulation, plasma triglyceride (TGA), and total cholesterol (TC)<sup>33</sup>. A clinical study found that administration of L-arginine 6.4 g/day for 18 months regulated blood glucose homeostasis by improving insulin sensitivity and  $\beta$  cell function, although it did not substantially lower the incidence of diabetes<sup>34</sup>. Meanwhile, Jabłeczka et al. (2012)<sup>35</sup> found that 6 g of L-arginine per day did not affect fasting blood glucose levels or HbA1c in diabetic individuals while boosting NO concentration and overall antioxidant status. Administration of 9 g and 630 mg/kg body weight of L-arginine orally has no adverse effect on humans and pigs, respectively<sup>36</sup>. This L-arginine administration is adequate for humans and pigs. However, ensuring that L-arginine supplementation does not disrupt the gastrointestinal tract's amino acid balance is critical.

L-arginine is a precursor for nitric oxide synthase (NOS), which acts as a catalyst for synthesizing nitric oxide (NO), and L-citrulline is a second reaction product. The process involves essential cofactors such as tetrahydrobiopterin (BH<sub>4</sub>) and nicotinamide adenine dinucleotide phosphate (NADPH). If intracellular Ca<sup>+</sup> increases, the endothelial NOS (eNOS) is active. The eNOS is one of three NOS isoforms mainly found in endothelial cells, and it promotes endothelium-dependent and triggered vascular relaxation<sup>32</sup>. Reduced NO production

or availability diminishes endothelium-dependent arterial relaxation and endothelial dysfunction. This condition is a general characteristic of diabetes, atherosclerosis, hypertension, and other disorders<sup>37</sup>.

L-arginine has various metabolic benefits as a NO precursor in the body. After NO is formed through the L-arginine-citrulline pathway, it can enhance glycolysis through the AMP-activated protein kinase (AMPK) pathway and enhance lipolysis via both the cyclic guanosine monophosphate (cGMP) and AMPK pathways. Through the peroxisome proliferator-activated receptor coactivator 1- (PGC-1), the arginine-nitric oxide can also stimulate mitochondrial biogenesis and the formation of brown fat tissue or brown adipose tissue (BAT). In addition, NO can affect insulin sensitivity through the phosphoinositide-3-kinase (PI3K) pathway<sup>29</sup>. Increasing insulin production by L-arginine is shown through stimulating  $\beta$  cell neogenesis by increasing insulin-immunopositive cells area. The increase in insulin sensitivity by L-arginine is carried out through the PI3K pathway. L-arginine converted to NO can increase the messenger molecule insulin receptor substrate (IRS) protein, increasing insulin receptor signaling, PI3K, and Akt kinase. The increasing Akt kinase can mediate insulin to stimulate GLUT4 to cell membranes so that extracellular glucose can enter the cell<sup>38</sup>.

L-arginine is not only beneficial for overcoming DM problems, but it is also beneficial for vascular function. The synthesis of NO from L-arginine by NOS plays a vital role in maintaining endothelial cell function in hypertensive DM patients. The following are the reasons: 1) NO diffuses from the endothelium to the capillary smooth muscle, relaxing it by activating guanylate cyclase (GC) and increasing intracellular cGMP. High concentration of cGMP in vascular muscle cells inhibits Ca transport which can support the relaxation of all vascular systems and increase volume in the lumen of blood vessels; 2) High amounts of cGMP<sup>39</sup> inhibit platelet aggregation on the endothelial surface of the vascular wall, 3) NO has an anti-inflammatory impact in the vascular system via regulating gene expression and inhibiting cytokine cells<sup>40</sup>. According to to<sup>41</sup>, L-arginine also protects pancreatic cells from methylglyoxal dysfunction by inhibiting the expression of arginase, oxidative stress, and endothelial dysfunction and inhibiting the excessive synthesis of methylglyoxal from high blood glucose concentrations in DM.

