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REVIEW

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Structural, functional, nutritional composition and analytical profiling of *Triticum aestivum* L.

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Abstract

Wheat is considered as the most important cereal grain globally. It has a vast economic importance as it is used in producing bread, pastries, and household flour and serving as food for livestock among other uses. Different biological activities of wheat were correlated with the presence of polyphenols due to their antioxidant activities and other preventative capabilities. Wheat can also be used as an antidiabetic, anti-inflammatory, anticancer, antimicrobial, and antiaging agent. Omics has established itself during the past 20 years as a crucial tool for comprehending the internal systems of various plant systems including wheat using LC–MS, GC–MS, and UV spectrophotometry as analytical techniques. The current review represents in depth search regarding wheat cultivation, botanical description, economic significance, quantitative phytochemical characterization, and biological importance. Additionally, a critical assessment of the cited omics research on wheat was conducted with an emphasis on the analytical instrument, methods of analysis and results interpretation.

Keywords Wheat, Polyphenols, Omics, LC–MS, GC–MS

Introduction

An estimated 35 % of the world's population depends on wheat as their main crop. More than two-thirds of the world's wheat is consumed for human consumption, while just a fifth is used for animal feed [19]. It is mostly composed of 75–80% carbohydrates, 9–18% protein, fiber, several vitamins (particularly B vitamins), calcium, iron, and a variety of macro- and micro-nutrients [23]. Also, the germ part is composed of almost 50%g/100 g dry matter total carbohydrates and various micronutrients such as phosphorus, magnesium, zinc, iron, manganese, thiamin (B1), riboflavin (B2) and pyridoxine (B6) [4, 8, 35]. Moreover, the outer layer of the seed (bran) contains 67.5%g/100 g dry matter carbohydrates and 48.2%g/100 g dry matter [45]. It exceeds the number of all other grain crops (including rice, maize….etc.) in terms of acreage, application, usability, consumption and industrial production, so it could be considered as world's most important cereal grain crop [22]. Wheat is a crop with a large yield that is simple to store and is particularly climate adaptable. Because of the vast genetic diversity of wheat, it can grow in temperate, Mediterranean, and subtropical areas in both hemispheres [10].

Omics is a vital tool in understanding the internal systems of several plant functions [20] and was indeed used for comprehension of the composition of different wheat parts such as whole seeds, bran, germ and leaves [23, 26, 66]. In order to improve human health and wellbeing, it is essential to thoroughly investigate the food and nutrition

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domain in the third millennium. This is because a nutraceutical's complete profile, rather than just its individual components, allows for more informed choices regarding the best diet for the treatment of various diseases such as diabetes, obesity, hypercholesterolemia and cancer.

Therefore, we present an updated review of bread wheat, addressing its cultivation, botanical description, economic importance, phytochemical characterization, and biological significance. Additionally, a critical assessment of the cited omics research on wheat was conducted, with an emphasis on the analytical instruments, methods of analysis and results interpretation.

Cultivation

There are millions of cultivars of wheat and they are cultivated in two seasons: winter and spring Winter wheat is planted in, between October and December, and grows during the winter to be harvested in the spring or early summer. It takes around 7 to 8 months to get matured. Spring wheat is planted from March to May and harvested between July and September [40]. Wheat must be harvested at full maturity immediately after physiological maturity, which is known from the yellowing of the upper phalanx, which bears the spike in about 50% of the field. Irrigation is prohibited before harvest about 10–15 days, and the harvest is before sunset or in the early morning so as not to break the grain or crack the ears, taking care of transportation and separation of the grains (threshing) operations to reduce crop losses. It is also preferable to use tractor-driven threshers to ensure that fine straw is obtained and threshing is performed as quickly as possible [7].

The top 10 countries producing wheat worldwide are as follows: China, India, Russia, United States, France, Australia, Canada, Pakistan, Ukraine and Germany [61]. Global wheat production has been increasing since 2011/2012 till today, with worldwide production of 697 million metric tons in 2011/2012 and 778.6 million metric tons in 2021/2022 [57].

Botanical description of *Triticum aestivum*, L.

Wheat aerial parts include a central stem emerging from the mature wheat plant, from which leaves arise on opposite sides and terminates in the ear. As for the leaf, its structure consists of the leaf blade and the sheath, which are formed from separate meristems. Leaves grow on alternating sides of the stem and are numbered such that all even-numbered leaves grow on one side of the plant. Transverse branches protrude from the main stem of the wheat plant. They can grow leaves on opposing sides of their central stem in the same way as the main stem produces leaves, and they can also create an ear at the end. The mature wheat plant has two distinct root types. The first is the seminal roots, the first root type to emerge, that develop from the root primordia present in the grain. The second type is the nodal roots that emerge at the same time as the tiller development. As for the wheat kernel, it is made up of the bran coat and endosperm that surrounds the embryo (germ). The pericarp, testa, and aleurone are the three layers that make up the outer layer of kernel (bran). Bran contains the largest amount of insoluble fiber, B vitamins, trace minerals and small amount of protein. The endosperm, the middle layer of kernel, contains mostly carbohydrates and protein that are necessary for the plant's development as well as flour manufacturing, and small amount of B vitamins, iron and soluble fiber. Although the embryo, the inner part of the grain, makes up a minor portion of the grain, it contains root radicle and shoot apex. It is also rich in trace minerals, unsaturated fats, B vitamins, antioxidants, phytochemicals and a small amount of protein [2, 42].

