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Variation of the ferulic acid concentration and kernel weight in CIMMYT bread wheat germplasm and selection of lines for functional food production

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ABSTRACT

Investigating the variation in ferulic acid concentration (FAC) is crucial for developing functional wheat products with potential health benefits. This study examined the variation in FAC of 267 advanced breeding lines from the International Bread Wheat Screening Nursery (IBWSN) across three different environments. The results revealed a wide range of FAC values, with measurements ranging from 590.47 to 943.81 μg/g in Gansu, 497.04–893.47 μg/g in Inner Mongolia, and 435.54–986.43 μg/g in Xinjiang. These FAC values were found to be comparable to those of present wheat varieties. Estimated broad-sense heritability of FAC was 0.68, indicating that genotypic factors play a major role in determining FAC. The correlation between FAC and thousand kernel weight (TKW) was found to be dependent on the specific environment. The study successfully identified 16 advanced breeding lines that exhibited consistently high FAC and TKW across multiple environments. These findings suggest the potential applicability of these lines in production of functional wheat products.

1. Introduction

Epidemiological evidences from recent years have robustly indicated that whole grain consumption can mitigate the risk of chronic diseases such as cardiovascular disease (CVDs), obesity, type II diabetes, and some types of cancer (O'Hearn et al., 2023; Tiozon et al., 2022; Wu et al., 2023). These health benefits have been largely ascribed to micronutrients, dietary fibers and phytochemicals present mainly in bran fractions (Okarter & Liu, 2010; Seal et al., 2021; Zhao et al., 2023). Ferulic acid is one of the most abundant phytochemical in wheat grains and its health-promoting effects have been widely recognized (Fernandez-Orozco et al., 2010; Tian et al., 2022). Due to consumers' strong desire to maintain good health condition through improved diet, high ferulic acid concentration (FAC) is becoming a desirable trait in wheat breeding and field production for development of functional wheat products (Sardella et al., 2023; Shewry et al., 2012). In recent years, a substantial amount of studies have investigated FAC variations of present wheat varieties and generally ascribed the variances to genetic and environmental factors (Fernandez-Orozco et al., 2010; Laddomada et al., 2021; Liu et al., 2022; Nigro et al., 2017; Tian & Li, 2018). However, most previous studies focused solely on FAC but have not investigated the relation between high FAC and yield component traits such as thousand kernel weight (TKW). Practically, FAC enrichment should not impact yield negatively, cultivation and the following food processing of high FAC wheat lines will not be sustained unless these lines have favorable agronomic traits (Martin & Li, 2017). Thus, it is imperative to understand relation between FAC and yield potential and further identify wheat lines with consistently high FAC and yield potential across multiple environments for production of functional wheat products.

In developing countries, 70% of wheat varieties are derived from germplasm developed by the International Maize and Wheat Improvement Centre (CIMMYT), i.e., directly released as a variety or serving as a parent in breeding programs. CIMMYT germplasm have also been

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widely used for wheat quality improvement in China and Australia (Lantican et al., 2016). The International Bread Wheat Screening Nursery (IBWSN) was initiated by CIMMYT in 1967 and each year it is distributed 200–400 advanced breeding lines to about 200 locations worldwide (Juliana et al., 2017). Before distribution, these wheat lines have been tested for wide adaptation, good disease resistance, high yield potential and good processing quality in multiple trials in Mexico and cooperating locations globally. The main goals of this study are to 1) investigate the phenotypic variation of FAC in CIMMYT's IBWSN advanced breeding lines 2) explore the relationship between FAC and TKW and 3) further identify wheat lines with both enhanced FAC and TKW for production of high FAC wheat products. Our findings have the potential to guide breeding strategies for phytochemical enrichment and provide valuable information for farmers and food producers interested in wheat-based functional foods.

2. Materials and methods

2.1. Plant materials

In this study, a total of 267 advanced breeding lines of CIMMYT's 53rd IBWSN were planted in three locations of Chinese spring wheat production area in 2021: Tianshui, Gansu Province (Gansu); Bayannur, Inner Mongolia Autonomous Region (Inner Mongolia); and Changji, Xinjiang Uygur Autonomous Region (Xinjiang). They were grown in randomized complete blocks in each environment with two replications. Each plot was a 1.0 m long row with an inter-row spacing of 20.0 cm. Field managements followed local practices. After harvest, wheat grains from the two plots were combined and their TKW were determined using a Wanshen SC-A Seed Detector (Wanshen Detection Technology, Hangzhou, China). Finally the wheat grains were milled into whole meal flour using a CT 293 Cyclotec™ laboratory mill (FOSS, Hillerød, Denmark) and stored at −20 °C until analysis.

