Fagopyrum Mill-A Review of Phytochemistry and Pharmacological Effects

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Keywords: F. esculentum; F. tatarium; F. cymosum; Phytochemistry; Pharmacology.

Abstract. OBJECTIVE: The present review is an attempt to update our knowledge about the phytochemistry and diverse pharmacological effects of the three types of Fagopyrum Mill against various pathological targets including cancer, high cholesterol, cardiovascular, inflammation, pain, diabetes and etc, and then arouse people,s attention and provide new research direction. ethods：This review was carried out using a comprehensive and systematic literature search on the ethnomedicinal uses, phytochemistry and pharmacological activities of the Fagopyrum Mill. We collected literatures on Springer Link, Elsevier, PubMed and CNKI between 2005 and 2015. Literature sources included papers published in international journals, reports from international, conference papers and books. ESULTS: This review showed that the Fagopyrum Mill contains active constituents, including ployphenols, alkaloids, terpenoids, steroids, proteins, minerals and phenylpropanoid glycosides. At the same time, the Fagopyrum Mill are well known to possess a wide spectrum of pharmacological properties such as anti-fatty liver, anti-diabetic, antioxidant, anticancer and neuroprotective activities. onclusion: In this review, the ethnomedicinal uses, phytochemistry, pharmacological activities have been summarized. Although bioactivities of chemical constituents isolated from buckwheat are substantiated by using in vitro and in vivo studies including animal models and cell culture studies, the mechanisms of some pharmacological properties are still uncertain. It is recommended that further pharmacological and phytochemical analysis should be conducted on those species which lack previous references in literature.

Introduction

Traditional Chinese Medicine (TCM) has been used to maintain people's health, as well as to prevent, diagnose, improve or treat physical and mental illnesses all over the world for thousands of years. Buckwheat is a commonly eaten food in Asia and Western countries in the form of groats, flour, and noodles. The leaves and stems of the buckwheat plant are also edible and have been used as a traditional medicine in eastern Asia. The use of buckwheat for the management of diseases can be traced back to Jin Dynasty 1,800 years ago. The Fagopyrum Mill, a member of family Polygonaceae, currently has about 19 species 1, which are mainly distributed in the North Temperate Zone. Among these species, a total of three types of buckwheat are used as medicine in China：Fagopyrum esculentum Moench，Fagopyrum tataricum (L.) Gaench and Fagopyrum cymosum (Trev.) Meisn. Since they are rich in ployphenols, alkaloids, terpenoids, steroids, proteins, minerals and phenylpropanoid glycosides, they appear to be suitable components of medical products from the therapeutic aspect. The major roles of different species of buckwheat played in health-promoting are anti-oxidative, anti-inflammatory, anti-hypertensive, anti-diabetic, anti-cancer and so on2, 3. We have found limited literature data concerning the pharmacological effects of different species of buckwheat. Clinical evidence has also shown that the consumption of buckwheat and buckwheat-derived foods is positively associated with the prevention of various chronic diseases and improvement of general health. We collected literatures on Springer Link, Elsevier, PubMed and CNKI between 2005 and 2015. The present review is an attempt to update our knowledge about the phytochemistry and diverse pharmacological effects of the three types of Fagopyrum Mill against various pathological targets including cancer, high cholesterol, cardiovascular, inflammation, pain, diabetes and etc, and then provide new research direction.

Phytochemistry

Many constituents of Fagopyrum esculentum, Fagopyrum tataricum and Fagopyrum cymosum have been isolated, including ployphenols, alkaloids, terpenoids, steroids, proteins, minerals and phenylpropanoid glycosides; these are listed in Table1. One of the most effective constituents present in Chinese Herbal Medicines are ployphenols which are biologically active and possess a wide range of pharmacological properties such as antibacterial, antivirus, anti-inflammation and anti-oxidation properties. As an important member of flavonoids, rutin owned remarkable antioxidant activity. No rutin was found in cereals and pseudocereals except buckwheat, which can be used as a good source of dietary rutin 4. F. tataricum owned the highest rutin content. Especially, the rutin content and the antioxidative activity of F. tataricum seeds are more than 100 times and 3 or 4 times higher than those of F. esculentum. Trans-p-hydroxy cinnamic methyl ester, 3,4-dihydroxy benzamide and protocatechuic acid methyl ester were found in F. cymosum for the first time, since F. cymosum were effective in the treatment of diverse cancers, they are worthy for further research. Fagopyrin (alkaloids), unique to buckwheat, is widely distributed in parts of these three species 5. However, few literatures focus on its pharmacological activities or side effects. It is unavoidable to intake a large sum of fagopyrin, along with ingestion of buckwheat. Hence, we need to be clear about pharmacological activities or side effects of fagopyrin. In addition, tatarisides A–G (seven new active ingredients), isolated from F. tataricum root, had inhibitory ability against the growth of several cancer cell lines. Tatarisides A–G, the unique ingredients of F. tataricum, may bring about specific pharmacological activities.

