



Review

The impact of processing on the release and antioxidant capacity of ferulic acid from wheat: A systematic review

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ARTICLE INFO

Keywords:

Bioaccessibility
Bioavailability
Phenolic acid
Bioprocessing
Thermal processing
Milling

ABSTRACT

The antioxidant capacity and bioaccessibility of ferulic acid (FA)¹ in wheat are highly limited by the lack of free ferulic acid (FFA).² However, many studies claim that wheat processing can efficiently increase FFA content and ultimately influence the overall antioxidant capacity. Hence, this systematic review investigated changes in FFA content, antioxidant capacity and bioaccessibility of wheat after different processing treatments. A literature search of two databases (PubMed and Web of Science) was undertaken covering the last 20 years, yielding 1148 articles. Studies which employed bioprocessing, thermal processing and milling of wheat were considered. After exclusion criteria were applied, 36 articles were included. These covered single processing methods (n = 25, bioprocessing: n = 9, thermal processing: n = 9, milling n = 7) and combined processing methods (n = 11, bioprocessing & thermal processing = 7, bioprocessing, thermal processing & milling = 2, thermal processing & milling = 2). The total ferulic acid (TFA)³ content, degree of covalent bond hydrolysis and the percentage of FFA degraded or transformed to other compounds dominated the final changes in FFA content, antioxidant capacity and bioaccessibility. This systematic review is the first to comprehensively summarize the best efficient processing method for releasing FA and increasing antioxidant capacity and or bioaccessibility in wheat. The combination of particle size reduction, pre-hydrolysis thermal processing (except at high temperature and extended duration) and enzymatic hydrolysis (ferulic acid esterase (FAE)⁴ or fermentation) has the highest potential of releasing FA. However, the literature on the bioaccessibility of FA in wheat is limited and more work is required to demonstrate the link between the release of FA by processing and the consequent health benefits.

1. Introduction

Ferulic acid (4-hydroxy-3-methoxycinnamic acid, FA, Fig. 1) has generated interest around the world because of its antioxidant capacity, which has been linked to anti-inflammatory, anti-aging, anticancer, antidiabetic, antihypertensive and neuroprotective effects (Bami et al., 2017; Hassanzadeh et al., 2017; Kikugawa et al., 2016; Wang et al., 2017). Ferulic acid occurs in many plants including vegetables, coffee, nuts, and cereals (Boz, 2015; de Oliveira Silva & Batista, 2017; Srinivasan et al., 2007). The phenolics in cereal grains are mainly divided into two types: hydroxybenzoic acid derivatives and hydroxycinnamic acid derivatives (Karamac et al., 2002; Masisi et al., 2016; Mattila et al.,

2005). The most abundant hydroxycinnamic acid in cereal is FA (Coghe et al., 2004; Gani et al., 2012; Kandil et al., 2012). In Europe, wheat is the most staple cereal compared with other cereals. Therefore, FA in wheat has been studied widely over the last 50 years.

Ferulic acid is important due to its antioxidant activity, which means FA and its derivatives can potentially protect DNA and lipids from oxidation through reactive oxygen species (Dragan et al., 2018). The antioxidant capacity of FA has led to its therapeutic applications in oxidative stress-related diseases such as Alzheimer's disease, diabetes, cancer, hypertension, and atherosclerosis etc (Kumar & Pruthi, 2014). There have been a number of studies on the beneficial effects of FA. For example, Mori et al. studied the anticancer properties of FA by feeding

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¹ FA: ferulic acid.

² FFA: free ferulic acid.

³ TFA: total ferulic acid.

⁴ FAE: Ferulic acid esterase.

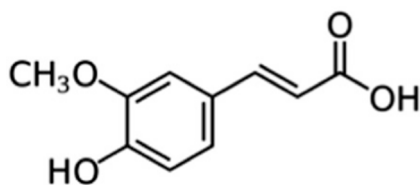


Fig. 1. Chemical structure of FA.

FA to rats at a dose of 0.5 g/kg/day, after exposure to 4-nitroquinoline-1-oxide for 5 weeks in drinking water at a dose of 0.02 g/kg/day, and the results demonstrated that FA had chemo preventive activity on oral cancer (Mori et al., 1999). Sultana et al. investigated the neuroprotective effect of FA and claimed that FA not only modulated oxidative stress but also reduced the risk of neurodegenerative diseases such as Alzheimer's disease (Sultana et al., 2005). Furthermore, FA was shown to specifically act on blood vessels in spontaneously hypertensive rats which led to a relaxation response in vascular endothelial cells mediated by Nitric Oxide (Srinivasan et al., 2007). Ferulic acid has also been used in the food industry and in environmental protection. For example, FA was added in baking as a cross-linking agent to increase shelf-life, while the condensation reaction between FA and tyramine was used to test environmental stress in plants (Kumar & Pruthi, 2014). However, in nature, FA is commonly covalently bound to other chemicals, and is seldom found in a free form. To obtain higher amounts of FFA and increase its bioavailability, many processing methods have been applied by the food industry, especially in the production of wheat-based foods.

For the purpose of this systematic review, which aims to examine the effect of processing on the release of FFA, a variety of methods were considered (bioprocessing, milling and thermal processing). Bioprocessing is a method to release FA using enzymes or the activity of cells, which mainly consists of enzymatic treatment and fermentation (Coda et al., 2015). For example, xylanase hydrolyses the β -1, 4 bonds in the main chain of arabinoxylan, generating soluble xylo-oligosaccharides. Fermentation, studied by Zhang et al, was highly associated with the type of microbial species. Among the microorganisms (*Bacillus* species, yeasts, and filamentous fungi) used, *Bacillus* species negatively impacted FFA release, while yeasts demonstrated an opposite effect, 3 out of 5 filamentous fungi strains increased FFA, one fungi strain decreased FFA while the other strain did not show a significant difference compared to untreated wheat bran (Zhang et al., 2014). Thermal processing is any form of heating in wheat processing, and includes baking, roasting, microwaving, boiling, and steaming and their effects varies (Duodu, 2011). For instance, it has been suggested that autoclaving can help the release of phenolic compounds (Randhir et al., 2008). However, a decrease of FFA has also been detected after thermal processing (Fares & Menga, 2012). Milling is a method that can not only lead to improved extraction from flour but also improve digestibility and sensory attributes (Duodu, 2011). Milling comprises of two stages, the first stage is debranning, where the outer layers of wheat grains are removed, and the second stage involves reduction of particle size. The impact of different methods of milling on FA release will be examined in this review.

As mentioned above, in wheat bran, FA is mainly covalently bound to arabinoxylans (>99 %) and is not released during digestion, thus leading to the low bioaccessibility of FA in wheat (El-Seedi et al., 2012; Zhao & Moghadasian, 2008). However, the bioavailability of FFA is high because of its low molecular weight (194.18 g/mol) and high absorption into plasma (74 %) (King et al., 1999; Zhao et al., 2004). The definition of bioavailability is the final ratio of a bioactive that reaches circulation and this in turn is determined by bioaccessibility (Anson, van den Berg, et al., 2009; Galanakis, 2017). Bioaccessibility is the amount of a compound released from the food matrix during digestion in a form that can be absorbed. Therefore, bioavailability and bioaccessibility of FA are increased with the release of FA (which can be impacted by processing

methods above). The aim of this review is to examine the impact of different processing methods on FA release from wheat to determine the best way of increasing FFA content and thus increasing its bioavailability and bioaccessibility.

2. Methods

A systematic search was conducted using the databases, Web of Science (1900–2020) and PubMed (1966–2020) in March 2021 using the search terms: (Cereal OR Rice OR Wheat OR Barley OR Maize OR Sorghum OR Bran) AND Ferulic acid AND (Process* OR Thermal* OR Heat* OR Cook* OR Mill* OR Irradiate* OR Malt* OR Ferment* OR Bioprocess*) AND (Bioactivity OR Bioavailability OR Antioxidant* OR Mechanism OR Metabolism OR Digest*).