Wheat growth stages

Wheat growth occurs over 5 stages. The first stage is germination, where the wheat kernel absorbs water (imbibition) and plant development starts once the embryo is fully imbibed. The coleoptile elongates, pushing the growth point toward the soil surface after the first three seminal roots are generated. The first leaf then appears, and this stage ends with the appearance of the first tiller. The second stage is tillering, where the appearance of tillers and the development of a secondary or crown root system follow the formation of the crown. During the growing season, the crown root system provides the majority of the plant's nutrients and water. Primordia at nodes give rise to roots, leaves, tillers, and spikelets that make up the wheat plant's head. Each produced tiller represents the possibility of a wheat plant developing a new stem with its own group of leaves, roots, and head. The plant's root and shoot development are coordinated, so the number of crown roots generated is proportional to the number of leaves produced. At the end of the tillering stage, wheat plant undergoes a significant change in its development. At this point, the main shoot and tillers' growth tips stop creating new leaves and begin producing reproductive structures. The end of the vegetative and beginning of the reproductive periods are signaled by the conversion of the growth point. The following stage then starts, which is stem elongation (stem jointing), where the nodes from which leaves develop are telescoped at the crown. Once jointing begins, the internode region lengthens, causing the nodes and growth point to

move upward from the crown, resulting in a long, stiff stem that will carry the head. On a wheat plant, each successive tiller has one less leaf than the one before it. This synchronizes the onset of the major stem and tiller elongation stages. The synchronization of growth and development at this stage ensures that the maturity of all heads on the plant is only a few days apart. Heading is the fourth stage of wheat growth. The heading stage lasts from when the tip of the head emerges from the flag leaf sheath until the head has fully emerged. Afterwards, pollination and fertilization start, where all heads of a well synchronized wheat plant flower and the embryo and endosperm begin to form shortly after fertilization. The developing endosperm then starts as a milky fluid that becomes more solid with time. During this stage, the kernel size grows fast. Then, the kernel accumulates the majority of its dry weight and by the end of this stage, all nutrients have been transported from the leaves, stems, and spike to the growing seed. Even though it still contains around 30% water, the growing kernel is physiologically mature. The final stage is the ripening stage, where the seed loses moisture and whatever dormancy it may have had [16]. Different wheat stages were reported to contain several polyphenols including phenolic acids, flavonoids, lignans, stilbenes, non-phenolic metabolites and other polyphenols [67].

Economic importance

Mexico accounted for 1.29 billion USD in global wheat export revenue in 2021, followed by the Philippines with 885.44 USD and China with 764.21 USD [58]. Additionally, Russia earned 8.879 billion USD from wheat exports, followed by the US with 7.3 billion USD and Canada with 6.78 billion USD [54].

Among the most common used types, is the hexaploid wheat (*Triticum aestivum* L.), which is often known as common bread wheat that is favored for bread production. It is grown in humid climates that characterize soft grains, enriched with protein of 8–10% and low gluten contents [23]. Gluten consists of gliadin (prolamin) and glutenin (glutelin). After intake, the numerous prolamins (such as glutenin and gliadin) that make up gluten must be digested within the small intestinal lumen; however, they are long peptide molecules that are difficult for humans to digest because they are rich in proline and glutamine. These prolamins cause certain diseases such as coeliac disease (CD), non-coeliac gluten sensitivity (NCGS), gluten ataxia (GA)and dermatitis herpetiformis (DH) [12, 44]. The majority of the wheat flour produced is used to make bread, cakes, crackers, biscuits, pastries, and household flours are made using this type as well. Among the used forms of wheat are wheat germ flour, wheat germ oil, bran, whole grains, whole grain flour and wheatgrass [23].

For extracting starch from corn and wheat, industry has developed certain techniques. Using a low-water-input centrifugation method, modern production factories can extract 40–50 tons of flour per hour. Wheat starch is now used in wide array of products including: food additives such as sweeteners in beverages, binders in soups and sauces, moistening agents in baked goods. Also, texture agents in numerous dairy products, green chemistry (fermentation), bioplastics, paper manufacturing, ethanol production, baby food, energy drinks, emulsifiers, animal feed (milk powder), piglet starter feed, aquaculture feed pellets, etc. [23].

Gluten is a "first-class byproduct" made by the wheat starch industry. Gluten is presently the cheapest "green protein" available to any food or feed company due to increased wheat starch output around the world. Gluten powder has been added to flour to increase rheological and technical qualities to the levels required by baking industry. Wheat is also used as an animal feed grain and this is directly influenced by the price relationship between wheat and other crops, which means that in years when harvests are affected by climatic circumstances and excess grain is unfit for human use, it will be fed to livestock. Low-grade grain is also used to make alcohol, adhesives, paper additives, soaps, rubbers, cosmetics, and varnishes, with wide range of applications adding to its rising demand and production [23].

Wheat stabilization

Wheat germ is a valuable by-product of the milling process since it is a naturally available supply of tocopherols, phytosterols, minerals, vitamins, and essential amino and fatty acids. The nutritional value of wheat germ does, however, rapidly decline during storage due to the high enzymatic activity and high unsaturated oil content, severely reducing the shelf-life of the product. To guarantee a stable WG, oxidative enzymes (lipase and lipoxygenase) must be inactivated or removed, or both. The best way to preserve wheat germ is to first inactivate the enzymes through heat treatment, then store it in a deep freezer at − 18°C [5].

Wheat germ physical stabilization might be subdivided into several subclusters: heat treatments (steaming, fluidization, spouted bed, and roasting/toasting), radiation mediated treatment (microwaving), infrared radiation treatment and gamma radiation and thermal/mechanical treatments (cooking-extrusion and de-oiling) [5]. Chemical stabilization include enzyme (lipase and lipoxygenase) denaturation either by acidification (hydrochloric

acid, acetic acid, calcium hydroxide) or alkalization [0% decrease in lipase activity at pH = 10 or 93% at pH = 12 or oil removal by either organic solvent (e.g. hexane) or supercritical CO_2 extraction [5].