Furthermore they are rich in minerals, trace elements 6 and amino acid 3, 7, which are essential to nutritional support and immune stimulation. Buckwheat has a high potential to be used as human food and to be utilized as a pharmacological agent in medicine.

Pharmacology

Over the past decade, numerous researchers have investigated the pharmacological activities of F.esculentum, F.tatarium and F.cymosum. This review provides a comprehensive summary of the main pharmacological properties of them.

Table1 Compounds isolated from F. esculentum, F. tatarium and F. cymosum

Classification	Chemical component	Species	Part of plan
Ployphenols	3, 4-dihydroxybenzoic acid	*F.cymosum*	Rhizome
	Gallic acid	*F.cymosum*	Rhizome
	(-)-epicatechin-3- *O*-gallate acid ester	*F.cymosum*	Rhizome
	Procyanidin B-2	*F.cymosum*	Rhizome
	Procyanidin C-1	*F.cymosum*	Rhizome
	pratol	*F.cymosum*	Rhizome
	luteolin-7,4′ -dime-thylether	*F.cymosum*	Rhizome
	3,6,3′ ,4′ -tetrahydroxy-7-methoxyflavon	*F.cymosum*	Rhizome
	Rutin	*F.esculentum*	Whole plant
		F.tatarium	Whole plant
		F.cymosum	Flowers, leaves and
	Quercetin	*F.esculentum*	Seed
		F.tatarium	Whole plant
	Isoquerectin	*F.tatarium*	Bran
	Quercitrin	*F.esculentum*	Sprout
	Luteolin	*F.esculentum*	Sprout
	Myricetin	*F.tatarium*	Whole plant
	Ferulic acid	*F.esculentum*	Grain and green-flc
		F.tatarium	Inflorescences
	Trans-*p*-hydroxy cinnamic methyl ester	*F.cymosum*	Rhizome
	3,4-dihydroxy benzamide	*F.cymosum*	Rhizome
	Protocatechuic acid	*F.cymosum*	Rhizome
		F.tatarium	seed
	Protocatechuic acid methyl ester	*F.cymosum*	Rhizome
	Kaempferol	*F. tatarium*	seeds
	Isokaempferol	*F. tatarium*	seeds
	kaempferol-3-O-rutinoside	*F. tatarium*	seeds
	quercetin-3-dirhamnoside	*F. tatarium*	seeds
	orientin	*F. tatarium*	sprout
	isoorientin	*F. tatarium*	sprout
	isovitexin	*F. tatarium*	sprout
Steroids	Hecogenin	*F.cymosum*	Rhizome
	β -sitosterol	*F.cymosum*	Rhizome
		F.tatarium	Grain
	β -sitosterol palmitate	*F.tatarium*	Grain
	stigmast- 4-thene-3,6-dione	*F.tatarium*	Grain
	daucosterol	*F.tatarium*	Grain
	ergosterol peroxide	*F.tatarium*	Grain
Triterpenoids	glutinone	*F.cymosum*	Rhizome
	glutinol	*F.cymosum*	Rhizome
Minerals	Mg	*F.tatarium*	Grain
		F.esculentum	Seed
	P	*F.tatarium*	Grain
Triterpenoids	glutinone	*F.cymosum*	Rhizome
	glutinol	*F.cymosum*	Rhizome
Minerals	Mg	*F.tatarium*	Grain
		F.esculentum	Seed
	P	*F.tatarium*	Grain
		F.esculentum	Seed
	S	*F.tatarium*	Grain
	K	*F.tatarium*	Grain
		F.esculentum	Seed
	Ca	*F.tatarium*	Grain
		F.esculentum	Seed
	Mn	*F.tatarium*	Grain
		F.esculentum	Seed
	Fe	*F.tatarium*	Grain
		F.esculentum	Seed
	Cu	*F.tatarium*	Grain
		F.esculentum	Seed
	Zn	*F.tatarium*	Grain
		F.esculentum	Seed
	Al	*F.tatarium*	Seed
		F.esculentum	Seed
	Se	*F.tatarium*	Seed
		F.esculentum	Seed
	Ni	*F.tatarium*	Seed
		F.esculentum	Seed
Amino acid	Aspartic acid	*F.esculentum*	Seed
		F.tatarium	Seed
	Threonine	*F.esculentum*	Seed
		F.tatarium	Seed
	Serine	*F.esculentum*	Seed
		F.tatarium	Seed
	Glutamic acid	*F.esculentum*	Seed
		F.tatarium	Seed
	Glycine	*F.esculentum*	Seed
		F.tatarium	Seed
	Alanine	*F.esculentum*	Seed
		F.tatarium	Seed
	Cysteine	*F.esculentum*	Seed
		F.tatarium	Seed
	Valine	*F.esculentum*	Seed
		F.tatarium	Seed
	Methionine	*F.esculentum*	Seed
		F.tatarium	Seed
	Isoleucine	*F.esculentum*	Seed
		F.tatarium	Seed
	Leucine	*F.esculentum*	Seed
		F.tatarium	Seed
	Tyrosine	*F.esculentum*	Seed
		F.tatarium	Seed
	Phenylalanine	*F.esculentum*	Seed
		F.tatarium	Seed
	Lysine	*F.esculentum*	Seed
		F.tatarium	Seed
	Histidine	*F.esculentum*	Seed
		F.tatarium	Seed
	Arginine	*F.esculentum*	Seed
		F.tatarium	Seed
	Proline	*F.esculentum*	Seed
		F.tatarium	Seed
Terpenoids	Carotenoids	*F.tatarium*	sprouts, leaves and
Phenylpropanoid glycosides	chlorogenic acid	*F.tatarium*	sprouts
	Tatarisides A–G	*F.tatarium*	root