Studies were only included if they considered FA, antioxidant capacity and/or bioaccessibility and processing concurrently. Studies containing these keywords but focused on the effect of FA on processing were excluded. Any research not related to changes in FA content induced by processing (e.g.: transformation of FA to its di-form or other compounds like vanillic acid) were excluded. Any studies which referred to malting, brewing, germination or sprouting were excluded because they contained irrelevant cereals. Any studies relevant to food additives such as coffee addition or bean addition were excluded. If the study did not report the FA content and antioxidant capacity and/or bioaccessibility before and after the processing, or the study detected FA but did not provide sufficient details, they were excluded. Studies referring to milling but showing no specific differences in parameters such as particle size or layers of wheat, were excluded. Finally, if the starting material did not contain wheat, the research was excluded because other cereals are not common staple foods in Europe.

The PRISMA flowchart (Fig. 2) shows that 1148 articles were identified based on the search criteria. After removal of duplicates, 983 articles were retrieved and subjected to title and abstract screening. This resulted in the exclusion of 677 articles: 95 articles were reviews; for 4 articles the full text was not available; one of the articles was not published in English; 419 articles had no relevance to FA, cereal and processing; 89 articles contain no human food-grade processing; 8 articles included food additives; 16 articles examined the effect of FA on processing; 1 study focused on the effect of FAE release; 44 articles referred to malting, brewing, germination or sprouting. For the full-text screening, 270 articles were excluded (9 were unobtainable; 104 articles had no relevance to wheat; 5 articles examined food supplements; 13 articles were not relevant to food-grade processing; 4 studies examined the effect of milling but failed to assess particle size or different fractions of cereal; 2 articles described processes in cereal growing; 96 articles failed to detect FA content at all or before and after processing; 30 articles did not determine antioxidant capacity and/or bioaccessibility; 2 articles examined FA's antioxidant capacity on fungi; 5 articles did not report antioxidant capacity and/or bioaccessibility or FA content in detail). Finally, 36 articles were included in the systematic review.

3. Results

The results are summarized in Tables 1-6, Tables 1-3 demonstrate the effect of single processes on FA content and antioxidant capacity and/or bioaccessibility in wheat, while Tables 4-6 show the effect of combined processing methods. Of the 36 studies included, 25 focused on the effect of a single processing method (bioprocessing: n = 9, thermal processing: n = 9, milling: n = 7). The remaining studies (n = 11) examined the effect of combined processing on FA content in wheat (bioprocessing and thermal processing = 7, bioprocessing, thermal processing, and milling = 2, thermal processing, and milling = 2).

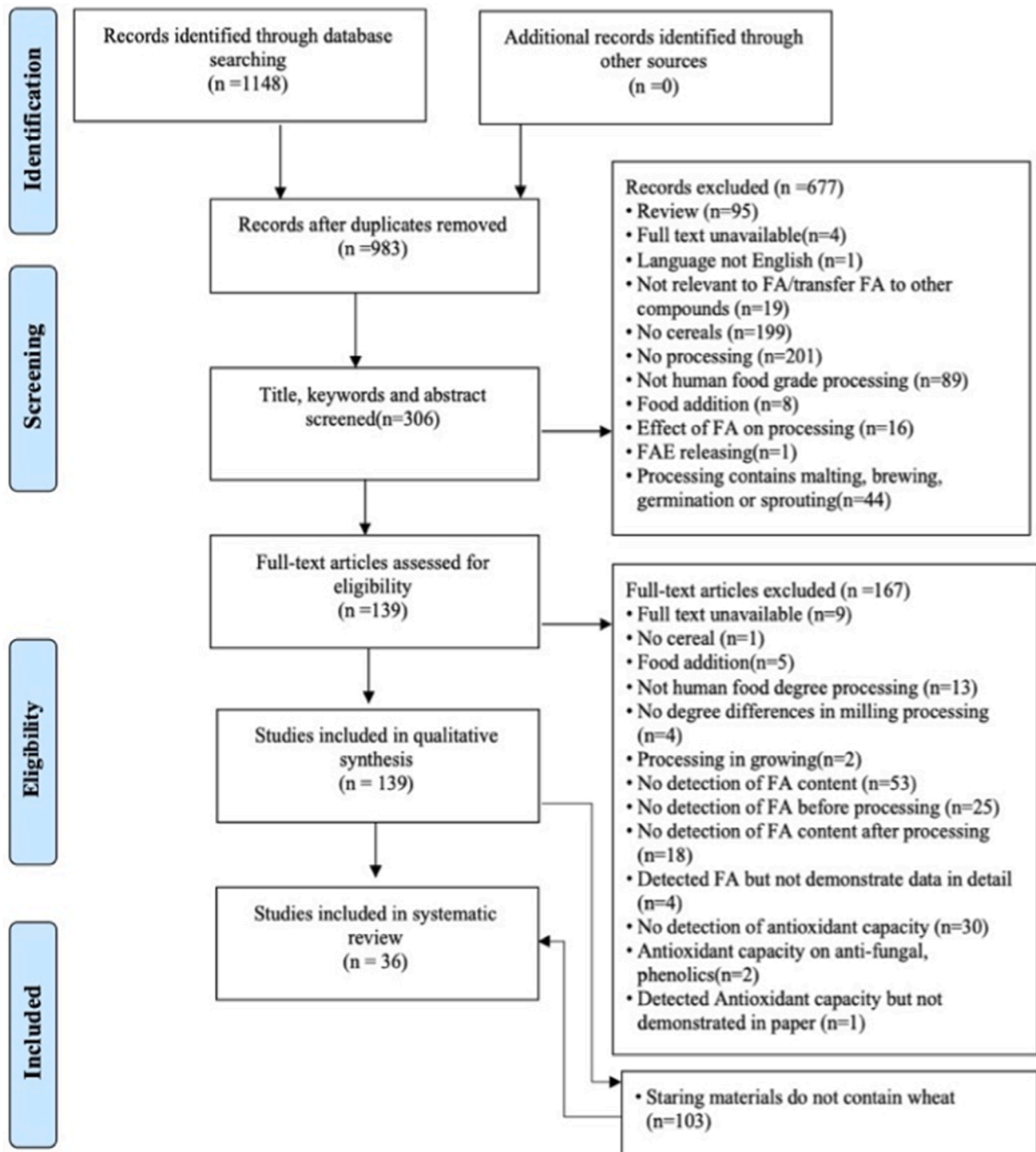


Fig. 2. PRISMA flowchart of the study selection procedure.

3.1. Effect of single processes on FA content and antioxidant capacities

3.1.1. Milling

Seven studies examined the effect of milling on FA content and its antioxidant capacity and/or bioaccessibility in wheat (Table 1). Three articles studied the effect of particle size, while the remainder focused on the effect of debranning or pearling. Of these three studies, two reported that reducing particle size positively impacted FFA content (Alzuwaid et al., 2020; Zaupa et al., 2014). Alzuwaid et al. indicated that when the particle size decreased from 800 to 425 μm , the TFA content detected increased significantly (Alzuwaid et al., 2020). Similar results were

found by Zaupa et al, who compared the FFA content in samples with different particle sizes and showed that reduction of particle size had a positive effect on FA (Zaupa et al., 2014). The highest amount of FFA in Table 1 (300 $\mu\text{g/g}$ from the inner part of the aleurone, particle size < 20 μm) was observed in this study (Zaupa et al., 2014). The remaining study which examined particle size demonstrated the opposite effect. Higher FFA content ($11.55 \pm 0.77 \mu\text{g/g}$) was detected in wheat with a larger particle size (thick bran) than in the smaller particle size sample (fine bran, $1.40 \pm 0.17 \mu\text{g/g}$) (Yilmaz et al., 2018). However, particle size and definition of “thick bran” or “fine bran” were not well described, which may in part account for some of the differences between these results

Table 1
Effect of milling on FA content and antioxidant capacities in wheat.