Recently, fermentation of wheat germ by lactic acid bacteria (e.g. sourdough fermentation) was proposed as a mean for wheat germ stabilization through enzyme inactivation as consequence of acidification [5].

In order to preserve the majority of oil triacylglycerols in their intact state, Megahed discovered that exposure to heat treatment of 70 °C for 30 min. reduced the lipase activity [36].

Wheat polyphenols classification

Natural polyphenols, a class of compounds with a widespread phenolic hydroxyl structure in nature, are mostly found in plants, including wheat. They mostly consist of flavonoids, phenolic acid, tannin, and other compounds, and have potent antioxidative properties that eliminate the free radicals produced by the body, hence reducing cardiocerebral syndrome and postponing aging. In addition to their potent antioxidative capabilities, polyphenols also possess anticancer, bacteriostatic, liver-protecting, anti-infection, cholesterol-lowering, immunity-enhancing effects and prevent numerous biological diseases,

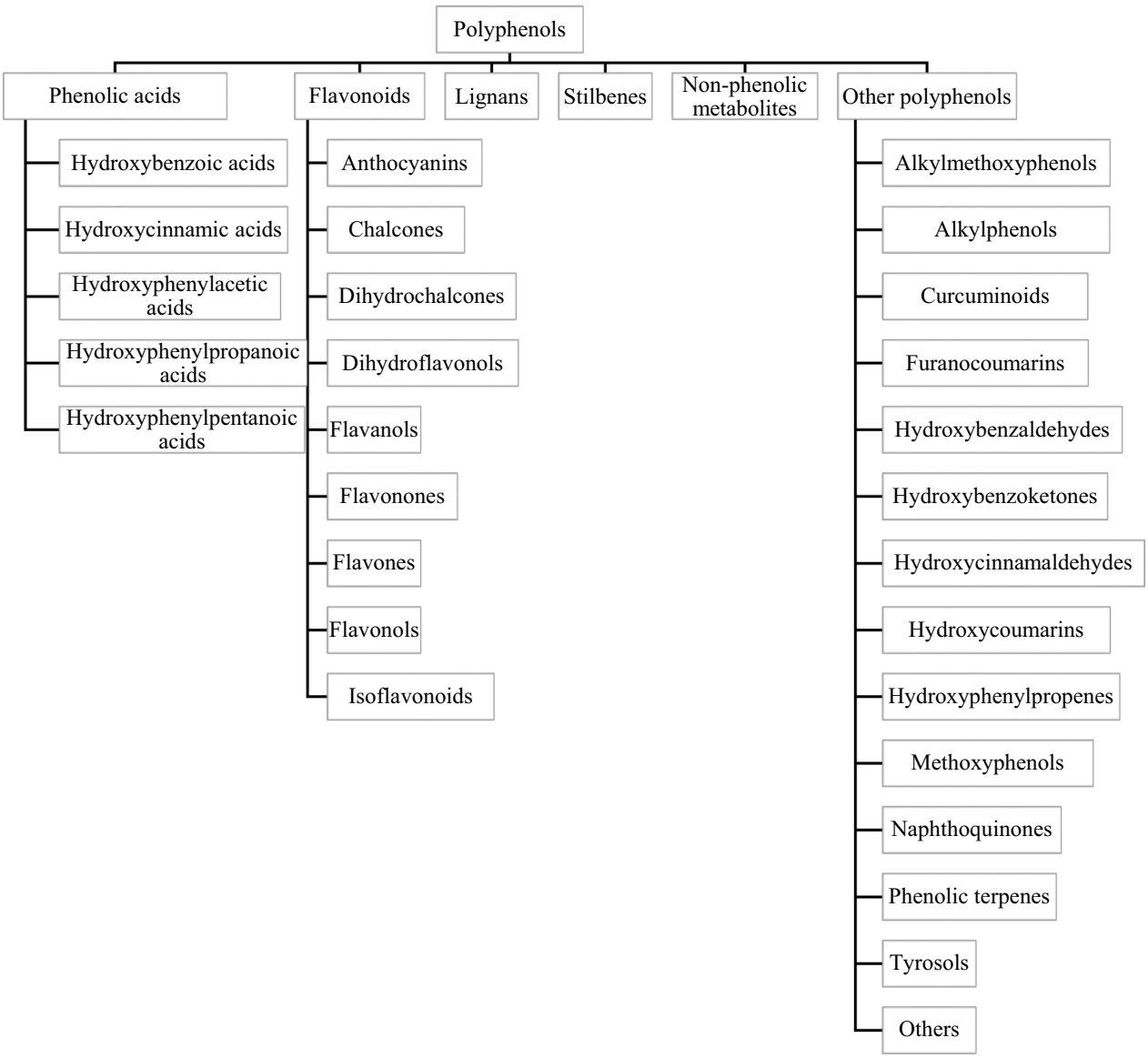


Fig. 1 Schematic diagram shows polyphenols classification

including type 2 diabetes. Cereals contain polyphenols in free, soluble, and insoluble binding forms [52]. The classification of wheat polyphenols is shown in Fig. 1.

Chemical composition of different wheat stages

The phytochemical composition of different wheat parts and stages with the major identified compounds is shown in Table 1.

Pharmacological activities and health benefits

Various pharmacological activities of different parts of wheat are shown in Table 2. Among these activities are anti-diabetic, anti-inflammatory, anti-cancer, anti-microbial, laxative and anti-aging effects.

