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## A review on the role of buckwheat in the management of hypertension

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**Abstract**

Buckwheat (BW) is a gluten-free pseudo cereal that belongs to the Polygonaceae family. BW grain is a highly nutritional food component that has been shown to provide a wide range of beneficial effects. Main effects of buckwheat on human health are its anti-hypertensive, hypoglycaemic, hypocholesterolemic, neuroprotective and antioxidant effects. Thus, it is considered an alternative food component in dietary treatment for chronic and metabolic diseases, such as diabetes, hypertension and celiac disease. Also, its rich nutrient content supports daily diet and provides a better eating profile. As a result, buckwheat is accepted as a functional food, suggested to improve human health and is used in the treatment of diseases. Buckwheat is rich in anti-hypertensive compounds is a potential antihypertensive food, and a significant number of reports concerning its blood pressure lowering (BPL) effects have been reported. In the present study, reports of *in vitro* studies, preclinical and clinical trials dealing with the antihypertensive effect of buckwheat. There are numerous reports of potential health benefits of consuming buckwheat, which may be in the form of food, dietary supplements, home remedies or possibly pharmaceutical drugs. It is a good source of many vitamins and minerals and has balanced nutritional value. Because of its nutrient content and many positive effects on human health, buckwheat has become a functional food, recently. The aim of this review is to explain some positive effects of buckwheat on human health for managing the hypertension. The literature also indicates that buckwheat is safe to consume and may have various beneficial effects on human health.

**Keywords:** Buckwheat, hypertension, blood pressure lowering effect, health effect, functional food, rutin and quercetin

**Introduction**

Buckwheat (*Fagopyrum esculentum*), a member of the Polygonaceae family, is a possible antihypertensive diet with a large number of studies on its blood pressure lowering (BPL) benefits<sup>[1, 2]</sup>. It is a member of the buckwheat pseudo-cereals family, which has many of the same features as grains including wheat, rice, and barley<sup>[3]</sup>. Buckwheat has gained popularity as a raw food material in recent years as a result of its "rediscovered" nutrient value and health advantages. The most commonly grown species among the main nine agriculturally important types are common buckwheat and Tartary buckwheat (also known as bitter buckwheat)<sup>[3]</sup>. Buckwheat grain is a very nutritious food grain that has been demonstrated to provide a range of health benefits. Buckwheat has been linked to lower plasma cholesterol levels, neuroprotection, anticancer, anti-inflammatory, and antidiabetic benefits, as well as improve hypertension conditions. Addition, BW has been shown to have prebiotic and antioxidant properties<sup>[4]</sup>. Food sources are buckwheat species<sup>[5]</sup>. Buckwheat is now mostly grown in the northern hemisphere, with Russia and China being the leading producers. Its use is also on the rise in the United States, Canada, and Europe<sup>[6]</sup>. Buckwheat is considered as a nutritionally valuable food source due to the high protein, lipid, dietary fibre, and mineral content, and other health-promoting components. As a result, it's growing in popularity as a possible functional food. Buckwheat is superior to other grains in terms of amino acid content and nutritional value, and it is also one of the most biologically valuable protein sources. Buckwheat also includes minerals including zinc, copper, manganese, selenium, potassium, sodium, calcium, and magnesium, as well as vitamins like B1, B2, B3, and B6; flavonoids, polyphenols, inositol, organic acid, and a high amount of dietary fibre<sup>[7]</sup>. Buckwheat seeds are commonly consumed as groats, flour, and noodles in Asia and Western countries. Buckwheat plant leaves and stems are edible and are used as a herbal medicine in eastern Asia. Buckwheat and its components have been shown to have antihypertensive properties in a single oral dose test in rats, an *in vitro* angiotensin I-converting enzyme (ACE) inhibitor assay, and aortic vasorelaxation preparation. In spontaneously hypertensive rats, neo-fermented buckwheat sprouts (neo-FBS) include angiotensin-converting protein (ACE) inhibitors and vasodilators with blood pressure-lowering (BPL) effects (SHRs)<sup>[8]</sup>.

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There have been various claims of buckwheat's possible health advantages, which can come in the form of food, nutritional supplements, home remedies, or prescription medications. The utilization of buckwheat again for treatment of hypertension has grown in popularity during the last decade. This pseudocereal is high in BPL compounds such as rutin [10] and-aminobutyric acid (GABA), which help to reduce blood pressure [11]. Rutin improves blood vessel flexibility in spontaneously hypertensive rats (SHRs), but GABA reduces blood pressure. Buckwheat also contains 2''-hydroxynicotianamine, a very powerful angiotensin I converting enzyme (ACE) inhibitor with an IC<sub>50</sub> of 0.08 M [13]. As a result, buckwheat is among the most studied cereals in terms of extracting functional elements for the treatment of high blood pressure as well as other cardiovascular diseases. Because various biochemical reactions followed by germination could promote their production, these BPL compounds are generally obtained from buckwheat sprouts, where they are more plentiful than in unsprouted seeds [14]. In fact, at a dosage of 600 mg/kg/day for 5 weeks, germinated buckwheat grains, which contain 1.92 times more rutin than buckwheat seeds, have been shown to have antihypertensive effects in SHRs [15]. Hypertension, typically known as high or increase the blood pressure, is a disorder in which the blood vessels have an abnormally high pressure for an extended amount of time. WHO [16] has highlighted hypertension as one of the most important risk factors for morbidity and mortality in the globe, with an estimated nine million people dying each year [9]. High blood pressure (BP), also known as hypertension, is defined as a clinic blood pressure of 140/90 mmHg or higher confirmed by a subsequent ambulatory blood pressure monitoring daytime average (or home blood pressure monitoring average) of 135/85 mmHg or higher by the National Institute for Health and Care Excellence (NICE) [10]. Because of its part of this increase, hypertension is a serious public health concern [18, 19].

High blood pressure is responsible for approximately 7.5 million fatalities per year, or 12.8 % of all deaths worldwide [20]. In 2025, it is predicted that 1.56 billion adults would've had hypertension [21]. Chronic heart disease, stroke, and coronary heart disease are all linked to high blood pressure. High blood pressure is linked to an increased risk of stroke and coronary heart disease. Heart failure, peripheral vascular disease, renal impairment, retinal bleeding, and visual impairment are among the complications, in addition to coronary heart disease and stroke [22]. It is a silent killer since no symptoms are visible in the early stages until a Heart attacks, strokes, and chronic renal failure are examples of significant medical crises [23-25]. Since most people are unaware of high blood pressure, the only approach to spot it is through measurements. Although the majority of hypertensive patients are asymptomatic, some persons with HTN have headaches, light headedness, vertigo, impaired vision, or fainting episodes [26]. Hypertension is caused by a variety of factors. These factors differ from nation to country, and even within a single country, there are differences between urban and rural areas [27]. Hypertension prevention is critical in lowering the risk of these chronic illnesses. Antihypertensive foods are attracting more attention since they are predicted to reduce hypertension while having fewer adverse effects than antihypertensive medication [28].