Ref	PD		DFAT	HFFAC (Treatment)	FAC in control	FARP	DA/BI	HAC/B (Treatment)	AC/B change	Results	Key Findings
(Alzuwaid et al., 2020)	Coarse bran	Roller milling	TFA	/	/	/	TEAC	570 mmol TEAC/kg (coarse bran 20 %, fine bran 20 %, 425 20 %, 180 20 %, < 180 20 %)	P > 0.001	AC has no significant changes Particle size: a. 800 to 425 µm: FA increased (highest FA: 800 µg/g (425 µm)) b. 425–250 µm: FA decreased significantly c. 250–180 µm: FA increased slightly d. under 180 µm: FA decreased significantly	When particle size reducing to 425 µm, TFA was highest. When particle size below 425 µm, TFA decreased. The impact of particle size on antioxidant capacity was not significant.
(Anson, van den Berg, et al., 2009)	Fine bran, 425, 315, 250, 180 and < 180 µm Flour, bran and aleurone fractions milling to particle size < 200 µm	Falling number milling coarse bran, screen to different particle sizes (Fine bran: 800 µm)	FFA, TFA	19 µg/g (bran)	/	/	Bioaccessibility	0.56 % (bran)	+0.56 %	- FFA (bran) > FFA (aleurone) > FFA (flour) - TFA (aleurone) > TFA (bran) > TFA (flour) - Bioaccessibility of FA has same trend with FFA	- Debranning decreased FFA and its bioaccessibility significantly - High TFA did not mean high FFA and bioaccessibility
(Chen et al., 2013)	Bran TADD samples Whole wheat samples (Control) Aleurone	Quadrumat senior mill, > 500 µm Dehull for 1, 3 and 5 min and three grain moisture levels, 15, 20 and 11 % (the original wheat moisture level) by using a TADD (Venables Tangential Abrasive Dehulling Device) moisture-time Wheat kernels grinding by coffee grinder at medium speed 3 times in 30 intervals Commercial sample from Cargill Co	FFA	15.0 ± 0.6 µg/g sample (TADD-11-1)	4.8 ± 0.2 µg/g sample DW	/	ORAC DPPH	478.7 ± 21.8 µmol TE/g of extract (TADD-11-1) 42.6 % inhibition (TADD-11-1)	+201 % +335 %	- Moisture: - 11–15 %: FFA decreased - 15–20 %: FFA increased - Abrasion time: - Before 3 mins, FFA increased - Aleurone contains the second highest AC and FAC - The highest contribution of FFA to ORAC and DPPH results. - DPPH decreased with the longer dehulling time - Under same dehulling time, a. moisture:11 % to 15 %, FFAC decreased significantly, b. moisture:15 % to 20 %, FFAC has no significant differences. - Dehulling time 1–3 min	- Moisture: a. Under15%, negatively impacted FFA b. Over 15 %, positively impacted FFA - Longer abrasion time decreased AC

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Table 1 (continued)

Ref	PD		DFAT	HFFAC (Treatment)	FAC in control	FARP	DA/BI	HAC/B (Treatment)	AC/B change	Results	Key Findings
(Liyana-Pathirana et al., 2006)	Milling	Sequential removal of bran layers from wheat kernels by abrasion, pearled from 10 to 50 % in 10 % increments, to get the pearled wheat and corresponding by products (particle size is 1000 µm)	FFA, CFA	4.98 ± 001 µg/g of crude extract (10 % by product, CWAD)	0.43 ± 0.01	15 %	ORAC	207 ± 4 µmol/g of defatted material (CWRS 10 % by product)	218 %	a. 15 % moisture, FFAC: no significant difference b. 20 % moisture, FFAC decrease significantly - AC of wheat decreased by peeling significantly - FAC in 30 % pearled grains was significantly lower than 10 % and whole grain. - FAC in flour is the lowest in all samples	- Pearling negatively impacted FAC
(Pasha et al., 2014)	Defat	Blend sample with hexane (1:5, /v 5 min, 3 times)									
	Milled through Brabender Quadrumat Senior Mill to get: Break flour, reduction flour, bran, and shorts		CFA	/	/	/	TAC	58.3 % (Shafaq-06)	/	- FAC in bran was highest (Break flour (3rd), reduction flour (4th), and shorts flour (2nd)) - The AC of milled samples did not detect	- Debranning decreased FAC. - AC was not impacted by debranning degree
(Yilmaz et al., 2018)	Milling	Milled on an experimental mill for separation into fine bran, thick bran, and flour fraction	FFA, TFA	11.5 ± 0.77 µg/g (Sarıçanak-98, thick bran)	/	1 %	TEAC	6.38 ± 0.11 µmol Teq/g (Sarıçanak-98, thick bran)	/	- The highest FA and AC were found in thick bran - The lowest AC was found in flour	- FFA in sample with larger particle size was higher - The AC mainly existed in outer bran
	Bread making	5.0 % pressed yeast, 1.5 % salt, 1.0 % sugar, 1.0 % fat and water + white wheat flour, fermentation at 32 °C and 80 % RH, 1 h. Baking at 250°C, 25 min.									- Reducing particle size of samples negatively impacted AC.
(Zaupa et al., 2014)	Milling	1. 3 subsequent steps of debranning: tradition milling by roller millers; 2. air separation: "IN" sample (particle size < 100 µm); "OUT" sample (particle size 300–425 µm.); 3. IN and OUT samples fractions were subsequently ultra-micronized by jet milling to get IN-M particle sizes < 20 µm) and the OUT-M (particle sizes < 100 µm) fractions,	FFA, TFA	300 µg/g	50 µg/g	36 %	FRAP	12 mMol Fe2+ / 100 g dry weigh	33 %	- FFA in Ultra-micronized sample (IN-M, OUT-M) was significantly higher than normal branning (IN, OUT) - FFA and TFA in IN and IN-M samples were significantly higher than OUT and OUT-M. - Reduced particle size a. IN: decreased TAC b. OUT: increased TAC	- Reducing particle size helped FFA releasing.
	Control	Standard wheat fraction, particle size 100–600 µm, produced by roller miller									

1 Ref: references.

2 PD: processing design.

3 DFAT: detected ferulic acid type.

4 HFFAC: highest free ferulic acid content.

5 FAC in control: ferulic acid content in control sample.

6 FARP: ferulic acid releasing percentage.

7 DA/BI: detected antioxidant capacity/bioaccessibility index.

8 HAC/B: highest antioxidant capacity/ bioaccessibility.

9 AC/B change: antioxidant capacity /bioaccessibility change.

10 TEAC: TEAC: Trolox equivalent antioxidant capacity.

and those of the other two studies. Alzuwaid et al. and Zaupa et al. found that the antioxidant capacity of wheat was not affected by particle size, while Yilmaz et al. showed that reducing particle size had a negative effect on antioxidant capacity (Alzuwaid et al., 2020; Yilmaz et al., 2018; Zaupa et al., 2014). The other 4 articles describing the effect of debranning/ pearling on FFA content and antioxidant capacity, all showed that FA is concentrated in the outer layers of wheat and that the removal of the outer layers of the bran decreased the TFA/ FFA content and antioxidant capacity in wheat (Anson, van den Berg, et al., 2009; Chen et al., 2013; Liyana-Pathirana et al., 2006a; Pasha et al., 2014).

To summarise, on the one hand, reducing particle size beneficially improved the release of FFA, especially when the initial particle size was bigger than 20 μm (Zaupa et al., 2014). When the particle size was smaller than 20 μm , the effect of reducing particle size was limited, which may be because mechanical treatment cannot break the chemical bonds between FA and the backbone polysaccharide (Rosa et al., 2013). However, only one article examined the impact of particle size under 20 μm , and so only limited conclusions about the effect of reducing particle size under 20 μm on FFA were drawn (Zaupa et al., 2014). On the other hand, debranning negatively impacted FFA, which decreased FA content dramatically. For the effect of milling on antioxidant capacity, debranning/ pearling had an obvious negative effect, while the effect of particle size reduction cannot be summarised due to limited number of studies.