2.2. Reagents and chemicals

Analytical standard of ferulic acid was purchased from MACKLIN (Shanghai, China). Other general chemicals and ultra-performance liquid chromatography (UPLC) mobile phases (water with 0.1% formic acid and acetonitrile with 0.1% formic acid) were purchased from Thermo Fisher Scientific (Waltham, MA, USA). CORTECS Phenyl Column (90 Å, 1.6 μm, 2.1 mm × 50 mm) was purchased from Waters Corporation (Milford, MA, USA).

2.3. Extraction of total ferulic acid in whole meal flour

Extraction of total ferulic acid was performed according to a previous report (Lu et al., 2014) with some modifications in our lab (Tian et al., 2021). In brief, 1 g of whole wheat flour was extracted with 10 mL of 2 M NaOH solution under dark condition for 3 h. The mixture was then acidified with 6 M HCl to pH = 1–2 and extracted three times with ethyl acetate. The combined organic phase was evaporated to dryness with a rotary evaporator and then re-dissolved with 3 mL HPLC grade methanol. The supernatant was filtered through 0.22 μm polytetrafluoroethylene (PTFE) filter, stored at −20 °C and analyzed within 3 days.

2.4. Separation and quantification ferulic acid

The quantification of ferulic acid was performed with a Waters ACQUITY UPLC-PDA system (Waters Corporation, Milford, MA, USA) equipped with an ACQUITY UPLC BEH C18 column (2.1 mm × 50 mm) according to our previous report (Tian et al., 2021). The mobile phase A was water with 0.1% formic acid and mobile phase B was acetonitrile with 0.1% formic acid. The flow rate was kept at 0.4 mL/min and the percentage of mobile phase B was kept at 6% from 0 to 1.0 min, which then increased linearly to 14% from 1.0 min to 3.0 min and increased linearly to 18% from 3.0 min to 4.0 min. The column was re-equilibrated for 2.0 min between each injection. The PDA detector was set to record the absorption at 280 nm. Ferulic acid was quantified using the external calibration curve and expressed as μg ferulic acid per gram of whole meal flour.

2.5. Statistical analysis

In this study, FAC determination for each sample was conducted with two replicates and additional replicate was performed if the first two replicates showed a standard deviation higher than 10%. Data analysis and visualization was conducted using Python version 3.8 (Beaverton, OR, USA).

2.6. Estimation of broad-sense heritability of FAC

Analysis of variance (ANOVA) was conducted using the PROC MIXED method in SAS V9.3 (SAS Institute Inc., Cary, NC, USA). Broad sense heritability (H_b^2) for FAC was calculated from the ANOVA, using the formula $H_b^2 = \sigma_g^2/(\sigma_g^2 + \sigma_{ge}^2/r + \sigma_\varepsilon^2/re)$, where σ_g^2, σ_{ge}^2 and σ_ε^2 were estimates of genotypic, genotype (line) × environment interaction and residual error variances, respectively, and e and r were the number of environments and replicates, respectively.

3. Results and discussions

3.1. Phenotypic variation of FAC in IBWSN wheat lines

Generally, there are three major methods for extraction, classification, and quantification of ferulic acid. Method A classified ferulic acid as soluble-free, soluble-conjugated, insoluble-bound (Moore et al., 2005; Okarter et al., 2010); Method B classified ferulic acid as free, ester-linked to mono- and/or oligosaccharides, ester-linked to soluble polysaccharides, and ester-linked to insoluble polysaccharides (Vaidyanathan & Bunzel, 2012); Method C determines total ferulic acids through one-step extraction (Lu et al., 2014). Since the majority of ferulic acid exists in insoluble forms, method C is becoming more frequently used for genetic resource studies due to its simplified protocol. In this study, distribution pattern of FAC and TKW are presented in Fig. 1 and tabulated in Table S1 (supplementary material). Generally, FAC values followed a relative normal distribution suggesting that FAC was a complex trait with many contributing factors. In Gansu, the FAC ranged from 590.47 to 943.81 μg/g (1.60-fold) with an average of 747.96 μg/g; In Inner Mongolia, FAC ranged from 497.04 to 893.47 μg/g (1.80-fold), averaging at 711.27 μg/g. Xinjiang exhibited the broadest range, from 435.54 to 986.43 μg/g (2.26-fold), with a mean concentration of 789.89 μg/g. Sample from Xinjiang had both the highest maximum and average FAC but the difference between three environments were not large in magnitude.