Omics studies on wheat

Different analytical methods were used for profiling and fingerprinting of wheat including q-Tof LC–MS, GC–MS and UV-spectrophotometry. GC–MS/MS was used to do a comparative metabolomic investigation of the wheat embryo and endosperm during seed germination [21]. 82 different metabolites were identified in the embryo and endosperm overall. Different dynamic changes in metabolites between the embryo and endosperm during seed germination were revealed by principal component analysis (PCA), metabolite-metabolite correlation, and hierarchical cluster analysis (HCA). It was concluded that the embryo comprised mainly proteins and lipid metabolism, while the endosperm stores starches during seed germination [21].

In an untargeted liquid chromatography-mass spectrometry-based metabolomics analysis of wheat grain conducted by Abbiss et al., whole seeds grown in China were first ground using a laboratory blender and then the powder-like ground material was used for further extraction using an extraction solution that consisted of acetonitrile with 2-aminoanthracene, miconazole, $^{13}C_6$-sorbitol and d_6-transcinnamic acid as internal standards. Mixing was performed using a homogenizer and the mixture was centrifuged for 5 min at 4 °C and the supernatant was collected. About 500 biologically significant features per ion polarity were obtained using a combined approach that used four acquisition modes (reversed phase, lipid-amenable reversed phase, positive and negative ionization), with roughly half of these significantly different in intensity between wheat varieties. Significant variations in metabolite content in the grains of various wheat varieties indicate different biochemistry, which may be related to disease resistance and stress tolerance and other phenotypic features that are crucial for grain yield and quality [1]. The contents and spatial distribution of metabolites in the grains of six representative bread wheat varieties farmed in China were investigated in a study by Zhu et al. using triple TOF LC–MS/MS. The whole grains were ground into fine powders and were mixed with 70% methanol containing acyclovir and roxithromycin as internal standards. This was followed by vortexing and sonication at 22 °C for 20 min and centrifugation at 4 °C for 10 min, and the supernatant was used for further analysis. 1202 metabolites were discovered using LC–MS/MS, and their profiles, spatial patterns, and differences among the six wheat cultivars were analyzed. Furthermore, changes in nutritional and bioactive metabolite profiles were discovered among the six cultivars, with wheat bran being identified as a significant source of health-beneficial chemicals [66]. In a targeted proteomics study, the most abundant gluten was extracted from wheat, rye and barely grains flours step wise three times each with salt solution for 10 min at 22 °C then centrifuged and the supernatant containing albumins and globulins was discarded. The sediments were extracted with ethanol/water 3 times for 10 min at 22 °C to obtain the prolamin fractions. For the glutelins, the resulting sediments were extracted three times each with 2-propanol/water/0.1 mol/L Tris–HCl, pH 7.5, containing 2 mol/l (w/v) urea and 0.06 mol/L (w/v) Dithiothreitol (DTT) for 30 min at 60 °C under nitrogen. These gluten proteins were enzymatically cleaved into peptides and were collected by centrifugation and were lyophilized to be resuspended later in 1% FA for LC–MS/MS analysis [32]. A study by Khakimov et al. presented a GC–MS metabolomic profiling of phenolics and organic acids in grains, the feasibility of which was proved by comparing the metabolite profiles of the main northern European cereal crops: wheat, barley, oat, and rye. All major cereal phenolics, both free and conjugated, were extracted using 85% methanol and vortexed for 20 s followed by incubation at 30 °C and centrifugation for 3 min. The combined extracts were hydrolyzed using hydrochloric acid at 96 °C for 1 h with stirring and the hydrolyzed extracts were extracted with diethyl ether. The obtained ether fractions were dried under nitrogen gas flow ad used for GC–MS analysis. After that, each sample was spiked with the internal standard (ribitol) and the derivatization was with trimethylsilyl cyanide (TMSCN) with incubation for 40 min at 40 °C. The derivatization and injection were fully automated by the GC–MS system [26]. A study was conducted to improve the method for GC–MS determination of major sterols in Turkish bread wheat grain. The extraction method of lipid in this study depended on alkaline hydrolysis. The ground wheat was then saponified using ethanol and potassium hydroxide for 2 h at 80 °C. Then the non-saponifiable fraction (the total plant sterols) in the combined solution were extracted two times: firstly, with diethyl ether and secondly with n-hexane. The organic phase (hexane and diethyl ether)

Table 1 Phytochemical composition of different wheat parts and stages

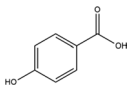
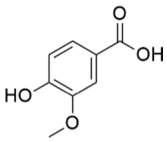
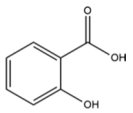
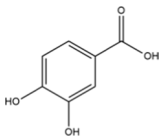
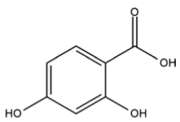
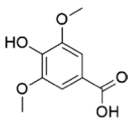
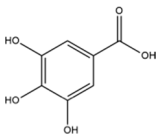
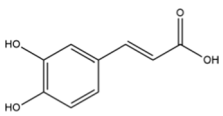
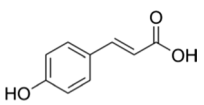
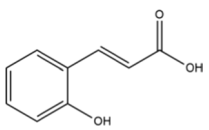
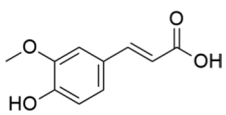
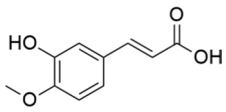
Chemical Class	Subclass	Compound	Structure	Wheat part	Amount (represented as mean)	References
Phenolic acid	Hydroxybenzoic acid	*p*-Hydroxybenzoic acid		Grain	0.8 µg/g	[33, 48]
		Vanillic acid		Grain, wheatgrass	36 µg/g, 42.6 µg/g	[27, 33]
		Salicylic acid		Wheatgrass	Nd	[62]
	Dihydroxybenzoic acid	Protocatechuic acid (PCA)		Grain	Nd	[33]
		2,4-Dihydroxybenzoic acid		Grain	Nd	[33]
	Trihydroxybenzoic acid	Syringic acid		Grain, leaf	18.5 µg/g, 48.5 µg/g	[27, 33]
		Gallic acid		Grain, leaf	41.4 µg/g, 135 µg/g	[27, 43, 48]
	Hydroxycinnamic acid	Caffeic acid		Grain	0.4 µg/g	[33, 49]
		p-Coumaric acid		Grain, leaf	85 µg/g, 0.1024 mg/g	[27, 33]
		2-Hydroxycinnamic acid		Grain	Nd	[33]
		Ferulic acid		Grain, wheatgrass	1.711 mg/g	[33]
		Isoferulic acid		Grain, wheatgrass	Nd	[63]