The goal of this study is to describe some positive effect of buckwheat on public health via literature studies.

## Types of hypertension

### 1. Primary hypertension

Primary hypertension, also known as essential hypertension, is a kind of high blood pressure. This is the case for the vast majority of hypertensive individuals. Despite years of investigation, a precise aetiology for hypertension has yet to be identified. Genetics, nutrition, lifestyle, and age are considered to all have a role. Smoking, drinking too much alcohol, stress, being overweight, eating too much salt, and not getting enough exercise are all lifestyle issues. Changes in your food and lifestyle can help you decrease your heart rate and blood pressure your risk of hypertension issues.

### 2. Secondary hypertension

Secondary hypertension occurs when your blood pressure is caused by an identifiable-and potentially reversible-cause. The secondary causes only up to 5 to 10% of hypertension. Younger folks are more prone to it. Secondary hypertension affects around 30% of people aged 18 to 40.

### 3. Other types of hypertension

Subtypes that fit within the categories of primary or secondary hypertension include:

1. Resistant hypertension
2. Malignant hypertension
3. Isolated hypertension

### Diagnosis of hypertension

The first step is to confirm the hypertension diagnosis. The recommendation advised taking at least two blood pressure readings on at least two times, using a standard measuring procedure and approved equipment, including a properly sized cuff [30]. For the diagnosis of white coat hypertension or masked hypertension, the 2017 ACC/AHA hypertension guideline advised the use of ambulatory BP measurement or home BP monitoring [30]. When blood pressure is elevated at a hospital or clinic but normal in an ambulatory BP monitoring technique or at home, white coat hypertension is diagnosed. Masked hypertension is indicated when blood pressure is normal at a hospital or clinic but rises in an ambulatory blood pressure monitoring technique or at home. Ambulatory blood pressure monitoring may measure blood pressure as patients go about their daily routines and can calculate mean blood pressure over the course of the monitoring session, mean blood pressure during the day and night, and diagnose symptomatic hypotension [30]. Once the diagnosis has been established, a thorough history should be conducted to determine any concomitant conditions and contributory variables, such as lifestyle, CV risk factors linked to hypertension, and features that might indicate secondary causes of hypertension. The presence of carotid, abdominal, or femoral bruits on examination raises the risk of renal artery stenosis. Aortic coarctation or severe aortoiliac disease is indicated by diminished femoral pulses or a difference in arm and thigh blood pressure. Abdominal striae, moon faces, and significant interscapular fat accumulation are all signs of Cushing disorder. Primary hypertension is indicated by a steady rise in blood pressure that is coupled with weight gain and a favourable family history, whereas secondary hypertension is indicated by multiple patients with target organ damage. The initial laboratory study, as indicated in Table 2, should look for any existing conditions that might alter the patient's reaction to the medicine, as well as assess for target organ damage. The aldosterone/renin ratio is an effective primary aldosteronism screening test [31]. Estimating dietary salt and

potassium consumption, calculating creatinine clearance, and quantifying aldosterone excretion can all benefit from 24-hour urine collection during ingestion of the patient's usual diet. The measurement of urinary metanephrines or plasma metanephrines over the course of 24 hours is a useful screening tool for individuals with Pheochromocytoma [32]. Renal artery stenosis imaging should be reserved for patients who have a high level of suspicion. In terms of target organ damage, resistant hypertension is related to increased 24-hour urine albumin production and left ventricular mass index [33].

### Classification of blood-pressure in adult according to acc/aha 2017 hypertension guidelines [34]

According to the 2017 ACC/AHA hypertension recommendations, normal blood pressure is 120/80 mmHg. Elevated blood pressure is defined as systolic blood pressure of 120-129 mmHg and diastolic blood pressure of 80 mmHg, and it should be managed with lifestyle changes. Stage 1 hypertension is defined as a systolic blood pressure of 130-139 mmHg or a diastolic blood pressure of 80-89 mmHg, and stage 2 hypertension is defined as a systolic blood pressure of 140 mmHg or a diastolic blood pressure of 90 mmHg, as indicated in Table 1.

**Table 1:** Classification of blood pressure in adults according to ACC/AHA 2017 hypertension guidelines

Blood Pressure Category	Definition
Normal	Systolic BP < 120 mm Hg and diastolic BP < 80 mm Hg.
Elevated	Systolic BP 120-129 mm Hg and diastolic BP < 80 mm Hg.
<b>Hypertension</b>	
Stage 1	Systolic BP 130-139 mm Hg and diastolic BP 80-89 mm Hg.
Stage 2	Systolic BP ≥ 140 mmHg and diastolic BP ≥ 90 mm Hg.

### Basic investigation of hypertension

**Table 2:** Following are Basic investigation of hypertension [35, 36, 37, 38, 39]

Sr. No.	Investigation
1.	Complete blood count-TLC, DLC, HB%, RBC
2.	Renal function test-Blood urea, serum creatinine, potassium, sodium, calcium, uric acid
3.	Blood sugar level
4.	Urinalysis
5.	Lipid profile
6.	Thyroid function test
7.	Electrocardiography
8.	Urine albumin to creatinine ratio
9.	Measure plasma aldosterone/rennin ratio
10.	Measurement of 24 hours urinary metanephrines.

### Treatment of hypertension

Non-pharmacologic and pharmacological treatments are used to treat hypertension. If you have a CV, DM, or CKD, your treatment options are limited. The 2017 AHA/ACC guideline advocated calculating a 10-year risk of cardiovascular disease in patients with stage one hypertension who did not have these comorbidities. If the risk is less than 10%, it is appropriate to undertake lifestyle changes on their own for 3 to 6 months. Both lifestyle adjustment and medicine are suggested for stage 2 hypertension with pre-existing conditions such as diabetes mellitus (DM), CKD, and a 10-year risk of CV event of 10% or higher.

### Non-pharmacological treatment

Following are the non-pharmacologic way to treatment of hypertensions.

#### Dietary Salt Restriction

The limit dietary salt intake is below 1500 mg per day [40]. Dietary salt restriction is related with a decrease of 5 to 10 mmHg in systolic blood pressure and 2 to 6 mmHg in diastolic blood pressure in general hypertensive patients.