3.1.2. Thermal processing

The positive effect of thermal processing on FA release was reported in 7 studies (Table 2). The FFA content after treatment by roasting, baking or steam explosion were similar, showing a steady increase or an increase followed by a significant decrease in FFA. For example, Lu et al. showed that 10 % of FA ($11.5 \pm 1.49 \mu\text{g/g}$) was released after baking (Lu et al., 2015). Puffing (360–390 °C, 4 min) significantly increased FFA content (Hidalgo et al., 2016). Similar results were observed by Liu et al., who showed that after treatment at 215 °C for 120 s the FFA content increased from 55.7 ± 3.8 to $586.3 \pm 37.2 \mu\text{g/g}$ (+916 %), which is the highest FFA increase observed in Table 2 (Liu et al., 2016). Furthermore, Olivos et al. demonstrated a slight increase in FFA after 25–45 min baking at 205°C but a significant decrease occurred when baking time was extended to 45 min (Santa Cruz Olivos et al., 2021). Zou et al. also observed a peak in FFA content after roasting for 10 mins followed by a dramatic decrease (Zou et al., 2015). Other thermal processing methods such as boiling followed by drying steadily decreased FFA content, probably because of the leaching of phenolics into the water (Podio et al., 2019; Yilmaz & Koca, 2017). However, there are only 3 studies using boiling in this review, and the results vary. Two of them showed a positive effect on FFA release while the other one demonstrated an opposite effect. The limited number of studies makes it difficult to draw a conclusion on the effect of water/solvent in FFA release. Therefore, at suitable temperatures and processing time, thermal processing can beneficially impact FA release in wheat.

Seven studies demonstrated a positive effect of thermal processing on antioxidant capacity (Călinoiu & Vodnar, 2020; Chen et al., 2016; Hidalgo et al., 2016; Liu et al., 2016; Lu et al., 2015; Podio et al., 2019; Santa Cruz Olivos et al., 2021). 2 studies showed a decrease in antioxidant capacity after thermal processing (Yilmaz & Koca, 2017; Zou et al., 2015) see Table 2. Six studies demonstrated that antioxidant capacity was positively related to FFA content (Călinoiu & Vodnar, 2020; Chen et al., 2016; Liu et al., 2016; Lu et al., 2015; Santa Cruz Olivos et al., 2021; Yilmaz & Koca, 2017). A further 3 studies showed different results: Hidalgo et al. demonstrated that both baking and puffing increased antioxidant capacity significantly (Hidalgo et al., 2016). However, baking had no effect on FFA releasing, while puffing increased FFA dramatically. Conversely, Podio et al. and Zou et al. showed a negative relationship between FFA content and antioxidant capacity (Podio et al., 2019; Zou et al., 2015).

- 11 DW: Dry weight.
- 12 ORAC: Oxygen radical absorbance capacity.
- 13 TADD: Venables Tangential Abrasive Dehulling Device.
- 14 DPPH: 2,2-diphenyl-1-picrylhydrazyl (antioxidant capacity detection method).
- 15 CFA: conjugated ferulic acid.
- 16 CWAD: Canada Western Amber Durum, *Triticum turgidum* L. var. durum.
- 17 CWRS: Canada Western Red Spring, *Triticum aestivum* L.
- 18 RH: relative humidity.
- 19 "IN" sample (the inner part of aleurone, particle size < 100 μm).
- 20 OUT" sample: (the outer part of aleurone, also containing a residue of tissue cells coming from the outer layer close to the aleurone,
- 21 IN-M: IN ultra-micronized.
- 22 OUT-M: OUT ultra-micronized.

Table 2
Effect of thermal processing on FA content and antioxidant capacities in wheat.

Ref.	PD		DFAT	HFFAC (Treatment)	FAC in control	FARP	DAC/BI	HA/B (Treatment)	AC/B change	Results	Key Findings
(Călinoiu & Vodnar, 2020)	Sample preparation	5:1v/w for bran with water and heat at 80 °C, 10 min	FFA	31.41 ± 0.33 µg/g DW	22.56 ± 0.13 µg/g DW	/	DPPH	48 % inhibition of the DPPH radical	26 %	- Significantly increase on FFA and AC was observed after 80°C boiling	- Boiling at 80°C positively impacted the FFA releasing and AC in wheat
(Chen et al., 2016)	Steam flash explosion	80 g sample treat at 2.5 MPa for 30 s, treated by saturated steam	FFA, CFA	97.7 ± 14.38 µg/g DW (2.5 Mpa, 30 s)	ND	4 %	DPPH ABTS	90 % (1.0 mg/ml) 55 % (1.0 mg/ml)	/ /	- Significantly increase on FFA and AC After treatment of 2.5 MPa, 30 s	- 2.5 MPa, 30 s, high temperature (accurate temperature did not show in study) has positive effect on FFA releasing and AC
(Hidalgo et al., 2016)	Biscuits making	Water biscuit: Four types of whole meal flour + water make to dough, rolled to 7 mm thickness using gauge strips and a rolling pin and cut with cookie cutter (inside diameter: 60 mm) baking at 205°C for 25/35 min	FFA, IFAT	/	/	11 %	ABTS	16 mmol TE/kg DM	129 %	- No significant changes observed on FFA after whole meal flour, dough and water biscuits baked at 205 °C for 25 and 35 min	- Both processing increased AC significantly - No significant changes were observed on FFA after baking at 205°C for 25/35 min
	Kernel puffing	Standard: cooker, 380 °C for 4 min. Puffing: 2.5 min with steam injected under pressure (8.5 bar). Optimal: 3–5 min at 360–390 °C, puffing was done under steam pressure between 7 and 10 bar for 1–4 min.					FRAP	18 mmol TE/kg DM (There is no significant difference between Monlis standard and optimal product)	260 %	- Both kernel puffing methods significantly increased FFA, the impact of optimal is importantly higher than standard method. - Impact of baking and puffing on AC are both significantly positive. - Impact of puffing on AC was significantly higher than baking	- Puffing increased FFA significantly (380 °C for 4 min/3–5 min at 360–390 °C)
(Liu et al., 2016)	Steam explosion	was performed 2.45 MPa, and 215°C for 30, 60, 90, and 120 s.	FFA, BFA	586.3 ± 37.2 µg/g (120 s)	55.7 ± 3.8 µg/g (untreated)	20 %	DPPH ABTS	79 ± 1.8 % (120 s) 78.6 ± 2.9 µmol/Trolox equivalent	997 % 2212 %	- With the explosion time extended, FFA and AC increased significantly (215°C, under 120 s, 2.45 MPa).	- Within 120 s, 215°C, time and FFA/AC is positive correlation
(Lu et al., 2015)	Baking	218°C, 21 min, upper crust: exposed to oven temperatures; bottom crust: the crust in contact with the loaf pan; crumb: everything except crust	FFA, CFA, TFA	11.5 ± 1.49 µg/g (whole meal, Louise, crumb)	2.31 ± 0.18 µg/g	10 %	antiproliferative effects	700,000 (9 mg/ml) Whole wheat dough	/	- Refine flour bread, FFA content: UC (upper crust) > C (crumb) > D(dough) - Whole flour bread: FFA content: C (crumb) > UC (upper crust) > D(dough) - Bread baking increased AC significantly	- 218°C, 21 min baking increased FFA and AC significantly. - FFA may be sensitive to high temperature and leading to the decrease of FFA in upper crust in whole meal bread
(Santa Cruz Olivos et al., 2021)	Biscuit's preparation	wheat meal flour (30 g dry weight basis for each water biscuit) + water, dough rolled to 7 mm thickness and cut with cookie cutter (inside diameter: 60 mm)	FFA, BFA	/	/	/	ABTS	17 mMol TE/kg DM		- 25–45 min baking, FFA increased significantly, after 45 min, no significant changes observed on FFA.	- Baking (205°C within 25–75 min) positive impacted AC - Within 45 min, thermal processing at 205°C increase FFA, when over 45 min,
	Baking						FRAP	25mMol TE/kg DM			(continued on next page)

Table 2 (continued)