Previous studies have compared nutraceutical qualities of "ancient varieties" and present wheat varieties (De Santis et al., 2018; Huertas-García et al., 2023; Montevecchi et al., 2019; Shewry et al., 2023). It is also necessary to compare phytochemical profiles of present varieties and advanced breeding lines (future varieties). In this study, FAC of CIMMYT spring wheat breeding lines ranged from 497.04 to 986.43 μg/g with an average of 749.71 μg/g across three environments. Using exactly same protocol, we found that FAC of 155 present Chinese winter wheat varieties ranged from 480.72 to 991.64 μg/g with an average of 755.07 μg/g (Table S2 in supplementary material). Under similar protocols, Liu et al. (2022) found that FAC of 136 Chinese bread wheat varieties ranged from 360 to 800 μg/g. Though reported FAC value was to some extent depend on extraction protocol (Tian et al., 2022), the magnitude of range and distribution pattern of these values were generally comparable. Taken together, current evidence suggests that breeding practices have not decreased FAC of advanced wheat breeding lines. Future breeding programs could aim to increase FAC at no expense

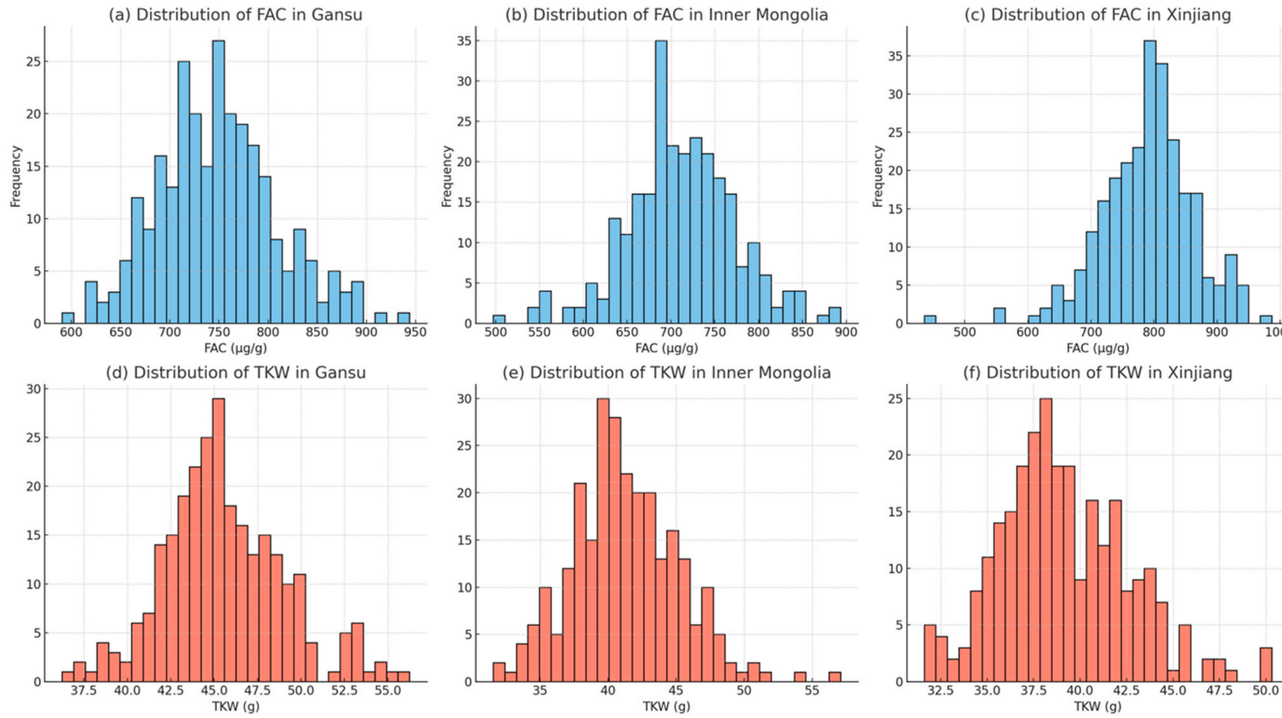

Fig. 1. Distribution of ferulic acid concentration (FAC) and thousand kernel weight (TKW) in Gansu, Inner Mongolia and Xinjiang.

of yield potential and processing quality.