1. Anti-fatty liver Activity. Oral administration of germinated F. esculentum caused significant reductions in triglycetides(TG) and total cholesterol(TC) levels in the liver after 8 weeks, and also down- regulated mRNA expressions of PPARγ and C/EBPα in hepatocytes in a dose-dependent manner of rats17, suggesting that germinated F. esculentum may be effective in the treatment of fatty liver. Germinated buckwheat was dried, pulverized and extracted with 70% ethanol for 24 h， rutin and quercitrin increased multi-fold by germination. Development of fatty liver is associated mainly with obesity. Flavonoids could suppress obesity by either inhibiting the signals that promote adipogenesis or decreasing adipose tissue mass, especially rutin effectively suppressed adipocyte differentiation from pre-adipocytes 5. Therefore, as a rich source of rutin, germinated buckwheat is likely to show anti-fatty liver potential. Moreover, it has been demonstrated by a targeted geneknockout strategy in mice that PPARγ and C/EBPα act in concert to generate fully mature adipocytes 18, 19. Oral administration of germinated buckwheat down-regulated mRNA expressions of PPARγ and C/EBPα in hepatocytes. Although further research is needed to draw a definite relationship between germinated buckwheat and its anti-fatty liver mechanism, it is clear that oral administration of germinated buckwheat lessened fatty liver.

2. Anti-atherosclerosis activity. Atherosclerosis is a chronic, maladaptive, nonresolving inflammatory response which underlies the leading cause of death in the world today. Macrophages play a central role in both the initiation and development stages of disease pathogenesis. It has been proved MiR-155 is multi-target molecule specifically expressed in atherosclerotic plaques and pro-inflammatory macrophages 20, suggesting its potential involvement in lesion progression. The study also demonstrated LDL and it s oxidized derivatives could modulate miR-155-mediated inflammatory and apoptotic responses in lesional macrophages at different stages of atherosclerosis. 80% methanol extract of Fagopyrum esculentum and Fagopyrum tataricum exhibited a dose–response effect in inhibiting low-density lipoprotein (LDL) peroxidation 21, suggesting that Fagopyrum esculentum and Fagopyrum tataricum may be potent candidates for the treatment of atherosclerosis. Of course, more mechanistic studies are required before Fagopyrum esculentum and Fagopyrum tataricum can be considered for further clinical use. In addition, buckwheat-enriched wheat bread was tested in normal weight patients on statin therapy over one-month dietetic intervention, significant decrease in total cholesterol and LDL-cholesterol, as well as the ratio of LDL/HDL cholesterol was obtained for the group of patients with high risk of developing cardiovascular diseases17.