Ref.	PD		DFAT	HFFAC (Treatment)	FAC in control	FARP	DAC/BI	HA/B (Treatment)	AC/B change	Results	Key Findings
		205°C for increasing times, 10 min steps from 25 to 75 min								- AC and time were positive correlation under 205°C within 25–75 min.	FFA kept stable, BFA decreased slightly
(Podio et al., 2019)	Pasta preparation	50 g of whole-wheat flour and 19 ml of NaCl 1 % w/v in ultrapure water, shape with 0.90 mm-thick, 2 mm wide and 15 cm long. Then dried at low temperature in two steps: 1st: 30 min at 30 °C without controlling the humidity in an air convection drier, 2nd: performed at 45 °C in a humidity-controlled (75 %) drier for 17.5 min	FFA, BFA	17.4 ± 19 µg/g (Raw whole noodle flour, ACA 315)	11.358 µg/g (whole flour, ACA315)	9 %	Bioaccessibility (in vitro)			- Pasta preparation increased FFA significantly, - Boiling treatment decrease the FFA content significantly, - AC of free form, a. No significant changes observed on BIOINTA 3004 FRAP during the whole process, b. TEAC decreased significantly in pasta preparation and has the opposite trend in cooking treatment.	- Pasta preparation (30 min, 30 °C or 45 °C 15 min) beneficially impacted FFA releasing - Boiling decreased FFA may be water-soluble FA loss in boiling. - There is a negative relationship between FFA content and AC of free fraction
	Boiling	8 g pasta in 400 ml of boiling ultrapure water, 8 min					TEAC (Total)	1.27 mmol TE/100 g (cooked pasta, BIOINTA 3004)			
							FRAP	0.7 mmol TE /100 g (cooked pasta, BIOINTA 3004)			
(Yilmaz & Koca, 2017)	Traditional cooking	Wheat: one unit of wheat + 2 units water cooked at 99-100°C for 20 min ; Durum: 1 unit durum + 3 units water,40 min, 99-100°C	TFA	/	/	/	DPPH	27 % reduction 0.1 g /ml	/	- TFA: durum > eikorn - All processing decreased TFA and AC significantly, except the micro cooking + air drying in Einkorn sample.	- All processing had negative effect on TFA and AC - TFA lost in the combination of traditional cooking and hot air drying was lowest.
	Microwave cooking	Einkorn: 1 unit einkorn wheat soaked with 1.75 units of water at 60°C, 1.5 h, microwave at 2450 MHz with output of 500 W for 6 min; Durum: 1 unit durum wheat soaked with 2.5 units of water at 60°C for 3 h. Microwave at the same condition for 7 min					ABTS	8 µmol/g TEAC	/		
	Autoclave cooking	Soaking processing of both were same with microwave cooking, cooking in autoclave at 121°C, 2.1 bar, 5 min					FRAP	7 µmol Fe 2 + equal. /g	/		
	Hot air drying	Cooked samples dried in ventilated oven at 60°C for 13-15 h until the water content = 10 %									
	Microwave drying	Cooked samples dried to 10 % water content in microwave oven at 500 W, traditional cooked samples: 60 min, autoclaved/ microwave cooked samples: 45 min									
(Zou et al., 2015)	Stabilization	Raw WG on a pilot scale fluidized bed drier with an air flow of 50 m ³ /h at 140 °C inlet and 100 °C outlet temperatures for 20 min	FFA	/	/	/	DPPH	6.90 ± 0.58 mg/ml (Stabilization)	- 4 %	- Both stabilization and roasting processing decreased AC significantly.	- Thermal processing negatively impacted AC of whole grain.
	Roasting	180°C: 5, 10, 20 min					ABTS	2.53 ± 0.13	-13 %	- Stabilization and roasting at 180°C under 10 min, FFA	- Roasting under 10 min, 180 °C, positively impacted FFA, over 10 min to

(continued on next page)

Table 2 (continued)

Ref.	PD	DEAT	HFFAC (Treatment)	FAC in control	FARP	DAC/BI	HA/B (Treatment)	AC/B change	Results	Key Findings
23	ABTS: 2,2'-azino-bis (3-ethylbenzothiazoline-6-sulfonic acid) (antioxidant capacity detection method).								increased significantly.	20 min, negatively impacted FFA
24	IFA: insoluble ferulic acid.								- After treated at 180°C for 20 min, FFA decreased significantly	- FFA is potentially sensitive to high temperature

23 ABTS: 2,2'-azino-bis (3-ethylbenzothiazoline-6-sulfonic acid) (antioxidant capacity detection method).

24 IFA: insoluble ferulic acid.

25 BFA: bound ferulic acid.

26 DM: dry matter.

27 ACA: ASOCIACIÓN de COOPERATIVAS ARGENTINAS (commercial Argentinean wheat).

28 BIOINTA: BIOCERES Instituto Nacional de Tecnología Agropecuaria-INTA (commercial Argentinean wheat).

29 WG: wheat germ.

3.1.3. Bioprocessing

Nine studies focused on the effect of bioprocessing on FA release and antioxidant capacity and/or bioaccessibility from wheat (see Table 3). Six demonstrated consistent positive effects on FA release after bioprocessing (Anson, Selinheimo, et al., 2009; Mao et al., 2020; Mateo Anson et al., 2011; Moore et al., 2009; Villalva et al., 2018; Yin et al., 2018). In 2 studies, different results were observed depending on the fermentation strains used (Antognoni et al., 2019; Zhang et al., 2014), and one study showed a trend for an increase in FFA followed by a decrease (Călinoiu et al., 2019). The effect of enzyme treatment was consistent. FFA content increased with enzyme treatment in all studies. For example, the combination of FAE with other enzymes (xylanase, β-glucanase, α-amylase and cellulase) was reported to increase FFA content (Mateo Anson et al., 2009; Villalva et al., 2018). Fermentation can also promote FA release. For example, Mao et al. showed that fermentation increased the FFA content from 8.67 ± 0.16 to 22.51 ± 0.66 μg/g (Mao et al., 2020). More specifically, the combination of enzyme treatment and fermentation demonstrated a significant positive effect on FA release. For instance, Villalva et al. observed that treatment with a combination of enzymatic hydrolysis and fermentation, significantly increased FFA content from 12.6 ± 1.3 μg/g to 70.1 ± 1.23 μg/g (556 %) (Villalva et al., 2018). The highest FFA concentration (100 μg/g) in Table 3 was also observed after combination treatment (Mateo Anson et al., 2009; Villalva et al., 2018). However, the effect of fermentation depends on the microbial strains used and fermentation time. Zhang et al. reported that *Saccharomyces cerevisiae*, *Saccharomycopsis fibuligera*, *Lichtheia corymbifera*, *Rhizomucor variabilis* and *Mucor circinelloides* all increased FFA content, while *Bacillus aylooluquefaciens*, *Aspergillus niger* and *Rhizopus oryzae* had a negative impact (Zhang et al., 2014). Călinoiu et al. found that during 6 days of fermentation, the FFA content reduced after an initial increase, with a peak on the 3rd day of 34.2 ± 0.2 μg/g (Călinoiu et al., 2019). In addition, the bioaccessibility of FA increased significantly after bioprocessing (Anson, van den Berg, et al., 2009b; Mateo Anson et al., 2009). Seven studies reported a beneficial effect of bioprocessing on antioxidant capacity (Călinoiu et al., 2019; Mao et al., 2020; Mateo Anson et al., 2009, 2011; Moore et al., 2007; Yin et al., 2018; Zhang et al., 2014), while the remaining article reported no significant differences (Antognoni et al., 2019; Villalva et al., 2018). Taken together, these results suggest that bioprocessing increases FFA content and antioxidant capacity in wheat.

3.2. Combined processing

Table 4 contains 7 studies which examined the effect of the combination of bioprocessing and thermal processing on FFA content and antioxidant activity in wheat. Three studies demonstrated a beneficial effect of combined processing (Bautista-Expósito et al., 2020; Lu et al., 2015; Yu et al., 2015). In particular, Bautista-Expósito et al. examined the impact of autoclaving followed by enzymatic hydrolysis and showed that combined processing was more efficient than either single process (Bautista-Expósito et al., 2020). These results demonstrated that the use of enzymes or thermal treatment alone, significantly promoted FA release. However, the combination of enzymes and thermal processing (thermal processing followed by enzyme treatment) was 7 times more efficient and finally generated 3835.34 ± 119.78 μg/g FFA, which is the highest FFA content of all the studies included in this review. Konopka et al. also observed FFA increase from 0.52 μg/g to 5.8 μg/g after sourdough fermentation and baking processes (Konopka et al., 2014). In contrast, Yu et al. found that the bread-making process had a negative effect on FA release, which may have been caused by the baking of the bread (Yu, 2015). This idea is also supported by the observation that FA in the crumb was significantly higher than in the crust (Konopka et al., 2014). It appears that the combination of thermal processing and bioprocessing is potentially the most effective method for releasing FA.

The two studies included in Table 5 concentrated on the effect of the

Table 3
Effect of bioprocessing on FA content and antioxidant capacities in wheat.