## CONCLUSIONS

Young and old coconut water is a natural food containing various bioactive components that can potentially improve type 2 diabetes mellitus metabolism. The various compounds contained in coconut water include minerals (Mg), amino acids (BCAA and arginine), vitamins (B1 and C), and phenolic antioxidants. The primary mechanism of how coconut water can help to improve metabolism in type 2 diabetes mellitus condition is through the antioxidant activity of phytochemicals, minerals, and vitamins in coconut water. Moreover, arginine as an NO precursor has a superior effect in improving type 2 diabetes mellitus metabolism. The arginine-nitric oxide pathway helps maintain blood

glucose homeostasis, increase insulin sensitivity, and inhibit mammal oxidative stress.

## ACKNOWLEDGEMENT

This research was supported by Scholarship for Master-to-Doctorate Program for Superior Scholar (PMDSU), Directorate of Higher Education (DIKTI), Ministry of Research, Technology, and Higher Education of the Republic of Indonesia (RISTEKDIKTI), No. 1/E1/KP.PTNBH/2021, 8 March 2021.

## Conflict of Interest and Funding Disclosure

The authors state no conflict of interest. This research was supported by the Scholarship of Master-to-Doctorate Program for Superior Scholars (PMDSU), the Directorate of Higher Education (DIKTI) of the Ministry of Research, Technology, and Higher Education of the Republic of Indonesia (RISTEKDIKTI). The number of grant is No. 1/E1/KP.PTNBH/2021, 8 March 2021.

## REFERENCES

1. Tan, TC, Cheng, LH, Bhat, R., Rusul, G. & Easa, AM Composition, Physicochemical Properties and Thermal Inactivation Kinetics of Polyphenol Oxidase and Peroxidase from Coconut (*Cocos nucifera*) Water Obtained from Immature, Mature and Overly-Mature Coconut. *Food Chem.* **142**, 121–128 (2014).
2. Bhagya, D., Prema, L. & Rajamohan, T. Therapeutic Effects of Tender Coconut Water on Oxidative Stress in Fructose Fed Insulin Resistant Hypertensive Rats. *Asian Pac. J. Trop. med.* **5**, 270–276 (2012).
3. Geetha, V., Bhavana, K., Chetana, R., Gopala, KA & G, SK Studies on the Composition and In-Vitro Antioxidant Activities of Concentrates from Coconut Testa and Tender Coconut Water. *J. Food Process. Technol.* **07**, 1–5 (2016).
4. USDA. FoodData Central. *Food Data Central*. [fdc.nal.usda.gov](https://fdc.nal.usda.gov/). (2019).
5. Prathapan, A. & Rajamohan, T. Antioxidant and Antithrombotic Activity of Tender Coconut Water in Experimental Myocardial Infarction. *J. Food Biochem.* **35**, 1501–1507 (2011).
6. Syafriani, R., Sukandar, EY, Apriantono, T. & Sigit, JI The Effect of Coconut Water (*Cocos Nucifera* L.) and an Isotonic Drink on the Change of Heart Rate Frequency in the Rats Induced Hypertension. *Procedia Chem.* **13**, 177–180 (2014).
7. Kalman, DS, Feldman, S., Krieger, DR & Bloomer, RJ Comparison of Coconut Water and Carbohydrate-Electrolyte Sports Drink. *J.Int. Soc. Sports Nutr.* **9**, 1–10 (2012).
8. Mohamad, N.Eet al. Dietary Coconut Water Vinegar for Improvement of Obesity-Associated Inflammation in High-Fat-Diet-Treated Mice. *Food Nutr. Res.* **61**, (2017).
9. Preetha, PP, Girija Devi, V. & Rajamohan, T. Comparative Effects of Mature Coconut Water (*Cocos Nucifera*) and Glibenclamide on Some Biochemical Parameters in Alloxan Induced Diabetic Rats. *Brazilian J. Pharmacogn.* **23**, 481–487 (2013).