Table 1 (continued)

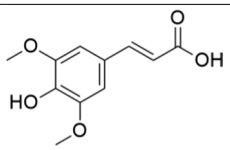
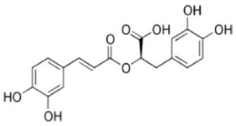
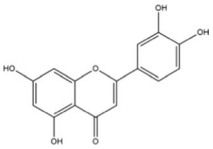
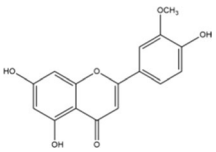
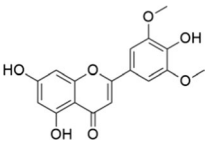
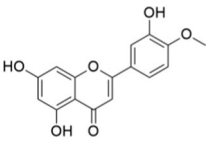
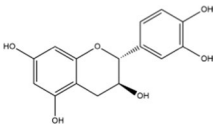
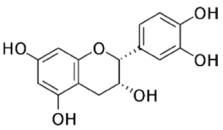
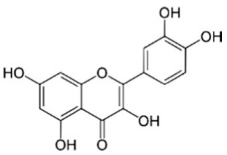
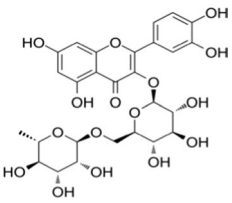
Chemical Class	Subclass	Compound	Structure	Wheat part	Amount (represented as mean)	References
		Sinapic acid		Grain, leaf	0.1 µg/g	[33, 49]
	Hydroxycinnamic acid, caffeic acid ester	Rosmarinic acid		Grain	Nd	[18]
Flavonoid	Flavone, tetrahydroxyflavone	Luteolin		Leaf	66.1 µg/g	[27]
	Methoxy-flavonoids	Chrysoeriol		Leaf	Nd	[55]
	O-Methoxyflavone	Tricin		Leaf, bran	253 µg/g, 33 µg/g	[38, 55]
	Methoxyflavone	Diosmetin		Grain	Nd	[18]
	Flavan-3-ol	(+)-Catechin		Grain	Nd	[46]
		Epicatechin		Grain	Nd	[18]
	Flavonol	Quercetin		Wheatgrass	Nd	[18]
		Quercetin 3-O-rutinoside (Rutin)		Wheatgrass	73.6 µg/g	[18, 27]

Table 1 (continued)

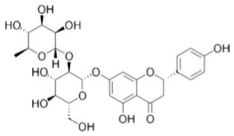
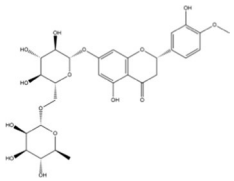
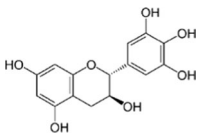
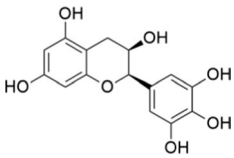
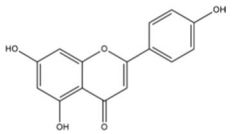
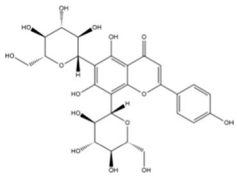
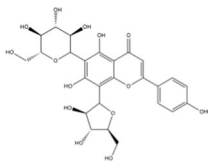
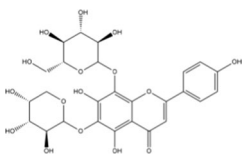
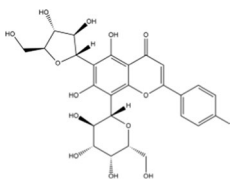
Chemical Class	Subclass	Compound	Structure	Wheat part	Amount (represented as mean)	References
	Flavanone	Naringin		Grain	nd	[18]
	Flavanone glycoside	Hesperidin		Grain	Nd	[18]
	Proanthocyanidin, flavan-3-ol	Gallocatechin		Grain	Nd	[67]
		Epigallocatechin		Grain	nd	[67]
	Flavone, trihydroxyflavone	Apigenin		Leaf	175.7 µg/g	[27]
	Flavone glycoside	Apigenin-6,8-di-C-glucoside (Vicenin-2)		Grain	Nd	[31]
	Flavonoid 8-c-glycosides	Apigenin-6C- glucoside-8C-arabinoside		Grain	468.2 µg/g	[49, 55]
		Apigenin-6C-arabinoside-8C-glucoside		Grain	304.7 µg/g	[49, 55]
		Apigenin-6C-arabinoside-8C-galactoside		Grain	Nd	[55]

Table 1 (continued)