#### Weight Loss

If a patient is overweight or obese, weight loss offers a demonstrable advantage in terms of lowering blood pressure and reducing the number of medications given [41]. Long-term weight loss studies have shown that a 10 kg weight loss is connected with a 6 mmHg systolic BP decrease and a 4.6 mmHg diastolic BP reduction.

#### Physical Activity

Regular aerobic exercise reduced systolic blood pressure by 4 mmHg and diastolic blood pressure by 3 mmHg on average. As a result, patients are advised to engage in 90 to 150 minutes of aerobic or resistance exercise each week [42]. As a result, all hypertensive patients are recommended to exercise.

#### Moderate Alcohol Intake

All hypertension patients are recommended to drink moderately—2 drinks per day for males and 1 drink per day for women—to lower systolic and diastolic blood pressure by 3 to 8 mmHg and 1 to 4 mmHg, respectively [43].

#### High Fibre and Low-fat Diet

Dietary strategy to stop hypertension (DASH) lowered systolic BP in hypertension patients by 11.4 mmHg and diastolic BP by 5.5 mmHg [44]. A diet high in fruits and vegetables not only lowers blood pressure but also increases endothelial function.

#### Withdrawal of Interfering Medications

Medicines that may interfere with blood pressure regulation, particularly NSAIDs, should be avoided or, if this is not possible, the lowest effective dose should be used. When starting therapy for hypertension with these drugs, keep a close eye on your blood pressure since you may need to change your antihypertensive regimen. Nonsteroidal anti-inflammatory medicines, oral contraceptive pills, corticosteroids, tricyclic antidepressant drugs, and monoamine oxidase inhibitors are only a few examples [45].

#### Pharmacological Treatment

The 2017 ACC/AHA guideline advised that antihypertensive medication treatment be started with two first-line drugs from distinct classes, either separately or in a fixed dosage combination, and that the goal blood pressure be less than 130/80 mmHg [46].

#### Initial drug selection

Angiotensin converting enzyme inhibitors (ACE inhibitors), angiotensin receptor blockers (ARBs), calcium channel blockers (CCBs) and thiazide type diuretics are the four types of antihypertensive medications, and each class of antihypertensive drugs lowers CV events [47]. Except for the major effect of beta blockers administered after MI reducing CAD event and calcium channel blockers reducing stroke, a meta-analysis of 147 randomized trials of 464,000 patients



with hypertension found that all major antihypertensive drug classes (diuretic, angiotensin converting enzyme inhibitors, angiotensin receptor blockers, beta blockers, and calcium channel blockers) cause reduction in CAD event and stroke for reduction in BP. According to the 2011 ACC/AHA hypertension guideline, the effectiveness, tolerability,

existence of certain comorbidities, and cost of antihypertensive medications in the treatment of adult hypertension are all factors to consider<sup>[48]</sup>.

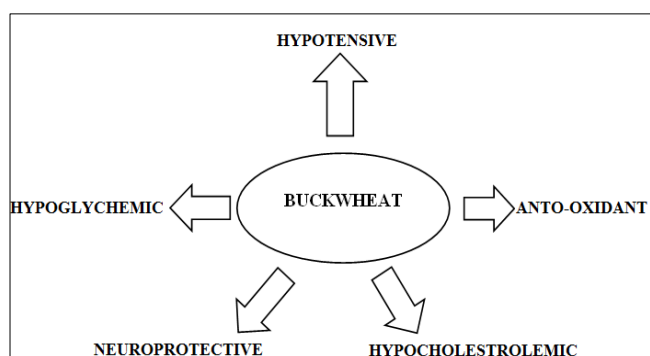
### New approach for treatment of hypertension

**Table 3:** New approach for treatment of hypertension are given as

Sr. No	New approach for treatment Of hypertension	Work
1.	<b>New Drugs for Treatment of Hypertension</b>	
	Antialdosterone Agent	Aldosterone is a mineralocorticoid that controls electrolytes and is linked to the development of hypertension and other diseases such as myocardial hypertrophy, myocardial fibrosis, and heart failure <sup>[49]</sup> .
	Vasopeptidase Inhibitors	The zinc metalloprotease neprilysin is a therapeutic target for hypertension and other forms of cardiovascular disease because it degrades the natriuretic peptides atrial (ANP) B type natriuretic peptides (BNP) and urodilatin and increase in circulating natriuretic peptide levels that results from neprilysin inhibition leads to natriuresis, vasodilatation, rennin-Angiotensin-aldosterone system inhibition, reduced sympathetic drive, and antiproliferative and antihypertrophic effects on heart <sup>[50]</sup> .
	Dopamine $\beta$ -Hydroxylase Inhibitor	Dopamine-hydroxylase is a therapeutic target for the treatment of hypertension and other cardiovascular problems because it catalyses the hydroxylation of dopamine to generate noradrenaline in the sympathetic nervous system.
2.	<b>Interventional Approach for Treatment of Hypertension</b>	
	Renal Denervation	With multiple published publications on RDN, this is a fast emerging study subject. The development, maintenance, and acceleration of arterial hypertension are all influenced by increased sympathetic activity <sup>[51]</sup> .
	Baroreflex Activation Therapy	Baroreflex activation treatment is a surgically implanted device that reduces sympathetic response and, as a result, lowers blood pressure by electrically activating carotid sinus baroreceptors.
	Carotid Body Ablation	Carotid body ablation investigations in animals and humans demonstrated increased carotid body sensitivity in hypertension, although the cause of the aberration is unknown <sup>[52]</sup> .
	Renal artery Stenting	For renal artery stenosis, percutaneous transluminal angioplasty with stenting is controversial. Recent clinical trials have found that using renal artery stenting in hypertensive patients with renal artery stenosis has little or no effect for blood pressure control, kidney function maintenance, or the avoidance of CV or renal events <sup>[53]</sup> .