3. Anti- celiac disease activity. Celiac disease (CD) is an autoimmune enteropathy triggered by the ingestion of gluten-containing grains (wheat, barley, rye and possibly oats) in genetically susceptible individuals. The consumption of gluten in CD causes self-perpetuating damage to the intestinal mucosal and its functionality becomes severely impaired, moreover CD is at least twice more common in cirrhotic patients than in the general population 22. Gluten-free food materials may protect patients from these damages. As this study reported that different buckwheat species are gluten-free pseudocereals 21, buckwheat grain and buckwheat grain products represent an alternative nutritious food source that is of paramount importance for people with celiac disease.

4. Neuroprotective activity. Neuromelanin-containing neurons are particularly susceptible to degeneration and their depigmentation is the feature of Parkinson's disease (PD) 23. Tyrosinase, which is a chief enzyme in melanin biosynthesis by means of the production of L-3, 4-dihydroxyphenylalanine (L-DOPA) and subsequent molecules, has ability to accelerate the stimulation of catecholamine quinone derivatives through its oxidase activity. Consequently, inhibition of tyrosinase is important in PD treatment 24. The F. esculentum seed extracts had notable inhibition towards tyrosinase 25, suggesting F. esculentum seed may be a potent candidate for the treatment of Parkinson's disease. Further research should be taken to investigate the mechanism before clinical use. Moreover, since oxidative stress and neuroinflammation have a crucial role in the initiation and progression of neurodegenerative diseases and neuronal cell death 26, the researchers proved that luteolin attenuated oxidative stress in neuroblastoma cells and suppressed inflammation in the brain tissues and regulates different cell signaling pathways 27, 28, suggesting that luteolin can be used as novel therapeutic agents for the treatment of

neurodegenerative diseases. F. esculentum sprouts contain a rich source of luteolin 29.

5 Anti-cancer activity. Carotenoid derivatives contribute to cancer prevention as well as bone health maintenance via the inhibition of the nuclear factor kappa B (NFkB) transcription system 30. Aberrant constitutive activation of NFkB transcription system plays a key role in inflammatory processes and therefore affects chronic diseases such as osteoporosis and cancer 31, 32. Therefore, inhibition of NFkB is considered a promising therapeutic approach for blocking tumor growth, reducing bone loss and increasing bone formation. IKK β and p65 subunit are the key proteins of the NFkB pathway, the study demonstrated carotenoid derivatives contribute to cancer prevention as well as bone health maintenance by inhibiting IKK β and p65 transcriptional activities. Fagopyrum tataricum expressed high levels of carotenoids in the sprouts, leaves and flowers 33, suggesting Fagopyrum tataricum can be a novel agent for inhibiting of NFkB. Also carotenoids serve as precursors of vitamin A, which is one of the most important micronutrients that affect the health of humans 34.

In addition, myricetin has potent anticancer-promoting activity and mainly targets Mitogen-activated protein kinase kinase (MEK) signaling, MEK generally plays a critical role in transmitting signals initiated by tumor promoters, including 12-O-tetradecanoylphorbol-13-acetate (TPA), epidermal growth factor (EGF) or platelet-derived growth factor, that may contribute to the chemopreventive potential of several foods including F.tatatium 35. Moreover, resveratrol also has been shown to have a potent chemopreventive effect in multiple carcinogenesis models by inducing apoptosis and inhibiting tumor promoter-induced cell transformation 36, suggesting that resveratrol, which is abundant in buckwheat 37, may be helpful in designing new generations of chemopreventive agents for control of human cancer.

Tatarisides A–G (1– 7), isolated and identified from tartary buckwheat roots, were evaluated in vitro for their inhibitory ability against the growth of human lung adenocarcinoma (A-549), human colon carcinoma (HCT116), human breast carcinoma (ZR-75-30) and human promyelocytic leukaemia (HL-60) cell lines38. They were found to possess marked inhibitory activity on four tested human cancer cell lines and can be regarded as potent tumour inhibitors and be beneficial in the therapy of cancer diseases. Especially, Tatarisides F possessed notable antitumor effect against H22 hepatocellular carcinoma (HCC) and showed protective effects against CTX-induced liver damages when co-administrated with CTX 39.