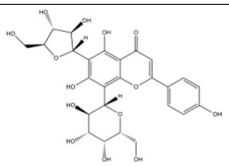
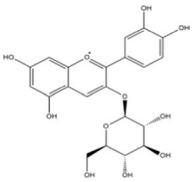
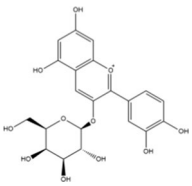
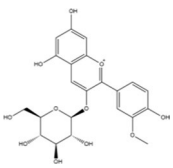
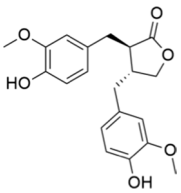
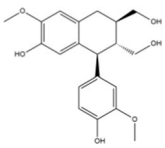
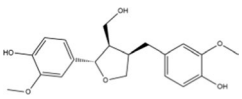
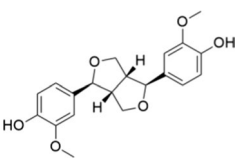
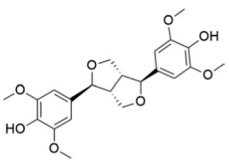
Chemical Class	Subclass	Compound	Structure	Wheat part	Amount (represented as mean)	References
		Apigenin-6C-galactoside-8C-arabinoside		Grain	0.13 mg/g	[49, 55]
	Anthocyanidin glycosides	Cyanidin-3-glucoside		Grain	Nd	[55]
	Anthocyanidin-3-o-glycosides	Cyanidin-3-galactoside		Grain	Nd	[55]
		Peonidin-3-glucoside		Grain	Nd	[55]
Lignan	Phenylpropanoid	Matairesinol		Bran, germ	0.09 µg/g	[49, 55]
		Isolariciresinol		Bran	Nd	[55]
	Tetrahydrofuran	Lariciresinol		Bran	0.6 µg/g	[49, 55]
		Pinoresinol		Bran	0.09 µg/g	[49, 55]
	Furanoid	Syringaresinol		Grain	3.7 µg/g	[49, 55]

Table 1 (continued)

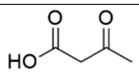
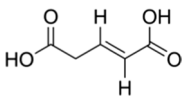
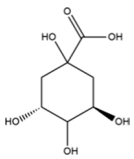
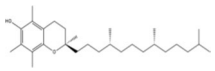
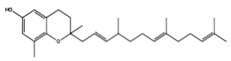
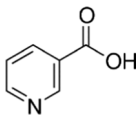
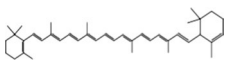
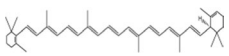
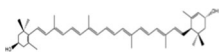
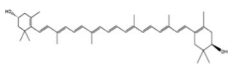
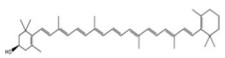
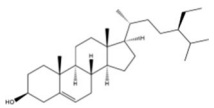
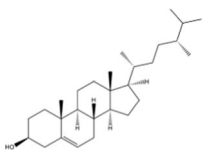
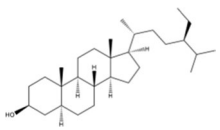
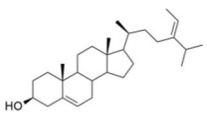
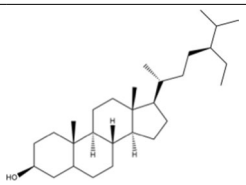
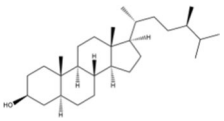
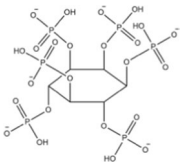
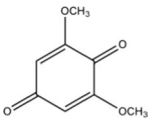
Chemical Class	Subclass	Compound	Structure	Wheat part	Amount (represented as mean)	References
Other polyphenol	Organic acid, monocarboxylic acid	Acetoacetic acid		Wheatgrass	Nd	[62]
	Organic acid, dicarboxylic acid	Glutaconic acid		Wheatgrass	Nd	[62]
	Cyclohexane carboxylic acid	Quinic acid		Wheatgrass	Nd	[62]
Vitamins	Vitamin E	Tocopherol		Grain, bran	3.91 µg/g	[39, 68]
	Vitamin E	Tocotrienol		Grain, bran	Nd	[39]
	Vitamin B3	Nicotinic acid		Wheatgrass	72.81 µg/g	[62, 68]
Carotenoid		β-Carotene		Bran, grain	0.211 µg/g	[34, 39]
		α-Carotene		Bran	Nd	[39]
		Lutein		Bran, grain	0.417 µg/g	[34, 39]
	Isomer of lutein	Zeaxanthine		Bran	0.067 µg/g	[34, 39]
		β-Cryptoxanthin		Bran	0.07 µg/g	[39, 53]
Phytosterol		β-Sitosterol		Wheat germ, bran	492.61 µg/g	[14, 55]
		Campesterol		Wheat germ, bran	45.66 µg/g	[14, 55]
		Stigmasterol		Wheat germ, bran	13.75 µg/g	[14, 55]
		Δ5-Avenasterol		Wheat germ, bran	161 µg/g	[47, 55]

Table 1 (continued)

Chemical Class	Subclass	Compound	Structure	Wheat part	Amount (represented as mean)	References
Phytostanol		Sitostanol		Wheat germ	69 µg/g	[47, 55]
		Campestanol		Wheat germ	127 µg/g	[47, 55]
Miscellaneous	Phosphorous source	Phytic acid		Wheat flour	8 mg/g	[15, 24]
Benzoquinone compound		DMBQ		Wheat germ	Nd	[28]

was combined, washed three times with 5% sodium chloride solution then washed with Milli-Q water until the washing water remained colorless upon addition of phenolphthalein, and organic phase was dried with sodium sulfate. The organic phase was evaporated to dryness using a rotary evaporator at 45 ℃. The concentrated extract was topped to 10 mL with chloroform and filtered through a 0.48 µm syringe filter. The optimum derivatization conditions was concluded to be 60 ℃ for 60 min using 50 µL of BSTFA with 1% TMCS [14]. Another study by Xing et al. aimed to determine the differences in the metabolite profiles of tender leaves of wheat, barley, rye and Triticale based on LC–MS. 50 mg of the tissue sample was soaked in methanol followed by the addition of L-2-chlorophenylalanine as the internal standard and the mixture was crushed then centrifuged for 15 min at 4 ℃. The supernatant was collected for further analysis [62]. All LC-based extraction methods reported were simple involving mixing with a hydroalcohol except for the proteomics-based study as it involved enzymatic cleavage of proteins which required an organic solvent (Tris–HCl). On the other hand, Khakimov et al. used hydrochloric acid for the hydrolysis of the extract at a high temperature for a long time, posing a possible hazard.