10. Preetha, PP, Devi, VG & Rajamohan, T. Hypoglycemic and Antioxidant Potential of Coconut Water in Experimental Diabetes. *Food Funct.* **3**, 753–757 (2012).
11. Santoso, U., Kubo, K., Ota, T., Tadokoro, T. & Maekawa, A. Nutrient Composition of Kopyor Coconuts (*Cocos nucifera* L.). *Food Chem.* **57**, 299–304 (1996).
12. Jayakumar, K., Rajasekaran, S., Nagarajan, M. & Vijayarengan, P. Bioactive Enzyme Activity and Medicinal Properties of Tender Coconut (*Cocos nucifera* L.). *int. J. Mod. Biochem.* **4**, 10–14 (2015).
13. Kailaku, SI, Alam Syah, AN, Risfaheri, Setiawan, B. & Sulaeman, A. Carbohydrate-Electrolyte Characteristics of Coconut Water from Different Varieties and Its Potential as a Natural Isotonic Drink. *int. J. Adv. sci. Eng. inf. Technol.* **5**, 174–177 (2015).
14. Barbagallo, M. Magnesium and Type 2 Diabetes. *World J. Diabetes* **6**, 1152–1157 (2015).
15. Depeint, F., Bruce, WR, Shangari, N., Mehta, R. & O'Brien, PJ Mitochondrial Function and Toxicity: Role of B Vitamins on the One-Carbon Transfer Pathways. *Chem. Bio. Interact.* **163**, 113–132 (2006).
16. Luong, K. vinh quoc & Nguyen, LTH The Impact of Thiamine Treatment in the Diabetes Mellitus. *J. Clin. med. Res.* **4**, 153–160 (2012).
17. Dakhale, GN, Chaudhari, HV & Shrivastava, M. Supplementation of Vitamin C Reduces Blood Glucose and Improves Glycosylated Hemoglobin in Type 2 Diabetes Mellitus: A Randomized, Double-Blind Study. *Adv. Pharmacol. sci.* **2011**, (2011).
18. Nasution, Z., Jirapakkul, W. & Lorjaroenphon, Y. Aroma Compound Profile of Mature Coconut Water from Tall Variety Through Thermal Treatment. *J. Food Meas. Charact.* **13**, 277–286 (2018).
19. Yep, SKet al. Antistress and Antioxidant Effects of Virgin Coconut Oil in Vivo. *Exp. Ther. med.* **9**, 39–42 (2015).
20. Daley, CA, Abbott, A., Doyle, PS, Nader, GA & Larson, S. A Review of Fatty Acid Profiles and Antioxidant Content in Grass-Fed And Grain-Fed Beef. *Nutr. J.* **9**, 1–12 (2010).
21. Srinivasan, V., Radhakrishman, S., Angayarkanni, N. & Sulochana, K. Anti-diabetic Effect of Free Amino Acids Supplementation in Human Visceral Adipocytes Through Adiponectin-Dependent Mechanism. *Indian J. Med. Res.* **149**, 41–46 (2019).
22. Nagato, C.et al. Branched-Chain Amino Acid Intake and the Risk of Diabetes in a Japanese Community. *Am. J. Epidemioloies.* **178**, 1226–1232 (2013).
23. Pinto, IFDet al. Study of Antiglycation, Hypoglycemic, and Nephroprotective Activities of the Green Dwarf Variety Coconut Water (*Cocos nucifera* L.) in Alloxan-Induced Diabetic Rats. *J.Med. Foods* **18**, 802–809 (2015).
24. Sandhya, VG & Rajamohan, T. Comparative Evaluation of the Hypolipidemic Effects of Coconut Water and Lovastatin in Rats Fed Fat-Cholesterol Enriched Diet. *Food Chem. Toxicol.* **46**, 3586–3592 (2008).
25. Dai, Y.et al. Effects of Coconut Water on Blood Sugar and Retina of Rats With Diabetes. *Peer J* **9**, 1–14 (2021).
26. Mahayothee, B.et al. Phenolic Compounds, Antioxidant Activity, and Medium Chain Fatty Acids Profiles of Coconut Water and Meat at Different Maturity Stages. *int. J. Food Prop.* **19**, 2041–2051 (2016).