### Effect of buckwheat on human health

Buckwheat's rich and diversified nutritional composition provides a number of health benefits. Buckwheat is considered to help prevent disorders including excessive cholesterol, hypertension, atherosclerosis, and diabetes. Rutin, which is found in high concentration in buckwheat, is utilised in medicine in many countries to prevent or minimise capillary deformations caused by hemorrhagic illnesses and hypertension<sup>[54]</sup>. Buckwheat products are utilised as food and medicine since it is employed in many functional foods manufactured across the world<sup>[55]</sup>. Positive effects of buckwheat on health are shown in Fig. (1)



**Fig 1:** Effect of buckwheat on health

#### 1. Antioxidant effect

In research, buckwheat's nutrition and functional features have served as a guide to studies that will be done to investigate its antioxidant effects. The antioxidant capacity of blood plasma samples collected from healthy persons who consumed 1.5 g buckwheat per kilogramme at once was measured in a research with 37 people<sup>[56]</sup>. Intake of 160

grammes of buckwheat honey in a litre of water or black tea, as well as buckwheat enhanced bread consumption, yielded comparable results<sup>[57]</sup>. Buckwheat's antioxidant effects were discovered to be related to its high phenolic component concentration in *in vitro* experiments<sup>[58, 59]</sup>. Zieliński and Kozłowska (2000) in their study, identified the antioxidant capacity of some cereals as buckwheat > barley > oats > rye<sup>[60]</sup>. Buckwheat sprouts contain a variety of flavonoids, including orientin, isoorientin, vitexin, isovitexin, rutin, and quercetin, but Tartary buckwheat exclusively contains rutin<sup>[61]</sup>. Buckwheat sprouts contain a variety of flavonoids, including orientin, isoorientin, vitexin, isovitexin, rutin, and quercetin, but Tartary buckwheat has solely rutin<sup>[61]</sup>. Buckwheat's high flavonoid and polyphenol content is known to have antioxidant properties, which may benefit human health<sup>[62]</sup>. Common buckwheat (*Fagopyrum esculentum* Moench) and tartary buckwheat (*Fagopyrum tataricum* Gaertn.) are often studied in terms of their overall composition, functional components, and antioxidant capabilities when considering the antioxidant content of buckwheat. Buckwheat decreases intracellular peroxide formation and cleans superoxide anions in liver cells, according to studies. Tartary buckwheat has been shown to significantly lower cellular oxidative stress caused by quercetin<sup>[64]</sup>.

#### 2. Hypocholesterolemic Effect

Buckwheat is increasingly being used as a cholesterol-lowering functional food<sup>[65]</sup>. Increased cholesterol consumption may lead to an increase in oxidative stress and plasma cholesterol levels. By increasing the regulation of low-density lipoprotein and oxidized LDL, this potential rise may contribute to the development of chronic illnesses such as atherosclerosis<sup>[66]</sup>. Buckwheat has been shown to control cholesterol levels and prevent the development of

cardiovascular illnesses in both *in vivo* and *in vitro* experiments [66, 67]. The effects of buckwheat protein on mice with hypercholesterolemia were investigated in a research. Buckwheat was found to lower protein plasma cholesterol levels more than other grains, limit sterol absorption from the intestines, increase the quantity of sterol eliminated from the body, and assist control the activity of liver cells linked to high cholesterol [67].

### 3. Hypoglycaemic Effect

The study of buckwheat's antihypertensive and anti-hypercholesterolemic qualities has led to a focus on the effects of buckwheat on diabetes [69]. In China, buckwheat is utilised in the nutritional therapy of diabetes [70]. Skrabanja *et al.* (2001) fed 10 healthy people boiling buckwheat grouts, 50 percent buckwheat flour enhanced bread, and white bread in a research. The study found that people who ate buckwheat products, particularly buckwheat groats, had lower postprandial plasma glucose and insulin production than those who ate white wheat bread [71]. Su-Que *et al.* (2013) randomly selected 10 diabetics who consumed buckwheat bread and found that their plasma glucose levels were 51 percent lower after 2 hours than those who consumed white bread [72].

### 4. Neuroprotective Effect

In animal experiments, buckwheat feeding was found to prevent the degeneration of brain functioning. In rats subjected to recurrent brain ischemia, 600 mg/kg buckwheat ingestion for 21 days reduced nitric oxide levels via blocking glutamate release and improved memory impairments by avoiding hippocampus cell necrosis and apoptosis [73]. In an *in vitro* investigation, ethyl acetate and ethanol extracts of root and buckwheat seed were found to have inhibitory effects on the development of neurological diseases by acting as antioxidants and inhibiting enzymes such as acetylcholinesterase, butyrylcholinesterase, and tyrosinase [74].

### Anti-hypertensive effect of buckwheat

In 2000, hypertension afflicted more than a quarter of the world's population (roughly 1 billion people) and this number is expected to rise to 1.56 billion by 2025 [75]. Blood pressure is controlled by the renin-angiotensin system. Angiotensinogen is converted to angiotensin I by plasma renin, which is then turned into angiotensin II by angiotensin converting enzyme (ACE) in the presence of angiotensin converting enzyme (ACE) [76].

Due to its high polyphenol content, buckwheat, a functional food with high rutin and quercetin content and used to prepare various functional meals, is thought to have an antihypertensive effect through modifying the renin-angiotensin system. Buckwheat sprouts also contain more phenolic compounds and have higher antioxidant activity than other grain sprouts [77].

Excess dietary salt consumption is regarded to be one of the most important factors in hypertension development. The amount of salt consumed and the kind of food consumed are both essential variables in the prevention and treatment of hypertension [78]. A study looked at the impact of high-salt diets on the blood pressure of hypertensive rats. The rats were divided into two groups: those who did not eat buckwheat and those who did eat it. According to the findings of the study, the high salt diet significantly increased blood pressure and serum Na<sup>+</sup> levels in the control group. Buckwheat has been proven to reduce blood pressure, protect against oxidative damage, and increase Na<sup>+</sup>/K<sup>+</sup> ATPase [79]. Buckwheat

reduces systolic blood pressure and oxidative stress in artery endothelial cells, resulting in antihypertensive effects [79]. Another study on hypertensive rats indicated that buckwheat sprout feeding boosted endogenous vasodilators such bradykinin and nitric oxide, as well as low blood pressure and strong antioxidant capacity, as compared to rats eating other cereals. A similar research looked at the effects of immunoreactivity on systolic blood pressure and aortic endothelial cells in mice after 5 weeks of buckwheat eating. Buckwheat consumption was shown to lower systolic blood pressure and oxidative stress by lowering immunoreactivity in aortic endothelial cells in the research [80].

*In vitro* and *in vivo* studies support the hypotensive effect found in persons who consume BW. ACE inhibitory activity in BW has been determined to be high [81]. The administration of 0.01-10 mg kg<sup>-1</sup> of lactic-fermented BWS to SHR rats decreased systolic and diastolic blood pressure, and this effect was associated with a decrease of the ACE activity and vasorelaxation effect on the blood vessel rings [82, 83].

Merendino *et al.* recently measured the levels of certain molecules involved in blood pressure control, as well as the antioxidant status, in normotensive Wistar Kyoto rats and SHR rats to assess the hypotensive and antioxidant responses to pasta containing tartary BWS. There was an increase in the expression of bradykinin (BK) and NO (vasodilators) in this research, as well as a decrease in endothelin-1 (ET-1) (vasoconstrictor) and an improvement in antioxidant status [84]. According to Koyama *et al.*, lactic fermentation in BWS increases the quantity of blood pressure-lowering chemicals such-aminobutyric acid (GABA) and tyrosine, which might help explain why lactic-fermented BWS lowers blood pressure in SHR rats [85].