In metabolomics-based studies using GC and LC techniques, run times can vary according to the used conditions. A study by Xing et al. analyzed the metabolomic profiles of wheat, barley, rye, and triticale seedlings with a run time of 17 min to result in finding 1800 features in positive mode and 4303 features in negative mode. 109 metabolites in positive mode and 124 metabolites in negative mode between these species were identified using the VIP and t-test values in the orthogonal projection to latent structure with discriminant analysis (OPLS-DA) model, with 69 of them being detected simultaneously in both modes [62]. Another study conducted by Zhu et al. with a run time of 25 min discovered 1202 metabolites using widely targeted LC–MS/MS, and their profiles, spatial patterns, and differences among the six wheat kinds [66]. Lexhaller et al. conducted a study to characterize and relatively quantitate wheat, rye, and barley gluten protein types by triple-TOF LC–MS/MS. The run time of the method was 88 min, where the relative quantitation of the most abundant gluten proteins was carried out using multiple reaction monitoring liquid chromatography-tandem mass spectrometry. These investigations also made it possible to identify peptides that were active towards celiac disease and known wheat allergens [32]. Determination of main plant sterols in Turkish bread wheat was done by Erdem et al. using GC–MS/MS with a run time of 22 min [14]. Another study by Khakimov et al. using GC–MS/MS with a run time of 25.5 min led to the semi-quantitative detection of a

Table 2 Pharmacological activities of different wheat parts

Wheat part	Pharmacological activity	Mechanism	References
Bran	Antidiabetic	- Alkylresorcinols, a component of bran, was concluded to probably have a hypoglycemic effect in diet-induced obesity and glucose intolerant male mice	[17, 56]
		- Treatment of high fat diet-treated mice with 5% bran or tocotrienols substantially reduced body weight gain	
	Anti-inflammatory	- Ferulic acid, a major phenolic compound found in wheat, has been found to suppress the inflammatory cytokine macrophage inflammatory protein-2 (MIP-2)	[59]
		- Wheat bran-rich diets were also found to decrease oxidative stress and inflammation in Zucker rats	
	Anticancer	- It was found to protect against colon cancer in both early and late stages of tumorigenesis in numerous animal studies	[24]
		- Its component, Phytic acid, can increase cell apoptosis and differentiation and affect colon morphometry	
	Antimicrobial	- A study investigated six types of wheat for their biological activity	[13]
		- It was concluded that antibacterial activity was exhibited by some types of wheat bran extracts against *Escherichia coli*, *Pseudomonas aeruginosa*, *Bacillus subtilis*, and *Staphylococcus aureus*	
		- Also, several extracts demonstrated antifungal activity against *Candida albicans* and *Aspergillus niger*	
	Laxative effect	- Crude bran fiber stimulated peristalsis more than the lesser amount of whole bran fiber residue, resulting in more defecations and feces than whole bran	[60]
Germ	Antidiabetic	- Due to the high level of polyunsaturated acids and vitamin E, wheat germ oil (WGO), it has been shown to aid in oxidative stress reduction	[3]
		- Policosanol, one of its components, aided in the reduction of high blood sugar and total cholesterol levels	
	Anticancer	- The effects of lectin present in wheat germ revealed a dose–response relationship, with the largest effects resulting from the highest concentrations at the longest culture period	[29, 51]
		- Avemar, a nontoxic wheat germ extract, which was approved by Hungary as a special nutrient for cancer patients, was found to inhibit glucose metabolism and affects the expression of several kinases, resulting in potent anticancer activity in cell lines	
		- Avemar was also effective in in vivo experimental models by improving immune system activity, such as stimulating natural killer (NK) cell activity (by lowering major histocompatibility complex class 1 (MHC I) molecule expression), enhancing macrophage tumor necrosis factor (TNF) production, and increasing CD54 molecule expression on vascular endothelial cells	
		- As a result of all of these factors, the tumor cells undergo apoptosis	
	Antimicrobial	- Wheat germ extract includes 2,6-dimethoxy-1,4-benzoquinone (DMBQ), which is extremely inhibitory to *Staphylococcus aureus* and *Bacillus cereus*	[28]
	Antiaging	- After treatment with fermented wheat germ (FWG), the amount of total cholesterol, triglycerides, and glucose in the serum of aged mice was lower	[64]
		- FWG consumption increased antioxidant activity and enhanced the levels of antioxidant enzymes including superoxide dismutase, glutathione peroxidase, and total antioxidant capacity while lowering malondialdehyde levels (a marker of oxidative stress) in several organs like the liver, brain, intestine, and serum	
Whole wheat grain	Antidiabetic	- It lowers the risk of diabetes and cardiovascular disease	[11, 65]
		- Wheat antioxidants and insoluble fiber are considered to be the major contributors to these positive benefits	
		- Another study proved that α-glucosidase inhibition increased with increasing germination time for wheat methanolic extracts containing starch	
	Anti-inflammatory	- The inclusion of whole wheat grain in diets was recommended due to its reduction of markers associated with inflammation	[25]
	Anticancer	- Arabinoxylan, a component of whole wheat grain, significantly inhibited the growth of mouse transplantable tumors in S180 tumor-bearing mice, while significantly promoting thymus and spleen indexes, spleenocyte proliferation, NK cells and macrophage phagocytosis activity, interleukin 2 production, and delayed-type hypersensitivity reaction	[6]
		- Arabinoxylan also enhanced peripheral leukocyte count and bone marrow cellularity	