Ref	PD		DFAT	HFFAC (Treated)	FAC in control	FARP	DA/BI	HAC/B (Treated)	AC/B change	Results	Key Findings
(Mateo Anson et al., 2011)	Control bread	82 % whole wheat flour, 16 % bran, 1 % yeast, and 1 % salt.	TFA, FFA	93.24 µg/g serving (bioprocessed)		13 %	Plasma total AC	2.5 µmol/L (after consumption 1.5–2.5 h)		Bioprocessed bread contains significantly higher FFA control bread Bioaccessibility of bioprocessed sample was significantly higher than controlled sample The highest plasm FA content observed after consumption 1.5–2.5 h and decreased rapidly after that	Enzyme treatment helped FFA releasing Enzyme treatment increased bioaccessibility FFA is readily to be absorbed to plasma and metabolized quickly
	Treated bread	Ingredients same with above, bran was enzyme treated: enzyme combination (enzyme activities of endoglucanase (cellulase), xylanase, β-glucanase, R-amylase and FAE: Veron CP = 91, 200, 435, 1, 0; Grindamyl A1000 = 0, 0, 0, 12, 0; Depol 740 L: 13, 200, 100, ND, 0.44)					Anti-inflammatory effects				
(Mateo Anson et al., 2009)	White bread	1 % yeast, 1 % salt, and 98 % white flour.	TFA, FFA	100 µg/g (fermentation + enzyme treatment)		8 %	Bioaccessibility	5.5 % (Fermentation + enzyme treatment)		- Fermentation increased FFA, and bioaccessibility - Combination of fermentation and enzyme has more significantly impact on FFA releasing and bioaccessibility	- Fermentation itself positive impacted FFA, but the combination of fermentation and enzyme is more efficient - Enzyme treatment and fermentation significantly improved FA releasing - Bioprocessing enhanced the colonic release and conversion of phenolic acids into their metabolite
	Whole-meal bread	1 % yeast, 1 % salt, and 98 % whole-meal flour									
	Whole-meal bread with native bran,	1 % yeast, 1 % salt, 16 % of bran and 82 % whole-meal flour									
	Whole-meal bread with fermented bran	1 % yeast, 1 % salt, 16 % of bran and 82 % whole-meal flour, Bran fermentation 22 % (w/w) bran and 0.27 % (w/w) Baker's Yeast (Finnish Yeast Ltd.) with water, 20 °C for 20 h									
	Whole-meal bread with fermented and enzymatic treated bran.	Above + 0.01 % (w/w) Grindamyl A1000 (Danisco), 0.36 % (w/w) Depol 740 L (Biocatalysts), and 0.14 % (w/w) Veron CP (Rohm GmbH). (Enzyme activities of endoglucanase (cellulase), xylanase, β-glucanase, α-amylase and FAE: Veron CP = 91, 200, 435, 1, 0; Grindamyl A1000 = 0, 0, 0, 12, 0; Depol 740 L: 13, 200, 100, ND, 0.44)									
(Antognoni et al., 2019)	LAB strains	<i>Lactobacillus fermentum</i> (MR13), <i>L. rhamnosus</i> (C249, C1272), <i>L. plantarum</i> (LB102, LB124, LB126, LB245, 29DAN, 83DAN, 6BHI, 98A), <i>L. brevis</i> (3BHI)	FFA, TFA	6 µg/g FW (98A)		3 %	FRAP	1 µM FRAP (29 DAN)	NB	- 98 A, LB126 and 290 A increased FFA significantly - 6 out of 12 of LAB strains improved FFA, while others had no significant effect	- 6 out of 12 of LAB strains beneficially impacted FFA releasing - Effect of fermentation on FFA releasing is highly associated with LAB strains species - No positive correlation was
	Inoculated dough	30 °C, 24 h									
	Final dough	30 °C, 34 h									
		30 % mature inoculated dough + 70 % uninoculated dough									

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Table 3 (continued)

Ref	PD		DFAT	HFFAC (Treated)	FAC in control	FARP	DA/BI	HAC/B (Treated)	AC/B change	Results	Key Findings
(Călinoiu et al., 2019)	Pre- processing	Sterilized at 121 °C, 15 min	FFA	34.2 ± 0.2 µg/g (3rd day of fermentation)	21.8 ± 0.1 (µg/g)	/	DPPH	45 % inhibition of the DPPH radical (in the 2nd and 3rd fermentation days, there is no significant differences between these two days)	25 %	- 1st –3rd day: Bioavailability and FFA increased significantly 3rd –6th days: Bioavailability and FFA significantly decreased 5th day, FFA is similar to the control sample, 6th day, FFA in fermented sample was significantly lower than control	observed between FFA and AC - Fermentation under 30°C positively impacted FFA and AC in first 3 days and followed by a significantly negative impact. - Over fermentation can lead to the degradation of FA
	WB (70 % humidity (w/w))	100 g WB + 5 ml yeast suspensions (107 CFU/mL) per 100 g of dry weigh, 30°C, 6 days									
	Control	100 g WB + 5 ml sterile water									
(Mao et al., 2020)	lactobacillus strains	Incubated in MRS and cultured at 37°C for 24 h	FFA	22.51 ± 0.66 µg/g Fermented wheat bran	8.67 ± 0.16 µg/g	/	TOAC	6.70 ± 0.12 µmol/g fermented sample		- FFA, AC: Solid fermented sample > raw > sterilized sample	- Sterilization negatively affect FFA and AC - Fermentation positively impacted FFA and AC
	Fermentation	Raw wheat bran sterilized by high pressure stream, the LAB containing sterile water was uniformly mixed with sterilized WB, the final moisture at 60 % incubated the mixture at 37°C for 36 h					DPPH	35.68 ± 1.41 %			
(Moore et al., 2007)	Yeast concentration	48 h treatment time and 3 types of yeast (Y1, Y2, Y3) at concentrations of 0, 0025, 0.05 0.1 and 0.2 g/g of wheat bran	FFA, TFA	65 µg/g (Y3 treated)	/	10 %	ORAC	23 µmol TE/g (Y3 treated)		- No significant differences were observed between Y1 and Y2 yeast of FFA, effect of Y3 yeast was significantly higher than Y1 and Y2 - Y1 increased ORAC significantly, decreased DPPH and no effect on ABTS and HOSC. - Y2 increased ORAC and DPPH significantly, no significant effect on ABTS and HOSC - Y3 treatment increased all AC index significantly	- Fermentation beneficially impacted FFA releasing - Fermentation potentially degrade FA to other antioxidant ingredients. - Types of yeasts influenced AC and releasing of FFA
	Fermentation time	0.1 g/g of what bran yeast fermentation for 0, 12, 24, 48 h					ABTS	8 µmol TE/g bran (Y3 treated)			
	Control	Treated using the procedures described above and with thermally inactive samples of the same yeast preparations used in the treatments					DPPH HOSC	0.5 % scavenged (Y3 treated) there are no significant differences between each sample			
(Villalva et al., 2018)	Bread preparation	White flour + 30 % native bran bread (Control) White flour + 30 % fermented bran bread White flour + 30 % enzyme treated bran bread (Enzyme: xylanase)	FFA, BFA	70.1 ± 1.23 µg/g (fermentation + enzyme treated bread)	12.6 ± 1.3 µg/g	6 %	TEAC	20.0 ± 1.2 µmol TE/g (fermentation + enzyme)	120 %	- FFA: fermentation ≈ enzyme ≈ fermentation + enzyme > whole meal bread ≈ no treated bread. - Total AC: combination treated/ fermentation treated bread > enzyme treated sample > non-treated bread.	- Fermentation, enzyme, and combination bioprocessing beneficially impacted FFA releasing. - Effect of fermentation, enzyme or

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Table 3 (continued)