Tsai *et al.* reported that extracts of several parts of BW, as well as rutin and quercetin, had a significant inhibitory effect on ACE activity [86].

Ushida *et al.* studied the effects of rutin-free tartary BW ext on isolated rat thoracic aortas [87].

A hydrolysate of BW protein produced a substantial ACE interference, according to Kawakami *et al.* [88].

*In vitro* and *in vivo* ACE inhibitory action was shown in tartary BW peptides produced during *in vitro* digestion, according to Li *et al.* [89].

Different peptides extracted from lactic-fermented BWS inhibited ACE activity in thoracic aorta tissue and reduced angiotensin II-mediated vasoconstriction, according to Koyama *et al.* [90].

### Conclusion

In conclusion, buckwheat is a food with rich nutrient content and important functional properties. It can show positive effect such as antioxidant, anti-inflammatory effects, on human health. It can also show significant effect on lowering the high blood pressure. Numerous reports have shown the potential benefit of consuming buckwheat for the management of hypertension. It can conclude that the literature indicates the buckwheat is safe to consume and may have beneficial effect on the hypertension.

### Conflict of interest

Author declares no conflict of interest, financial or otherwise.

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## References

- Guang C, Phillips RD. Plant food-derived angiotensin I converting enzyme inhibitory peptides. *Journal of Agricultural and Food Chemistry*. 2009;57:5113-5120.
- Krkoskova B, Mrazova Z. Prophylactic components of buckwheat. *Food Research International*. 2005;38:561-568.
- Giménez-Bastida JA, Zieliński H. Buckwheat as a functional food and its effects on health-A comprehensive review. *J Agric Food Chem*. 2015;63(36):7896-913.
- Li SQ, Zhang QH. Advances in the development of functional foods from buckwheat. *Crit. Rev. Food Sci. Nutr*. 2001;41:451-464.
- Christa K, Soral-Smietana M. Buckwheat grains and buckwheat products-Nutritional and prophylactic value of their components: A review. *Czech J Food Sci*. 2008;26:153-62. <http://dx.doi.org/10.17221/1602-CJFS>.
- Sammur D, Dennison P, Venter C, Kurukulaaratchy RJ. Buckwheat allergy: A potential problem in 21st century Britain. *BMJ Case Rep*. 2011, 1-3.
- Wronkowska M, Soral-Smietana M, Krupa-Kozak U. Buckwheat, as food component of a high nutritional value, used in the prophylaxis of gastrointestinal diseases. *Eur J Plant Sci Biotechnol*. 2010;4:1-7.
- Koyama M, Hattori S, Amano Y, Watanabe M, Nakamura K. Blood Pressure-Lowering Peptides from Neo-Fermented Buckwheat Sprouts: A New Approach to Estimating ACE-Inhibitory Activity. *PLoS ONE*. 2014;9(9):e105802. doi:10.1371/journal.pone.0105802.
- Kawasaki T, Itoh K, Ogaki T, Yoshimizu Y. A study on the genesis of hypertension in mountain people habitually taking Tibetan tea and buckwheat in Nepal. *J. Health Sci*. 1995;17:121-130.
- Kreft I, Fabjan N, Yasumoto K. Rutin content in buckwheat (*Fagopyrum esculentum* Moench) food materials and products. *Food Chem*. 2006;98:508-512.
- Suzuki A, Fujii A, Yamamoto N, Yamamoto M, Ohminami H, Kameyama A. Improvement of hypertension and vascular dysfunction by hydroxyhydroquinone-free coffee in a genetic model of hypertension. *FEBS Lett*. 2006;580:2317-2322.
- Abeywardena MY, Head RJ. Dietary polyunsaturated fatty acid and antioxidant modulation of vascular dysfunction in the spontaneously hypertensive rat. *Prostag. Leukotr. Ess. Fatty Acids*. 2001;65:91-97.
- Aoyagi, Y. An angiotensin-I converting enzyme inhibitor from buckwheat (*Fagopyrum esculentum* Moench) flour. *Phytochemistry*. 2006;67:618-621.
- Lin LY, Peng CC, Yang YL, Peng RY. Optimization of bioactive compounds in buckwheat sprouts and their effect on blood cholesterol in hamsters. *J Agric. Food Chem*. 2008;56:1216-1223. (8)
- Koyama M, Nakamura C, Nakamura K. Changes in phenols contents from buckwheat sprouts during growth stage. *J Food Sci. Technol*. 2013;50:86-93.
- Kim DW, Hwang IK, Lim SS, Yoo KY, Li H, Kim YS, *et al*. Germinated buckwheat extract decreases blood pressure and nitro tyrosine immunoreactivity in aortic endothelial cells in spontaneously hypertensive rats. *Phytother. Res*. 2009;23:993-998.
- Organisation WH. World Health Organization (2013), A global brief on hypertension. Report, 2013 April 2013. Contract No.: WHO/DCO/WHO/2013.
- Jamie Kitt, Rachael Fox, Katherine L. Tucker, Richard J. McManus. New Approaches in Hypertension Management: A Review of Current and Developing Technologies and Their Potential Impact on Hypertension Care. *Current Hypertension Reports*. 2019;21:44. <https://doi.org/10.1007/s11906-019-0949-4>.
- Erem C, Hacıhasanoglu A, Kocak M, Deger O, Topbas M. Prevalence of prehypertension and hypertension and associated risk factors among Turkish adults: trabzon hypertension study. *Journal of Public Health*. 2009;31(1):47-58. doi: 10.1093/pubmed/fdn078. [PubMed] [CrossRef] [Google Scholar]
- Ahmed A, Rahman M, Hasan R, *et al*. Hypertension and associated risk factors in some selected rural areas of Bangladesh. *International Journal of Research in Medical Sciences*. 2014;2(3):925. doi: 10.5455/2320-6012.ijrms20140816. [CrossRef] [Google Scholar]
- Mendis S. World Health Organisation; 2010. Global status report on non-communicable diseases, 2010. [http://www.who.int/nmh/publications/ncd\\_report2010/en/](http://www.who.int/nmh/publications/ncd_report2010/en/) [Google Scholar]
- Tabrizi JS, Sadeghi-Bazargani H, Farahbakhsh M, Nikniaz L, Nikniaz Z. Prevalence and associated factors of prehypertension and hypertension in Iranian population: the lifestyle promotion project (LPP) PLoS ONE, 2016, 11(10). doi: 10.1371/journal.pone.0165264.e0165264 [PMC free article] [PubMed] [Cross Ref] [Google Scholar]
- Mendis S. World Health Organisation; 2010. Global status report on non-communicable diseases 2010. [http://www.who.int/nmh/publications/ncd\\_report2010/en/](http://www.who.int/nmh/publications/ncd_report2010/en/) [Google Scholar]
- Chobanian AV, Bakris GL, Black HR, *et al*. Seventh report of the Joint National Committee on prevention, detection, evaluation, and treatment of high blood pressure. *Hypertension*. 2003;42(6):1206-1252. doi: 10.1161/01.HYP.0000107251.49515.c2. [PubMed] [Cross Ref] [Google Scholar]
- Wikipedia, Hypertension, <https://en.wikipedia.org/wiki/Hypertension>
- Prabakaran J, Vijayalakshmi N, Venkata Rao E. Prevalence of hypertension among urban adult population (25-64 years) of Nellore. *International Journal of Research & Development of Health*. 2013;1(2):42-49. [Google Scholar]
- Fisher ND, Williams GH. Hypertensive vascular disease. In: Kasper DL, Braunwald E, Fauci AS, *et al.*, editors. *Harrison's Principles of Internal Medicine*. 16th. New York, NY, USA: McGraw-Hill, 2005, 1463-1481. [Google Scholar].
- Rani R, Mengi V, Gupta RK, Sharma HK. Hypertension and its risk factors: A cross sectional study in an urban population of a North Indian District. *Public Health Research*. 2015;5(3):67-72. doi: 10.5923/j.phr.20150503.01. [CrossRef] [Google Scholar]
- Chen ZY, Peng C, Jiao R, Wong YM, Yang N, Huang Y. Anti-hypertensive nutraceuticals and functional foods. *Journal of Agricultural and Food Chemistry*. 2009;57:4485-4499.
- Vaishnavi Yuvraj Gande, Shrikrushna Subhash Unhale, Shubhangi Ingle, Priyanka lende, Prof. Dr. Pagore RR, Prof. Dr. Biyani KR. A review on types, treatment, awareness, prevention, pathophysiology and diagnosis of