Table 2 (continued)

Wheat part	Pharmacological activity	Mechanism	References
Wheatgrass	Antidiabetic	- Giving diabetic rats wheatgrass reduced their HbA1C levels and raised their Hb levels, demonstrating its potential for preventing diabetes complications	[37]
		- Increased glycolysis (increased liver hexokinase activity) might also possibly explain the reduction in blood glucose level in wheatgrass-treated rats	
		- In addition, the activities of hepatic glucose-6-phosphatase in diabetic rats were considerably enhanced	
	Anti-inflammatory	- Its anti-inflammatory was equivalent to diclofenac sodium in chronic inflammation	[41]
		- On the other hand, it showed no anti-inflammatory effect in acute models	
Bioprocessed bread	Anti-inflammatory	- The consumption of bioprocessed bread with improved phenolic compound bioavailability caused a significant reduction in pro-inflammatory cytokines in humans	[30]
Other	Antimicrobial	- A study compared the antimicrobial activity against *Escherichia coli*, *Salmonella typhimurium*, and *Staphylococcus aureus* of selected wheat varieties including winter wheat. The highest inhibitory activity was demonstrated by winter wheat against all strains tested, with S. aureus being the most sensitive strain with an MIC of 0.50 mg/mL	[9]

total of 247 analytes in wheat, barley, oat and rye using GC–MS, out of which 89 were identified based on RI and EI-MS library match [26]. Identified wheat metabolites are shown in Additional file 1.

The use of mobile phases can greatly affect the results of a LC-based study by affecting the retention times of the analytes in a sample. Zhu et al. used 0.1% formic acid in water (buffer A) and acetonitrile (buffer B) [66], while Lexhaller et al. used 5% DMSO, 0.1% FA, 94.9% water as buffer A and 5% DMSO, 0.1% FA, 90% acetonitrile, 4.9% water as buffer B to separate enzymatically cleaved gluten peptides [32].

Zhu et al. used the open access software Metaboanalyst for dimensionality reduction analysis of principal component analysis (PCA), sparse partial least squares discriminant analysis (sPLS-DA), and orthogonal partial least squares discriminant analysis (oPLS-DA) [66]. For protein identification in another study conducted by Lexhaller et al., the SCIEX.wiff raw files were directly used as input in the ProteinPilot 5.0 software (SCIEX) with the Paragon algorithm. The raw data were searched against a database comprising UniProtKB-Poaceae proteins appended with cRAP [32]. In the study by Khakimov et al., the raw GC–MS data was imported from netCDF format to.mat files into Matlab® ver. R2012b (8.0.0.783). The PARAFAC2 algorithm then resolved mass spectrum of each peak and compared against NIST05 library (NIST, USA) and Golm Metabolome Database [26]. Among these softwares, only Metaboanalyst was an open access software and NISTand Golm libraries were freely available. On the other hand, ProteinPilot 5.0 and Matlab were not open access softwares and this was considered as a major limitation is these studies.

Both LC-based studies conducted by Zhu et al. and Lexhaller et al. used C18 column. However, Zhu et al. used Accucore C18 (150 × 2.1 mm) for the separation of the identified compounds, mainly flavonoids, including sugars, polyphenols, phenolamides, lipids, and vitamins, while Lexhaller et al. used Trap column ChromXP C18 (3 µm, 12 nm, 10 × 0.3 mm) and column ChromXP C18 (3 µm, 12 nm, 150 mm × 0.3 mm) for the analysis of the gluten types peptides [32, 66]. As for GC columns, a 60 m capillary column with a moderately polar stationary phase (5% diphenyl and 95% dimethyl polysilox) was used in a study for analysis of plant sterols [14]. In another study by Khakimov et al., Phenomenex ZB 5MSi column (30 m × 250 µm × 0.25 µm) was used for the comprehensive and comparative metabolomic profiling of wheat, barley, oat and rye [26].

All GC-based metabolomics studies have the advantage of using libraries such as NIST and Golm databases which allowed for the identification of a wide number of metabolites compared to LC-based metabolomics study. On the other hand, LC-based studies do not have as much libraries for metabolite identification and are less accurate than GC databases due to the contribution of mobile phase chromatographic conditions, therefore changing the retention times according to these conditions thus eliminating one of the tools of accurate identification. Also, in GC, the Kovat's index using an alkane standard allows metabolite identification by specifying the number of carbon atoms in the compound. On the other hand, nonvolatile, polar, or thermally labile drugs cannot be directly analyzed by GC–MS techniques. Derivatization is required to increase the volatility and thermal stability of these compounds. Compared to the majority of LC-based techniques where samples can

be directly analyzed, this greatly extends the time required for sample analysis.

A study by Suchy et al. used an ultraviolet (UV) spectrophotometer to quantify monomeric-rich (single-chain, mostly gliadin), polymeric-rich (multichain, mostly low- and high-molecular weight glutenin), and total soluble protein (monomeric and polymeric protein) wheat proteins after being divided using an organic solvent. The method was found to be able to accommodate a large range of concentrations of protein fraction as a result of observing a strong linear relationship between the protein content in the fractions and the absorbance reading [50]. The use of UV spectrophotometric approach was convenient due to its simplicity, reliability and low-cost requirements.

Supplementary Information

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Additional file 1: Table S1. Identified metabolites using GC and LC-MS.

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Availability of data and materials
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Declarations

Competing interests
The authors have no competing interests to declare that are relevant to the content of this article.

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