Ref	PD	DFAT	HFFAC (Treated)	FAC in control	FARP	DA/BI	HAC/B (Treated)	AC/B change	Results	Key Findings	
(Yin et al., 2018)	Fermentation								- AC of free phenolic: no significant differences	combination processing is similar - Beneficially effect of bioprocessing was observed on bound phenolics, no effect was observed on AC of free phenolics	
	Baking										
	Flour preparation	FFA	/	/	/	DPPH	86.5 ± 3.6 % (<i>Aspergillus niger</i> fermentation)		- The highest FFA: <i>Aspergillus niger</i> fermented samples (416.6 ± 2.2) µg/g, 1413 % higher than the unfermented sample	- Fermentation demonstrated positive effect on FFA and AC - Effect of fermentation is highly associated with strains of microorganism	
	Fermentation					ABTS	99.6 ± 4.9 % (<i>Aspergillus niger</i> fermentation)		- Fermentation increased FFA and AC significantly - <i>Aspergillus niger</i> fermented samples contains the highest AC	- The most efficient strain: <i>Aspergillus niger</i> .	
(Zhang et al., 2014)	50 WB (70 % humidity), autoclaved at 121°C 20 min, inoculated with 5 ml of spore suspensions/ 100 g dry substrates. Incubated at 30°C for 6 days.	FFA, SFA	15.57 ± 0.23 µg/g (<i>Saccharomycopsis fibuligera</i> fermentation)	4.2 ± 0.2 µg/g	/	Total reducing activity	1151.5 ± 11.1 µg/g (<i>Aspergillus niger</i> fermentation)	175 µg/g (<i>Rhizomucor variabilis</i> / <i>Rhizopus oryzae</i>)	250 %	- Most effective: <i>Saccharomycopsis fibuligera</i>	- 5 out of 5 strains positively impacted FFA releasing
						DPPH	14 mg/ml (<i>Bacillus amyloliquefaciens</i>)		-13 %	- <i>Saccharomyces cerevisiae</i> , <i>Lichtheimia corymbifera</i> , <i>Rhizomucor variabilis</i> and <i>Mucor circinelloides</i> increased FFA - <i>Bacillus amyloliquefaciens</i> and <i>Aspegillus niger</i> decreased FFA - <i>Rhizopus oryzae</i> : no effect - All strains of microorganisms increased total reducing power, decreased DPPH and superoxide anion scavenging activity.	- Fermentation positively impacted total reducing power, negatively impacted DPPH.

30 WB: Wheat bran.

31 MRS: de Man, Sogosa and Sharpe agar.

32 TOAC: total antioxidant capacity.

33 HOSC: hydroxyl radical scavenging capacity.

Table 4
Effect of bioprocessing & thermal processing on FA content and antioxidant capacities in wheat.

Ref	PD		DFAT	HFFAC (Treated)	FAC in control	FARP	DA/BI	HAC/B (Treated)	AC/B change	Results	Key Findings
(Bautista-Expósito et al., 2020)	Commercial glycosidase cocktails samples (cellulase, xylanase)	Solid/solvent = 1:20; 40°C, 1000 rpm, 20 h, pH = 6	SFA	528.93 ± 84.87 µg/g of bran (Depol 670L)		NB	ORAC	22.67 ± 2.07 mmol Trolox/kg	/	FFA: Ultraflo XL + autoclave > Ultraflo XL > autoclave > control AC: Ultraflo XL + autoclave > autoclave > Ultraflo XL	No direct relationship was observed between FFA and TAC Both thermal (autoclave) and enzyme treatment positively impacted FFA, combination of both methods is more efficient than any single method.
	Autoclave	Before enzyme fermentation, was autoclaved at 121 °C at 1 atm for 30 min	FFA	3835.34 ± 119.78 µg/g of bran (autoclave + Ultraflo XL)		/	ABTS	17.04 ± 0.53 mmol Trolox/kg			
	Autoclave + UltrafloXL (a classic multi active β-glucanase and xylanase preparation)	Add Ultraflo XL at 1 % (enzyme to WB ratio, w/w) after autoclave						DPPH FRAP	5.09 ± 0.28 mmol Trolox/kg 0.94 ± 0.02 (T = 50°C, pH = 4, 20 min under Ultraflo XL)		
(Çelik & Gökmen, 2020)	Fermentation	Optimized Straight-Dough Bread Making"	BFA	/	/	/	ABTS	20.6 ± 0.5 mmol Trolox/kg (Refined Wheat bread crusty 30)		- No significant difference was observed between fermented sample and flour in AC - Heating: 5 to 30 min: AC increased significantly	- No significant effect was observed at fermentation and heating on AC and FFA releasing
(Konopka et al., 2014)	Heating (Crust 5,15,30)	Baking the ground, freeze-dried fermented dough samples in glass tubes in an oil bath at 200°C for 5, 15 and 30 min					DPPH	28.9 ± 0.9 mmol Trolox/kg (Refined Wheat bread crust 30)			
	Dough preparation	White yeast: 350 g flour, 10.5 g yeast, 3.5 g salt, 192 g water	FFA	5.8 µg/g (Crumb of sourdough bread)	0.52 µg/g (whole meal flour)	/	TEAC	14.4 µmol of TE/g(Sourdough)		- FFA: sourdough fermented > yeast fermented - FFA and AC: crumb > crust - After baking, FFA in crust decreased significantly, while no significant changes were observed in crumb	- Sourdough fermentation is more efficient than yeast fermentation on FFA releasing, both fermentation increased AC and FFA Thermal processing helped FFA releasing but over thermal processing may lead to degradation of FA and therefore results in FFA reducing in crust Baking negatively impacted AC
		White souldough: 175 g flour, 10.5 g yeas, 3.5 g salt. 319 g sourdough, 48 g water Whole meal yeast: 350 g flour + 10.5 g yeast, 3.5 g salt, 160 g water Whole meal sourdough: 175 g flour + 10.5 g yeast + 3.5 g salt + 295 g sourdough + 40 g water									
(Starzyńska-Janiszewska et al., 2019)	Baking Cooking	100 g grains boiled for 20 min (green spelt) or 25 min(spelt) in tap tater (1:3 w/v), pH = 4.5–5	SFA	/	/	/	ABTS	24.51 ± 0.41 µmol Trolox/g dm	9 %	- FFA: fermentation treated sample (80.18 ± 4.8 µg/g) > raw ≈cooked sample Cooking decreased AC significantly, Fermentation increased significantly	- No effect was observed on FFA from Cooking Fermentation improved FFA releasing. Cooking negatively influenced AC Fermentation positively impacted AC
	Fermentation	Cooked material inoculated with <i>R. oligosporus</i> , incubated at 31 °C for 30 h									
(Tian et al., 2021)	Bread fermentation	100 g whole wheat flour (70 % refined flour + bran + shorts fractions) + 2.0 g yeast + 6 g sucrose + 1.5 salt + 3 g shortening + 0.2 g malt flour, 90 min fermentation + 30 min proofing	SFA	/	/	/	ABTS, DPPH	24 µmol Trolox Equivalence/g sample (Turkey red, bread crust)	300 %	- AC: crust > loaf > crumb Fermentation increased FFA significantly No significant differences were	- Fermentation positively impacted FFA Thermal processing did not show impact on FFA releasing Both fermentation and thermal processing increased

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Table 4 (continued)

Ref	PD		DFAT	HFFAC (Treated)	FAC in control	FARP	DA/BI	HAC/B (Treated)	AC/B change	Results	Key Findings
	Baking	215°C, 24 min								observed on fermented and baked sample	AC Thermal processing is more efficient on AC
(L. Yu & Nanguet, 2013)	Dough preparation	5.3 g yeast, 6 g sucrose, 1.5 g salt, 3.0 shortening + 100 g flour, 30 °C water bath for 90 min, dough was punched and rolled before incubating for 52 min, + second punch + 25 min incubation, proof 33 ± 2 min	BFA	/	/		DPPH	5 µmol equivalent of Trolox/g	/	- DPPH: flour > bread ORAC: flour < bread Highest BFA: bread (whole wheat flour) (393.5 mg/g Dry sample)	- Bread making processing has beneficial effect on ORAC, but negatively impact DPPH. Bread making processing had negative effect on FFA releasing.
	Baking	215°C, 24 min					ORAC	60 µmol equivalent of Trolox/g	/	Bread processing increased BFA significantly.	
(Yu et al., 2015)	Dough preparation	100 g flour (14 % moisture basis), 3 g compressed yeast, 2.5 g gluten, 4 g whey powder, 4 g sugar, 2.4 g salt, 1 g malt, and 3 g pure lards fermented at 37.5 °C and 85 % humidity(30 + 65 min), proofing: 15 min	FFA, BFA	16.44 ± 0.57 µg/g (Bread crumb, Konini)	2.5 ± 0.2 µg/g (flour)	3 %	DPPH (Total)	600 µmol equivalent of Trolox/g	33 %	- During fermentation, FFA keep increase (from 30 min fermentation to 65 min treatment). In bread, FFA: crumb > loaf > crust The highest AC	- Fermentation and thermal processing helped FFA releasing The decrease of FFA in bread crust was potentially contributed to its strictly contact with high temperature and finally leading to the degradation of FFA
	Baking	200°C, 25 min					ABTS	680 µmol equivalent of Trolox/g	30 %	observed in bread crust, and followed by bread loaf, bread crumb	Fermentation and baking positively impacted the AC

Table 5
Effect of milling & thermal processing on FA content and antioxidant capacities in wheat.