3.2. Broad-sense heritability of FAC

Heritability is the proportion of variation in a particular trait that is attributable to genetic factors (Visscher et al., 2008). Heritability is of particular use in understanding traits that are very complex with many influencing factors. In this study, the broad-sense heritability of FAC and TKW were estimated to be 0.68 and 0.85, respectively, based on the ANOVA results (Table S3 and Table S4 in supplementary material). This value indicated significant effects of genotype on FAC values. The early study based on 26 wheat genotypes under six environments reported a low heritability (0.28) for ferulic acid, but authors still identified some wheat varieties with relative high and stable FAC (Fernandez-Orozco et al., 2010; Shewry et al., 2012). A previous study investigating 111 tetraploid wheat genotypes under two environments reported a broad-sense heritability of FAC as 0.70 (Laddomada et al., 2017). A following study characterizing FAC of six elite durum wheat varieties under drought and heat stress reported a FAC heritability of 0.69, suggesting that wheat FAC is relative constant across different environmental conditions (Laddomada et al., 2021). Overall, these results suggested that FAC is a trait with considerable heritability though the effects of environmental factors cannot be ignored. It is important to identify wheat verities or advanced breeding lines with high FAC and high yield potential.

3.3. Correlation between FAC and TKW

TKW, kernel number per spike (KNS) and spike number (SN) are three yield components in determination of yield performance. In this study, we focused on TKW because 1) the effect of TKW is usually most significant and because 2) TKW can be determined accurately while KNS and SN are hard to determine accurately for a small experimental plot size (Liu et al., 2023). The correlation between FAC and TKW is plotted in Fig. 2. In Gansu, a positive yet unsignificant ($P > 0.05$) correlation was found between FAC and TKW. The correlation was significantly negative in Inner Mongolia ($R = -0.30$, $P < 0.001$) and Xinjiang ($R = -0.18$, $P < 0.01$), but the strength of the inverse relationship was not strong. In an early study including 175 diversified wheat varieties, the correlation between FAC and TKW was reported to be −0.025 which was not significant (Li et al., 2008). In another 2-year study on FAC of 111 tetraploid wheat genotypes, the authors reported the correlation coefficient to be 0.01 (not significant, $P > 0.05$) and −0.19 (not significant, $P > 0.05$) for year of 2012 and 2013, respectively (Laddomada et al., 2017). Taken together, the correlation between FAC and TKW was weak and dependent on environment, not suggesting a strong relationship between FAC and TKW.

3.4. Identification of superior genotypes with high FAC and TKW

Besides the general correlation analysis, it is more important for wheat breeders and producers to identify varieties or advanced breeding lines with both high FAC and TKW and to understand its underlying mechanism. From the scatter plot (Fig. 2), it is apparent that some wheat lines retained both high FAC and TKW. In this study, we used top 25% as threshold and selected wheat varieties whose FAC and TKW are both among top 25% for at least 2 environments and the average. 16 out of 267 wheat lines met this criterion (Table 1), suggesting a good chance of selecting and producing high-FAC wheat without reduction of TKW. Further, according to bread-making experiments that were performed in Mexico before germplasm distributions, 10 out of these 16 wheat lines also had overall good bread-making quality (Table S5 in supplementary material). Line 8248391 (pedigree: ATTILA/3*BCN*2//BAV92/3/KIRITATI/WBLL1/4/DANPHE/5/KACHU/DANPHE) and line 8239764 (pedigree: BAJ #1/3/2*HUW234+LR34/PRINIA//PFAU/WEAVER/4/MUTUS/AKURI #1//MUTUS) exhibited FAC and TKW values that were among top 25% in all three environments. Line 8236134 (pedigree: KFA/2*KACHU*2//MUTUS*2/CHONTE) demonstrated remarkable TKW performance (>50 g in all environments, ranked 5th, 3rd and 1st, respectively) and fairly high FAC in Inner Mongolia (795.03 μg/g, ranked 21st) and Xinjiang (916.43 μg/g, ranked 13th). In addition, this wheat line also had high loaf volume and very good crumb structure according to the quality test performed in Mexico before distribution of these breeding lines (Table S5 in supplementary material). Overall, our