- hypertension. *International Journal of Advance Research and Innovative Ideas in Education*. 2020; April 6(2):1576-1586.
31. Whelton PK, *et al.* 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Journal of the American College of Cardiology*. 2018;71:e127-e248. <https://doi.org/10.1016/j.jacc.2017.11.006>.
  32. Schwartz GL, Turner ST. Screening for Primary Aldosteronism in Essential Hypertension: Diagnostic Accuracy of the Ratio of Plasma Aldosterone Concentration to Plasma Renin Activity. *Clinical Chemistry*. 2005;51:386-394. <https://doi.org/10.1373/clinchem.2004.041780>
  33. Sawka AM, Jaeschke R, Singh RJ, Young WF. A Comparison of Biochemical Tests for Pheochromocytoma: Measurement of Fractionated Plasma Metanephrines Compared with the Combination of 24-Hour Urinary Metanephrines and Catecholamines. *Journal of Clinical Endocrinology and Metabolism*. 2003;88:553-558. <https://doi.org/10.1210/jc.2002-021251>
  34. Oliveras A, *et al.* Urinary Albumin Excretion Is Associated with True Resistant Hypertension. *Journal of Human Hypertension*. 2010;24:27-33. <https://doi.org/10.1038/jhh.2009.35>
  35. Whelton PK, Carey RM, Aronow WS, Casey Jr, DE, Collins KJ, *et al.* 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Hypertension*. 2018;71:e13-e115.
  36. Sawka AM, Jaeschke R, Singh RJ, Young WF. A Comparison of Biochemical Tests for Pheochromocytoma: Measurement of Fractionated Plasma Metanephrines Compared with the Combination of 24-Hour Urinary Metanephrines and Catecholamines. *Journal of Clinical Endocrinology and Metabolism*. 2003;88:553-558. <https://doi.org/10.1210/jc.2002-021251>
  37. Oliveras A, *et al.* Urinary Albumin Excretion Is Associated with True Resistant Hypertension. *Journal of Human Hypertension*. 2010;24:27-33. <https://doi.org/10.1038/jhh.2009.35>
  38. Calhoun DA, *et al.* Resistant Hypertension: Diagnosis, Evaluation, and Treatment. A Scientific Statement from the American Heart Association Professional Education Committee of the Council for High Blood Pressure Research. *Hypertension*. 2008;51:1403-1419. <https://doi.org/10.1161/HYPERTENSIONAHA.108.189141>
  39. De la Sierra A, *et al.* Clinical Differences between Resistant Hypertensives and Patients Treated and Controlled with Three or Less Drugs. *Journal of Hypertension*. 2012;30:1211-1216. <https://doi.org/10.1097/HJH.0b013e328353634e>
  40. Campese VM, Mitra N, Sandee D. Hypertension in Renal Parenchymal Disease: Why Is It So Resistant to Treatment? *Kidney International*. 2006;69:967-973. <https://doi.org/10.1038/sj.ki.5000177>
  41. Aburto NJ, *et al.* Effect of Lower Sodium Intake on Health: Systematic Review and Meta-Analyses. *BMJ*. 2013;346:f1326. <https://doi.org/10.1136/bmj.f1326>
  42. Neter JE, *et al.* Influence of Weight Reduction on Blood Pressure: A Meta-Analysis of Randomized Controlled Trials. *Hypertension*. 2003;42:878-884. <https://doi.org/10.1161/01.HYP.0000094221.86888.AE>
  43. Cornelissen VA, Smart NA. Exercise Training for Blood Pressure: A Systematic Review and Meta-Analysis. *Journal of the American Heart Association*. 2013;2:e004473. <https://doi.org/10.1161/JAHA.112.004473>
  44. Xin X, *et al.* Effects of Alcohol Reduction on Blood Pressure: A Meta-Analysis of Randomized Controlled Trials. *Hypertension*. 2001;38:1112-1127. <https://doi.org/10.1161/hy1101.093424>
  45. Whelton PK, *et al.* Effects of Oral Potassium on Blood Pressure. Meta-Analysis of Randomized Controlled Clinical Trials. *JAMA*. 1997;277:1624-1632. <https://doi.org/10.1001/jama.1997.03540440058033>
  46. Calhoun DA *et al.* Resistant Hypertension: Diagnosis, Evaluation, and Treatment. A Scientific Statement from the American Heart Association Professional Education Committee of the Council for High Blood Pressure Research. *Hypertension*. 2008;51:1403-1419. <https://doi.org/10.1161/HYPERTENSIONAHA.108.189141>
  47. Whelton PK, *et al.* 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Journal of the American College of Cardiology*. 2018;71:e127-e248. <https://doi.org/10.1016/j.jacc.2017.11.006>
  48. Law MR, Morris JK, Wald NJ. Use of Blood Pressure Lowering Drugs in the Prevention of Cardiovascular Disease: Meta-Analysis of 147 Randomised Trials in the Context of Expectations from Prospective Epidemiological Studies. *BMJ*. 2009;338:b1665. <https://doi.org/10.1136/bmj.b1665>
  49. Aronow WS, *et al.* ACCF/AHA 2011 Expert Consensus Document on Hypertension in the Elderly: A Report of the American College of Cardiology Foundation Task Force on Clinical Expert Consensus Documents. *Circulation*. 2011;123:2434-2506. <https://doi.org/10.1161/CIR.0b013e31821daaf6>
  50. Ruilope LM. Aldosterone, Hypertension, and Cardiovascular Disease: An Endless Story. *Hypertension*. 2008;52:207-208. <https://doi.org/10.1161/HYPERTENSIONAHA.108.111211>
  51. Corti R, Burnett Jr JC, Rouleau JL, Ruschitzka F, Lüscher TF. Vasopeptidase Inhibitors: A New Therapeutic Concept in Cardiovascular Disease? *Circulation*. 2001;104:1856-1862. <https://doi.org/10.1161/hc4001.097191>
  52. Esler M, *et al.* Assessment of Human Sympathetic Nervous System Activity from Measurements of Norepinephrine Turnover. *Hypertension*. 1988;11:3-20. <https://doi.org/10.1161/01.HYP.11.1.3>
  53. Esler MD, *et al.* Renal Sympathetic Denervation in Patients with Treatment-Resistant Hypertension (The