6. Anti-DNA damage activity. The human body is continuously attacked by both exogenous and endogenous reactive oxygen species (ROS), causing oxidative damage to the cells. Of the ROS, the hydroxyl radical (OH) is usually high reactive and short-lived, and is known to cause damage to cellular components including DNA 40. However, Fagopyrum Mill may alleviate the damage, because it contains many kinds of antioxidants, such as rutin, quercitrin, quercetin, tocopherols and phenolic acids 23, 36, 41. Some researchers examined the protective effects of the ethanolic extracts from buckwheat (Fagopyrum esculentum and Fagopyrum Tartaricum) groats on DNA damage caused by hydroxyl radical 42. The result showed that 70% can effectively inhibit non-site-specific hydroxyl radical-mediated DNA damage and site-specific hydroxyl radical-mediated DNA strand breaks under in vitro conditions， suggesting that Fagopyrum esculentum and Fagopyrum Tartaricum can be used not only as the easily accessible source of natural antioxidants but also as an ingredient of the functional food related to the prevent ion and control carcinogenesis diseases.

7. Anti- hypertension activity. Hypertension is a major risk factor for cardiovascular disease and stroke, thus prevention of hypertension is important in reducing the risk of these debilitating ailments. Neo-FBS decreased both systolic and diastolic blood pressure in spontaneously hypertensive rats (SHRs) at a dose of 0.010 mg/kg, an effect comparable to 1.0 mg/kg captopril, an anti-hypertensive drug 43. Neo-fermented buckwheat sprouts (neo-FBS), was produced from buckwheat sprouts by lactic fermentation, orally administered neo-FBS (10 mg/kg) significantly decreased angiotensin I-converting enzyme (ACE) activity in the lung, thoracic aorta, heart, kidney, and liver of SHRs. Neo- FBS had a detectable relaxing effect on a phenylephrine-precont racted thoracic aorta in SHRs, suggesting that the ACE inhibition and vasorelaxation activities were found to be responsible for the excellent BPL effect of neo-FBS and neo-FBS may also have BPL effects

in human patients.

8. Anti-acne activity. It is reported that Propionibacterium and Staphylococci species are two predominant bacterial groups in sebaceous sites. The excessive growth of the two major bacteria and inflammation which caused by the reactive oxygen species are the most important physiological factors in the pathogenesis of acne 44. The extract of the tartary buckwheat bran (TBBE) was examined in vitro for the antibacterial activity against S. aureus (ATCC25923), S. epidermidis (ATCC12228), P. acnes (ATCC11827) and P. acnes (ATCC6919) 45. TBBE might be useful to develop new types of antibacterial substance and new skin care cosmetics to prevent or improve acne. TBBE was found to possess marked inhibitory activity on four tested bacterial strains, and the antibacterial activity of TBBE was potentially attributed to quercetin and isoquerectin or the interaction between quercetin, isoquerectin and rutin.

9. Anti- irritable bowel syndrome activity. Irritable bowel syndrome (IBS) is a chronic functional bowel disorder featured in abdominal pain and disturbed bowel habits. One of the pathomechanism is gastrointestinal motility dysfunction accompanied by visceral hyperalgesia 46. The study has demonstrated that F. cymosum soothed the visceral hypersensitivity of model rats, possibly by inhibiting the colonic epithelium inflammation and injury, as well as by facilitating membrane localization and expressions of colonic epithelial TJs which strengthened the colonic barrier, and have provided a theoretical basis for F. cymosum treated IBS due to its pharmacological values 25.

10. Anti-snake venom activity. The venom enzymes responsible for the toxic effects are phospholipase A2, proteases, and hyaluronidases, which play key roles in many inflammatory reactions, tissue necrosis and hemorrhagic activity 29, 33. Crude water and ethanol extracts of 88 plant species used against snakebites in traditional Chinese medicine was assessed for hyaluronidase-, phospholipase A2-, and protease inhibitor activity using G. blomhoffi, D. acutus, N. naja, and T. stejnegeri venoms 26, crude water extract of F. cymosum (Rhizome) presented marked inhibitory activity on G. blomhoffi, N. naja, and T. stejnegeri venoms, ethanol extracts of F. cymosum (Rhizome) possessed notable inhibitory activity on D. acutus, N. naja, and T. stejnegeri venoms.