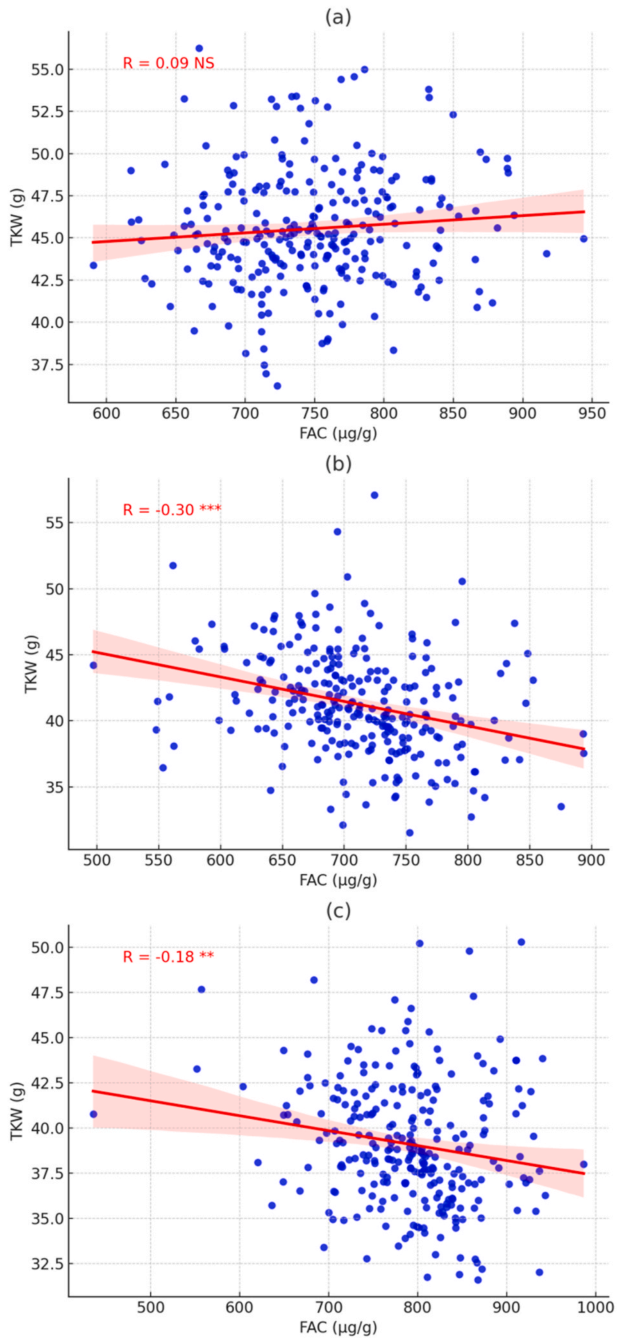

Fig. 2. Correlation plot of ferulic acid concentration (FAC) and thousand kernel weight (TKW) in (a) Gansu, (b) Inner Mongolia, and (c) Xinjiang. *, **, and *** denotes significane level at $P < 0.05$, $P < 0.01$ and $P < 0.001$, respectively.

results indicated it is a practical goal to produce new varieties with enhanced FAC and high TKW for production of functional wheat products.

4. Conclusions

FAC of CIMMYT advanced breeding lines ranged from 497.04 to 986.43 μg/g with an average of 749.71 μg/g across three environments. Broad-sense heritability of FAC is 0.68 suggesting that genotype is a major factor influencing wheat FAC. 16 out of 267 wheat lines retained high FAC and TKW, suggesting the possibility to develop new wheat varieties with improved nutraceutical value for functional wheat products. Further studies are necessary to thoroughly study the relationship between concentration of ferulic acid and other major phytochemicals as well as dietary fibers. The molecular mechanism of achieving high phytochemicals concentration and high TKW needs to be further investigated. Meanwhile, it is crucial to acknowledge the limitations of this study, as it was conducted across three locations for only one harvest year, and the *in vitro* antioxidant activities were not determined. Furthermore, it's important to recognize that other factors, besides TKW, exert influence on wheat grain yields. Therefore, for selected wheat lines with high FAC and TKW, a comprehensive study should be conducted under various geographic locations across multiple harvest years to further investigate their phytochemical profiles, antioxidant activities and grain yield performances. This holistic approach will serve as a robust foundation for the development of superior wheat varieties tailored for functional food applications.