- Symplicity HTN-2 Trial): A Randomised Controlled Trial. *The Lancet*. 2010;376:1903-1909. [https://doi.org/10.1016/S0140-6736\(10\)62039-9](https://doi.org/10.1016/S0140-6736(10)62039-9).
54. Wheatley K, *et al.* Revascularization versus Medical Therapy for Renal-Artery Stenosis. *New England Journal of Medicine*. 2009;361:1953-1962. <https://doi.org/10.1056/NEJMoa0905368>
55. Zhang C, Zhang R, Li YM, *et al.* Cholesterol-lowering activity of tartary buckwheat protein. *J Agric Food Chem* 2017;65(9):1900-6. <http://dx.doi.org/10.1021/acs.jafc.7b00066> PMID: 28199789
56. Zhang ZL, Zhou ML, Tang Y, *et al.* Bioactive compounds in functional buckwheat food. *Food Res Int* 2012;49:389-95. <http://dx.doi.org/10.1016/j.foodres.2012.07.035>
57. Schramm DD, Karim M, Schrader HR, Holt RR, Cardetti M, Keen CL. Honey with high levels of antioxidants can provide protection to healthy human subjects. *J Agric Food Chem* 2003;51(6):1732-5. <http://dx.doi.org/10.1021/jf025928k> PMID: 12617614
58. Gheldof N, Wang XH, Engeseth NJ. Buckwheat honey increases serum antioxidant capacity in humans. *J Agric Food Chem*. 2003;51(5):1500-5. <http://dx.doi.org/10.1021/jf025897t> PMID: 12590505
59. Oomah BD, Mazza G. Flavonoids and antioxidative activities in buckwheat. *J Agric Food Chem*. 1996;44:1746-50. <http://dx.doi.org/10.1021/jf9508357>
60. Giménez-Bastida JA, Zieliński H. Buckwheat as a functional food and its effects on health. *J Agric Food Chem*. 2015;63(36):7896-913. <http://dx.doi.org/10.1021/acs.jafc.5b02498> PMID: 26270637
61. Zieliński H, Kozłowska H. Antioxidant activity and total phenolics in selected cereal grains and their different morphological fractions. *J Agric Food Chem*. 2000;48(6):2008-16. <http://dx.doi.org/10.1021/jf990619o> PMID: 10888490
62. Nam TG, Lee SM, Park JH, Kim DO, Baek NI, Eom SH. Flavonoid analysis of buckwheat sprouts. *Food Chem*. 2015;170:97-101. <http://dx.doi.org/10.1016/j.foodchem.2014.08.067> PMID: 25306322
63. Saiyma Sheikh, Yasir Ali Arfat. A comparative study of buckwheat and wheat cookies and effect of baking on antioxidant and anti-proliferative activities. *Int. J Horticult Food Sci*. 2021;3(1):60-67.
64. Lee LS, Choi EJ, Kim CH, *et al.* Contribution of flavonoids to the antioxidant properties of common and tartary buckwheat. *J Cereal Sci*. 2016;68:181-6. <http://dx.doi.org/10.1016/j.jcs.2015.07.005>
65. Brajdes C, Bahrin G, Dinica R, Vizireanu C. Phenolics composition and their biochemical stability confirmation by *in vitro* gastrointestinal conditions simulation, for a new functional fermented beverage based on sprouted buckwheat. *Rom Biotechnol Lett*. 2013;18:8832-42.
66. Liu CL, Chen YS, Yang JH, Chiang BH. Antioxidant activity of tartary (*Fagopyrum tataricum* (L.) Gaertn.) and common (*Fagopyrum esculentum* Moench) buckwheat sprouts. *J Agric Food Chem*. 2008;56(1):173-8. <http://dx.doi.org/10.1021/jf072347s> PMID: 18072736
67. Yang N, Li YM, Zhang K, *et al.* Hypocholesterolemic activity of buckwheat flour is mediated by increasing sterol excretion and down-regulation of intestinal NPC1L1 and ACAT2. *J Funct Foods*. 2014;6:311-8. <http://dx.doi.org/10.1016/j.jff.2013.10.020>
68. Berger S, Raman G, Vishwanathan R, Jacques PF, Johnson EJ. Dietary cholesterol and cardiovascular disease: a systematic review and meta-analysis. *Am J Clin Nutr*. 2015;102(2):276-94. <http://dx.doi.org/10.3945/ajcn.114.100305> PMID: 26109578
69. Zhang C, Zhang R, Li YM, *et al.* Cholesterol-lowering activity of tartary buckwheat protein. *J Agric Food Chem*. 2017;65(9):1900-6.
70. Wieslander G, Fabjan N, Vogrincic M, *et al.* Eating buckwheat cookies is associated with the reduction in serum levels of myeloperoxidase and cholesterol: A double blind crossover study in daycare centre staffs. *Tohoku J Exp Med*. 2011;225(2):123-30. <http://dx.doi.org/10.1620/tjem.225.123> PMID: 21931228
71. Qiu J, Li Z, Qin Y, Yue Y, Liu Y. Protective effect of tartary buckwheat on renal function in type 2 diabetics: a randomized controlled trial. *Ther Clin Risk Manag*. 2016;12:1721-7. <http://dx.doi.org/10.2147/TCRM.S123008> PMID: 27920542
72. Zeng Y, Pu X, Du J, *et al.* Use of functional foods for diabetes prevention in China. *Afr J Pharm Pharmacol* 2012;6:2570-9. <http://dx.doi.org/10.5897/AJPP12.119>
73. Skrabanja V, LiljebergElmståhl HG, Kreft I, Björck IM. Nutritional properties of starch in buckwheat products: studies *in vitro* and *in vivo*. *J Agric Food Chem* 2001;49(1):490-6. <http://dx.doi.org/10.1021/jf000779w> PMID: 11170616
74. Su-Que L, Ya-Ning M, Xing-Pu L, Ye-Lun Z, Guang-Yao S, HuiJuan M. Effect of consumption of micronutrient enriched wheat steamed bread on postprandial plasma glucose in healthy and type 2 diabetic subjects. *Nutr J*. 2013;12:64.
75. Pu F, Mishima K, Egashira N, *et al.* Protective effect of buckwheat polyphenols against long-lasting impairment of spatial memory associated with hippocampal neuronal damage in rats subjected to repeated cerebral ischemia. *J Pharmacol Sci*. 2004;94(4):393-402. <http://dx.doi.org/10.1254/jphs.94.393> PMID: 15107579.
76. Gülpınar A, Orhan I, Kan A, Şenol F, Celik S, Kartal M. Estimation of *in vitro* neuroprotective properties and quantification of rutin and fatty acids in buckwheat (*Fagopyrum esculentum* Moench) cultivated in Turkey. *Food Res Int*. 2012;46:536-43. <http://dx.doi.org/10.1016/j.foodres.2011.08.01>
77. Kearney P, Whelton M, Reynolds K, Muntner P, Whelton P, He J. Global burden of hypertension: analysis of worldwide data. *Lancet*. 2005;365:217-223.
78. Chia-Ling J, Shih-Li H, Kuo-Chiang H. Angiotensin I-converting enzyme inhibitory peptides: Inhibition mode, bioavailability, and antihypertensive effects. *Biomed*. 2012;2:130-921 136.
79. Merendino N, Molinari R, Costantini L, *et al.* A new "functional" pasta containing tartary buckwheat sprouts as an ingredient improves the oxidative status and normalizes some blood pressure parameters in spontaneously hypertensive rats. *Food Funct*. 2014;5(5):1017-26. <http://dx.doi.org/10.1039/C3FO60683J> PMID: 24658587
80. Rodrigues SL, Souza Júnior PR, Pimentel EB, *et al.* Relationship between salt consumption measured by 24-h urine collection and blood pressure in the adult