11. Anti-rheumatoid arthritis activity. Rheumatoid arthritis (RA) is a chronic autoimmune disease that results in a chronic, systemic inflammatory disorder of many tissues and organs, and principally attacks flexible (synovial) joints. It is a disabling and painful condition, which can lead to substantial loss of function and mobility if not adequately treated 47. The study evaluated the anti-arthritic effect of 95% ethanol extract of EFC (extract of Fagopyrum cymosum) 48. The high dose level of EFC (160 mg/kg) significantly suppressed the swelling of hind paw of adjuvant arthritic rats and decreased the plasma viscosity. Moreover, EFC significantly reduced the production of IL-1 and TNF-α in the serum of AA, suggesting that F. cymosum is effective in preventing and suppressing the development and progression of arthritis, with reductions in inflammatory response.

12. Anti- pneumonia activity. Some researchers studied the mechanism of protective effect of Fagopyrum cymosum on lung injury induced by Klebsiella pneumonia in rats 49. The result demonstrated that the contents of IL-1beta, IL-6, IL-8, TNF-alpha, ICAM-1 and INF-gamma in serum and the expressions of TNF-a, ICAM-1, NF-kappaB p65 and MIP--2mRNA of Fagopyrum cymosum were significantly lower than those of model group, and the rats of Fagopyrum cymosum had less lung injury than those of model group. Namely, the lung injury induced by Klebsiella pneumonia is related to TNF-alpha, ICAM-1, NF-kappaB p65 and MIP-2mRNA. To decrease the excessive expression of TNF-alpha, ICAM-1, NF-kappaB p65 and MIP-2mRNA might be the main mechanism of protective effect of Fagopyrumcymosum on lung injury.

13. Anti-diabetic activity. Fagopyrum tataricum seed is used for the treatment of type 2 diabetes mellitus in Taiwan. Diabetes is a life-long disease characterized by high levels of blood sugar. The study investigated the antioxidant, anti-glycation, inhibitions of amylase and glucosidase by EEB (75 % ethanol extract of Fagopyrum tararicum seeds), which are related to hyperglycemia 50. The hydrolysis is carried out by a group of hydrolytic enzymes, namely α-amylase and α-glucosidase.

Inhibition of these enzymes is increasingly believed to be the best strategy for management of type 2 diabetes, however, Hydrolysis of dietary carbohydrates is the major source of glucose in the blood 51, 52. Furthermore, EEB inhibited α-glucosidase and α-amylase activity in a dose-dependent manner. Nonenzymatic glycation of proteins that promotes the irreversible formation of AGEs is also a significant factor associated with hyperglycemia 53. They found that EEB inhibited the generation of AGE, as well as the nonenzymatic glycation. This study proved that 75 % ethanol extract of buckwheat (EEB) play a potent inhibition role in main links of the formation of diabetes , hence EEB may use as protection and treatment agent in diabetic patients

Conclusions

Fagopyrum esculentum Moench，Fagopyrum tataricum (L.) Gaench and Fagopyrum cymosum (Trev.) Meisn, belonging to the Fagopyrum Mill (Polygonaceae), possess a wide spectrum of pharmacological properties such as neuroprotective, antimicrobial, antidiabetic, antioxidant, anti-inflmmatory, anti-fatty liver and anticancer activities, which are associated with its diverse chemical constituents, including flvonoids, alkaloids, phenolics, terpenoids, proteins, minerals, phenylpropanoid glycosides and certain active compounds that are still not identified. Although bioactivities of chemical constituents isolated from buckwheat are substantiated by using in vitro and in vivo studies including animal models and cell culture studies, the mechanisms of some pharmacological properties are still uncertain. It is recommended that further pharmacological and phytochemical analysis should be conducted on those species which lack previous references in literature. Moreover, the deficiency of clinical trials is one of the main factors resulting in the limitation of clinical use. Hence more research is required to find new active compounds and how they increase or decrease disease tolerance or resistance, what the changes are in plant metabolism, and how this can be used to control plant disease. And we also expect that the present review could update our knowledge and promote the future research for buckwheat on new pharmaceutical preparations or functional products and bioassays.

Declaration of interest

The authors declare that there was no conflict of interest with respect to the data collected and procedures used within the study.

Author contribution

All authors contributed equally to this project. All authors read and approved the final manuscript. f you follow the “checklist” your paper will conform to the requirements of the publisher and facilitate a problem-free publication process.

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