Table 1
List of CIMMYT's 53rd IBWSN advanced breeding lines with high ferulic acid concentration (FAC) and thousand kernel weight (TKW).

Sample GID	Gansu FAC (μg/g)	Inner Mongolia FAC (μg/g)	Xinjiang FAC (μg/g)	Average FAC (μg/g)	Average TKW (g)
8247203	893.48	789.81	927.08	870.12	44.80
8236134	778.28	795.03	916.43	829.91	51.44
8236642	889.34	707.63	842.53	813.17	44.08
8245094	734.96	770.48	910.85	805.43	44.19
8241002	759.27	852.57	857.79	823.21	48.73
8242371	796.84	698.94	913.35	803.04	44.08
8235681	783.58	765.55	803.08	784.07	44.65
8236681	849.64	709.35	797.84	785.61	46.71
8239176	853.42	754.67	878.67	828.92	44.60
8236760	830.26	690.12	885.20	801.86	45.35
8240418	806.03	665.69	873.13	781.62	45.47
8237586	742.69	766.53	910.39	806.53	46.00
8244280	831.93	837.60	683.38	784.30	48.73
8248391	832.55	847.97	940.21	873.57	46.81
8238810	749.68	716.33	892.21	786.08	47.15
8239764	785.93	831.08	862.52	826.51	48.67

CRediT authorship contribution statement

Wenfei Tian: Writing – review & editing, Writing – original draft, Visualization, Methodology, Formal analysis, Data curation, Conceptualization. **Xue Gong:** Writing – review & editing, Formal analysis. **Maria Itria Ibba:** Writing – review & editing, Resources. **Velu Govindan:** Writing – review & editing, Resources. **Shuanghe Cao:** Writing – review & editing. **Jindong Liu:** Writing – review & editing, Writing – original draft, Methodology, Formal analysis, Conceptualization. **Zhonghu He:** Writing – review & editing, Project administration, Methodology, Funding acquisition, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Raw data is attached in the supplementary material

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.lwt.2024.115829.

References

De Santis, M. A., Kosik, O., Passmore, D., Flagella, Z., Shewry, P. R., & Lovegrove, A. (2018). Comparison of the dietary fibre composition of old and modern durum wheat (*Triticum turgidum* spp. *Durum*) genotypes. *Food Chemistry, 244*, 304–310. https://doi.org/10.1016/j.foodchem.2017.09.143

Fernandez-Orozco, R., Li, L., Harflett, C., Shewry, P. R., & Ward, J. L. (2010). Effects of environment and genotype on phenolic acids in wheat in the HEALTHGRAIN diversity screen. *Journal of Agricultural and Food Chemistry, 58*(17), 9341–9352. https://doi.org/10.1021/jf102017s

Huertas-García, A. B., Tabbita, F., Alvarez, J. B., Sillero, J. C., Ibba, M. I., Rakszegi, M., & Guzmán, C. (2023). Genetic variability for grain components related to nutritional quality in spelt and common wheat. *Journal of Agricultural and Food Chemistry, 71*(28), 10598–10606. https://doi.org/10.1021/acs.jafc.3c02365

Juliana, P., Singh, R. P., Singh, P. K., Crossa, J., Huerta-Espino, J., Lan, C., Bhavani, S., Rutkoski, J. E., Poland, J. A., Bergstrom, G. C., & Sorrells, M. E. (2017). Genomic and pedigree-based prediction for leaf, stem, and stripe rust resistance in wheat. *Theoretical and Applied Genetics, 130*(7), 1415–1430. https://doi.org/10.1007/s00122-017-2897-1

Laddomada, B., Blanco, A., Mita, G., D'Amico, L., Singh, R. P., Ammar, K., Crossa, J., & Guzmán, C. (2021). Drought and heat stress impacts on phenolic acids accumulation in durum wheat cultivars. *Foods, 10*(9), 2142. https://doi.org/10.3390/foods10092142

Laddomada, B., Durante, M., Mangini, G., D'Amico, L., Lenucci, M. S., Simeone, R., Piarulli, L., Mita, G., & Blanco, A. (2017). Genetic variation for phenolic acids concentration and composition in a tetraploid wheat (*Triticum turgidum* L.) collection. *Genetic Resources and Crop Evolution, 64*(3), 587–597. https://doi.org/10.1007/s10722-016-0386-z

Lantican, M. A., Braun, H.-J., Payne, T., Singh, R., Sonder, K., Baum, M., van Ginkel, M., & Erenstein, O. (2016). *Impacts of international wheat improvement research. International Maize and Wheat Improvement Center (CIMMYT)*. https://repo.mel.cgiar.org/handle/20.500.11766/6023.