- population of Vitória (Brazil). *Braz J Med Biol Res.* 2015;48(8):728-35. <http://dx.doi.org/10.1590/1414-431x20154455> PMID: 26132095
81. Sofi F, Ghiselli L, Dinu M, *et al.* Consumption of buckwheat products and cardiovascular risk profile: A randomized, single-blinded crossover trial. *Nutr Food Sci.* 2016;6:3.
  82. Kim DW, Hwang IK, Lim SS, *et al.* Germinated Buckwheat extract decreases blood pressure and nitrotyrosine immunoreactivity in aortic endothelial cells in spontaneously hypertensive rats. *Phytother Res.* 2009;23(7):993-8. <http://dx.doi.org/10.1002/ptr.2739> PMID: 19140152\
  83. Lam H, Shimamura T, Sakaguchi K, Noguchi K, Ishiyama M, Fujimura Y. Assay of angiotensin I-converting enzyme-inhibiting activity based on the detection of 3-hydroxybutyric acid. *Anal. Biochem.* 2007;364:104-111.
  84. Koyama M, Naramoto K, Nakajima T, Aoyama T, Watanabe M, Nakamura K. Purification and identification of antihypertensive peptides from fermented buckwheat sprouts. *J Agric. Food Chem.* 2013;61:3013-3021.
  85. Nakamura K, Naramoto K, Koyama M. Blood-pressure-lowering effect of fermented buckwheat sprouts in spontaneously hypertensive rats. *J Funct. Foods.* 2013;5:406-415.
  86. Merendino N, Molinari R, Costantini L, Mazzucato A, Pucci A, Bonafaccia F. A new "functional" pasta containing tartary buckwheat sprouts as an ingredient improves the oxidative status and normalizes some blood pressure parameters in spontaneously hypertensive rats. *Food Funct.* 2014;5:1017-1026.
  87. Koyama M, Naramoto K, Nakajima T, Aoyama T, Watanabe M, Nakamura K. Purification and identification of antihypertensive peptides from fermented buckwheat sprouts. *J Agric. Food Chem.* 2013;61:3013-3021.
  88. Tsai H, Deng H, Tsai S, Hsu Y. Bioactivity comparison of extracts from various parts of common and tartary buckwheats: evaluation of the antioxidant- and angiotensin-converting enzyme inhibitory activities. *Chem. Cent. J.* 2012, 6.
  89. Ushida Y, Matsui T, Tanaka M, Matsumoto K, Hosoyama H, Mitomi A. Endothelium-dependent vasorelaxation effect of rutin-free tartary buckwheat extract in isolated rat thoracic aorta. *J Nutr. Biochem.* 2008;19:700-707.
  90. Kawakami A, Inbe T, Kayahara H, Horii A. Preparations of Enzymatic Hydrolysates 954 of Buckwheat Globulin and Their Angiotensin I Converting Enzyme Inhibitory Activities. In 955 Current advances in buckwheat research: proceedings of the 6th International Symposium on buckwheat in Shinshu, August 24-29, 1995, Toshiko, M.; Akio, U., Eds. Shinshu University Press, 1995: Shinshu, 1995, 927-934
  91. Li CH, Matsui T, Matsumoto K, Yamasaki R, Kawasaki T. Latent production of angiotensin I-converting enzyme inhibitors from buckwheat protein. *J Pept. Sci.* 2002;8:267-274.
  92. Koyama M, Hattori S, Amano Y, Watanabe M, Nakamura K. Blood pressure lowering peptides from neo-fermented buckwheat sprouts: a new approach to estimating ACE inhibitory activity. *PLoS One.* 2014;9:e105802.