27. Renjith, RS, Chikku, AM & Rajamohan, T. Cytoprotective, Antihyperglycemic and Phytochemical Properties of *Cocos nucifera* (L.) Inflorescence. *Asian Pac. J. Trop. med.* **6**, 804–810 (2013).
28. Bailey, CJ Treating Insulin Resistance: Future Prospects. *Diabetes Vasc. Dis. Res.* **4**, 20–31 (2007).
29. Hu, S.et al. L-Arginine Modulates Glucose and Lipid Metabolism in Obesity and Diabetes. *Curr. Protein Pept. sci.* **18**, 599–608 (2017).
30. Liang, M.et al .L-Arginine Induces an Antioxidant Response to Prevent Oxidative Stress Via Stimulation of Glutathione Synthesis and Activation of the Nrf2 Pathway. *Food Chem. Toxicol.* **115**, 315–328 (2018).
31. Thirumalai, T., Therasa, SV, Elumalai, EK & David, E. Intense and Exhaustive Exercise Induces Oxidative Stress in Skeletal Muscle. *Asian Pacific J. Trop. Dis.* **1**, 63–66 (2011).
32. El-Kirsh, AAA, Abd El-Wahab, HMF & Abd-Allah Sayed, HF The Effect of L-arginine or L-citrulline Supplementation on Biochemical Parameters and the Vascular Aortic Wall in High-Fat and High-Cholesterol-Fed Rats. *Cell Biochem. funct.* **29**, 414–428 (2011).
33. Fouad, AM, El-Senousey, HK, Yang, XJ & Yao, JH Dietary L-Arginine Supplementation Reduces Abdominal Fat Content by Modulating Lipid Metabolism in Broiler Chickens. *Animal* **7**, 1239–1245 (2013).
34. Monty, L.Det al. Effect of a Long-Term Oral L-Arginine Supplementation on Glucose Metabolism: A Randomized, Double-Blind, Placebo-Controlled Trial. *Diabetes, Obes. Metab.* **14**, 893–900 (2012).
35. Jabtecka, A.et al. The Effect of Oral L-Arginine Supplementation on Fasting Glucose, Hba1c, Nitric Oxide and Total Antioxidant Status in Diabetic Patients with Atherosclerotic Peripheral Arterial Disease of the Lower Extremities. *euro. Rev. med. Pharmacol. sci.* **16**, 342–350 (2012).
36. Hu, S.et al. Safety of Long-Term Dietary Supplementation with L-Arginine in Pigs. *Amino Acids* **47**, 925–936 (2015).
37. Potenza, M., Gagliardi, S., Nacci, C., Carratu, M. & Montagnani, M. Endothelial Dysfunction in Diabetes: From Mechanisms to Therapeutic Targets. *Curr. med. Chem.* **16**, 94–112 (2009).
38. Tahrani, AA, Bailey, CJ, Del Prato, S. & Barnett, AH Management of Type 2 Diabetes: New and Future Developments in Treatment. *Lancet* **378**, 182–



- 197 (2011).
39. McNamara, D.B. *et al.* L-Arginine Inhibits Balloon Catheter-Induced Intimal Hyperplasia. *Biochem. Biophys. Res. Commun.* **193**, 291–296 (1993).
40. DeCaterina, R. *et al.* Nitric Oxide Decreases Cytokine-Induced Endothelial Activation: Nitric Oxide Selectively Reduces Endothelial Expression of Adhesion Molecules and Proinflammatory Cytokines. *J. Clin. Invest.* **96**, 60–68 (1995).
41. Dhar, I., Dhar, A., Wu, L. & Desai, KM Arginine Attenuates Methylglyoxal- and High Glucose-Induced Endothelial Dysfunction and Oxidative Stress by an endothelial Nitric-Oxide Synthase-Independent Mechanism. *J. Pharmacol. Exp. Ther.* **342**, 196–204 (2012).