Li, L., Shewry, P. R., & Ward, J. L. (2008). Phenolic acids in wheat varieties in the HEALTHGRAIN diversity screen. *Journal of Agricultural and Food Chemistry, 56*(21), 9732–9739. https://doi.org/10.1021/jf801069s

Liu, S., Wang, C., Gou, J., Dong, Y., Tian, W., Fu, L., Xiao, Y., Luo, X., He, Z., Xia, X., & Cao, S. (2022). Genome-wide association study of ferulic acid content using 90K and 660K SNP chips in wheat. *Journal of Cereal Science, 106*, Article 103498. https://doi.org/10.1016/j.jcs.2022.103498

Liu, D., Zhao, D., Zeng, J., Shawai, R. S., Tong, J., Li, M., Li, F., Zhou, S., Hu, W., Xia, X., Tian, Y., Zhu, Q., Wang, C., Wang, D., He, Z., Liu, J., & Zhang, Y. (2023). Identification of genetic loci for grain yield-related traits in the wheat population Zhongmai 578/Jimai 22. *Journal of Integrative Agriculture, 22*(7), 1985–1999. https://doi.org/10.1016/j.jia.2022.12.002

Lu, Y., Luthria, D., Fuerst, E. P., Kiszonas, A. M., Yu, L., & Morris, C. F. (2014). Effect of processing on phenolic composition of dough and bread fractions made from refined and whole wheat flour of three wheat varieties. *Journal of Agricultural and Food Chemistry, 62*(43), 10431–10436. https://doi.org/10.1021/jf501941r

Martin, C., & Li, J. (2017). Medicine is not health care, food is health care: Plant metabolic engineering, diet and human health. *New Phytologist, 216*(3), 699–719. https://doi.org/10.1111/nph.14730

Montevecchi, G., Setti, L., Olmi, L., Buti, M., Laviano, L., Antonelli, A., & Sgarbi, E. (2019). Determination of free soluble phenolic compounds in grains of ancient wheat varieties (*Triticum* sp. Pl.) by liquid chromatography–tandem mass spectrometry. *Journal of Agricultural and Food Chemistry, 67*(1), 201–212. https://doi.org/10.1021/acs.jafc.8b05629

Moore, J., Hao, Z., Zhou, K., Luther, M., Costa, J., Yu, L., & Lucy). (2005). Carotenoid, tocopherol, phenolic acid, and antioxidant properties of Maryland-grown soft wheat. *Journal of Agricultural and Food Chemistry, 53*(17), 6649–6657. https://doi.org/10.1021/jf050481b

Nigro, D., Laddomada, B., Mita, G., Blanco, E., Colasuonno, P., Simeone, R., Gadaleta, A., Pasqualone, A., & Blanco, A. (2017). Genome-wide association mapping of phenolic acids in tetraploid wheats. *Journal of Cereal Science, 75*, 25–34. https://doi.org/10.1016/j.jcs.2017.01.022

O'Hearn, M., Lara-Castor, L., Cudhea, F., Miller, V., Reedy, J., Shi, P., Zhang, J., Wong, J. B., Economos, C. D., Micha, R., & Mozaffarian, D. (2023). Incident type 2 diabetes attributable to suboptimal diet in 184 countries. *Nature Medicine, 29*(4), 982–995. https://doi.org/10.1038/s41591-023-02278-8

Okarter, N., & Liu, R. H. (2010). Health benefits of whole grain phytochemicals. *Critical Reviews in Food Science and Nutrition, 50*(3), 193–208. https://doi.org/10.1080/10408390802248734

Okarter, N., Liu, C.-S., Sorrells, M. E., & Liu, R. H. (2010). Phytochemical content and antioxidant activity of six diverse varieties of whole wheat. *Food Chemistry, 119*(1), 249–257. https://doi.org/10.1016/j.foodchem.2009.06.021

Sardella, C., Burešová, B., Kotíková, Z., Martinek, P., Meloni, R., Paznocht, L., Vanara, F., & Blandino, M. (2023). Influence of agronomic practices on the antioxidant compounds of pigmented wheat (*Triticum aestivum spp. Aestivum L.*) and Tritordeum (× *Tritordeum martinii A. Pujadas, nothosp. Nov.*) genotypes. *Journal of Agricultural and Food Chemistry, 71*(36), 13220–13233. https://doi.org/10.1021/acs.jafc.3c02592

Seal, C. J., Courtin, C. M., Venema, K., & de Vries, J. (2021). Health benefits of whole grain: Effects on dietary carbohydrate quality, the gut microbiome, and consequences of processing. *Comprehensive Reviews in Food Science and Food Safety, 20*(3), 2742–2768. https://doi.org/10.1111/1541-4337.12728

Shewry, P. R., Brouns, F., Dunn, J., Hood, J., Burridge, A. J., America, A. H. P., Gilissen, L., Proos-Huijsmans, Z. A. M., van Straaten, J. P., Jonkers, D., Lazzeri, P. A., Ward, J. L., & Lovegrove, A. (2023). Comparative compositions of grain of tritordeum, durum wheat and bread wheat grown in multi-environment trials. *Food Chemistry, 423*, Article 136312. https://doi.org/10.1016/j.foodchem.2023.136312

Shewry, P. R., Charmet, G., Branlard, G., Lafiandra, D., Gergely, S., Salgó, A., Saulnier, L., Bedő, Z., Mills, E. N. C., & Ward, J. L. (2012). Developing new types of wheat with enhanced health benefits. *Trends in Food Science & Technology, 25*(2), 70–77. https://doi.org/10.1016/j.tifs.2012.01.003

Tian, W., & Li, Y. (2018). Phenolic acid composition and antioxidant activity of hard red winter wheat varieties. *Journal of Food Biochemistry, 42*(6), Article e12682. https://doi.org/10.1111/jfbc.12682

Tian, W., Wilson, T. L., Chen, G., Guttieri, M. J., Nelson, N. O., Fritz, A., Smith, G., & Li, Y. (2021). Effects of environment, nitrogen, and sulfur on total phenolic content and phenolic acid composition of winter wheat grain. *Cereal Chemistry, 98*(4), 903–911. https://doi.org/10.1002/cche.10432

Tian, W., Zheng, Y., Wang, W., Wang, D., Tilley, M., Zhang, G., He, Z., & Li, Y. (2022). A comprehensive review of wheat phytochemicals: From farm to fork and beyond. *Comprehensive Reviews in Food Science and Food Safety, 21*(3), 2274–2308. https://doi.org/10.1111/1541-4337.12960

Tiozon, R. J. N., Sartagoda, K. J. D., Serrano, L. M. N., Fernie, A. R., & Sreenivasulu, N. (2022). Metabolomics based inferences to unravel phenolic compound diversity in cereals and its implications for human gut health. *Trends in Food Science & Technology, 127*, 14–25. https://doi.org/10.1016/j.tifs.2022.06.011

Vaidyanathan, S., & Bunzel, M. (2012). Development and application of a methodology to determine free ferulic acid and ferulic acid ester-linked to different types of carbohydrates in cereal products. *Cereal Chemistry, 89*(5), 247–254. https://doi.org/10.1094/CCHEM-02-12-0013-R

Visscher, P. M., Hill, W. G., & Wray, N. R. (2008). Heritability in the genomics era—concepts and misconceptions. *Nature Reviews Genetics, 9*(4), 255–266. https://doi.org/10.1038/nrg2322

Wu, J., Alhamoud, Y., Lv, S., Feng, F., & Wang, J. (2023). Beneficial properties and mechanisms of natural phytochemicals to combat and prevent hyperuricemia and gout. *Trends in Food Science & Technology, 138*, 355–369. https://doi.org/10.1016/j.tifs.2023.06.021

Zhao, C., Tong, J., Gao, Z., Liu, J., Hao, Y., Xia, X., He, Z., Zhang, Y., & Tian, W. (2023). Genome-wide association study of alkylresorcinols content in 161 wheat cultivars. *Journal of Cereal Science, 111*, Article 103679. https://doi.org/10.1016/j.jcs.2023.103679