Ref	PD	DFAT	HFFAC (Treated)	FAC in control	FARP	DA/BI	HAC/B (Treated)	AC/B change	Results	Key Findings	
(Fares et al., 2010)	Debran processing	Friction debranning machine for nine subsequent time intervals of 20 s, named debranning fractions 1, 2, 3, 4, 5, 6, 7, 8, 9	FFA, TFA	Highest in pasta making: 11.0 µg/g (EP2 uncooked pasta)	3.27 µg/g	5.05 %	TEAC	1.3 µmol Trolox/g sample (cooked EP2 pasta)	86 %	FFA: fraction 1 > 9 > 4 > 5 > 6 > 7 > 8 > 2 > 3 No significant changes observed after cooking Cooking increased AC significantly.	Cooking beneficially impacted AC Effect of cooking on FFA is not significant Outer pericarp contains highest FA
	Pasta production	Total dough water content of 44–45 %, extrusion at 50 ± 5 °C, pressure 70 ± 10 atm, and vacuum 700 mm; EP1 made with 6 % of fraction 1, EP2 made with 10 % of fraction 1, EP3 made with 6 % of fractions 2 and 3, EP4 made with 10 % of fractions 2 and 3		Highest in debranning: 7.47 ± 2.59 µg/g (fraction 1)	6.44 ± 10.5 µg/g	0.36 %					
	Control pasta	100 % durum wheat semolina									
	Cooking condition	100 g pasta + 1 L boiling water to the while core in the strands disappeared after squeezing them between two glass plates									
(Pasqualone et al., 2017)	DB	6 % of the kernel weight was removed (1st debranning step), then a further 3 % was removed and collected (2nd debranning step), a further 3 % was detached and collected (3rd debranning step), up to 12 % of the kernel weight in total. DB: 2nd + 3rd fractions (180–425 µm)	FFA	1894.6 ± 35.4 µg/g (MB flour)	1281 ± 14.9 µg/g(B)		DPPH	39.3 % (there is no significant between 20 DB bread and 20B bread)	/	- In flour, FFA: MB > DB > B. - DPPH: MB ≈ DB > B. - In bread, FFA D bread > B bread > MB bread	- Smaller particle size is positive correlated to high FFA Thermal processing degraded FFA
	MB	DB goes to micronization and air classification treatment to obtain two sub fractions with different particle size, the thinner of the sub-fraction were MB (126–180 µm)									
	B, remilled semolina	B (coarse bran) and remilled semolina were obtained by conventional rolled milling without debranning pre-treatment (Remilled semolina: 126–180 µm, B: >500 µm)									
	Bread making	re-milled semolina were added to B, DB or MB + 20 g yeast + 20 g salt + water, mixed for 13 min, and leaven at 30°C, baked at 220°C for 30 min									

Table 6
Effect of bioprocessing, thermal processing & milling on FA content and antioxidant capacities in wheat.

Ref	PD		DFAT	HFFAC (Treated)	FAC in control	FARP	DA/BI	HAC/B (Treated)	AC/B change	Results	Key Findings
(Hemery et al., 2010)	Milling	Amb. Medium: coarse bran large scale conventional milling; (257.6 µm) Amb. Fine: a further milling on Amb. Medium (147.1 µm) Amb. Ultrafine: three successive grinding steps with a selection grid of 0.3 mm (51.41 µm) Cryo.ultrafine: cyrogenic grinding at-100°C by combing a cryogenic screw feeder with liquid nitrogen supply to the hammer mill (54.93 µm) FES Positive (26.51 µm)/negative (45.66 µm) /middle (88.28 µm): ultrafine bran obtained by cryogenic grinding, charged by impacting against each and against the walls of the charging liner, the bran containing positively or negatively charged particles are FES positive or FES negative, the two products mixed are FES middle faction White flour:106.7 µm Whole meal flour: 148.5 µm	BFA, TFA, FFA	17.9 ± 0.1 (µg/g DM) FES middle	1.2 ± 0.1 (1.8 %)	2 %	Bioaccessibility	31.8 ± 1.4 µg/g bread DM intake (3.0 %) (FES positive bread)	/	FFA: FES middle > Cryo. Ultrafine > Amb. Ultrafine > FES negative > Amb. Fine > Amb. Medium = FES positive > Whole bread > White bread Bioaccessble FA: FES negative > FES positive > Amb. Ultrafine > Amb. Fine > FES middle > Whole bread > Amb. Medium > white bread	Particle size decreased from 148.5 µm to 88.28 µm, FFA increased significantly, under 88.28 µm, FFA decreased but still higher than untreated flour. Bioaccessibility of FA is positive correlated with particle size decreasing
	Bread making	whole meal /white bread: 96.3 % white flour/ whole meal flour + 2 %salt + 1.76 % instant yeast fermentation at 30°C for 15 min, molded, fermentation at 30°C for 45mins. After proofing oven at 215°C, 65 °C dew point, 15 Hz convection, vertical top-down air flow, for 25 min Sample bread:15.9 % bran and 80.4 % white flour, others same with whole and white bread									
(Moore et al., 2009)	Milling	Coffee grinder to 20 and 80mesh	FFA, TFA	4.94 µg/g (204°C, 14 min, Lakin)	4.28 µg/g	2 %	ORAC	No significant difference		- Within 48 h, fermentation increased FFA significantly	- Within 48 h, fermentation positively impacted FFA
	Fermentation	whole-wheat flour preparations, water, honey, soybean oil, dry active yeast (Fleischmann's, Fenton, Missouri), and salt at w/w percentages of 52.04, 33.24, 10.30, 2.34, 1.13, and 0.95, fermentation at 4°C for 0 (control), 18, 48 h					ABTS	No significant difference		- Thermal processing increased AC and peak at 204°C, 14 min = 288°C, 7 min. Thermal processing a. Lakin: FFA increased significantly	- Thermal processing positively impacted FFA in Lakin. - Effect of thermal processing associated with wheat varieties.
	baking	7 min at 204 °C, 14 min at 204 °C, and 7 min at 288 °C					DPPH HOSC	No significant difference No significant difference		b. Trego: FFA decreased significantly	

34 20 DB: re-milled semolina added of a mix of second and third debranning fractions at 200 g/kg.

35 20B: re-milled semolina added of coarse bran at 200 g/kg.

36 FES: fraction from electrostatic separation.

combination of thermal processing and milling on FFA content and antioxidant capacity. Pasqualone et al. demonstrated that smaller particle size combined with thermal processing may lead to the degradation of FFA and decrease its antioxidant capacity (Pasqualone et al., 2017). Fares et al. demonstrated that debranning decreased FA content significantly, and although pasta processing increased FFA content, the final FFA content was significantly lower (Fares et al., 2010). To summarise, the combination of milling and thermal processing negatively impacts FA content and antioxidant capacity in wheat. However, the limited number of studies that examined these techniques suggests that further study is needed.

Table 6 summarizes studies into the combination of bioprocessing, thermal processing and milling on FFA content and antioxidant activity and/or bioaccessibility in wheat. Hemery et al. demonstrated that larger particles contained higher FA content, but smaller particle size led to higher bioaccessibility (Hemery et al., 2010). Additionally, the highest amount of FFA found in this study was found in uncooked "middle size" flour ($17.9 \pm 0.1 \mu\text{g/g}$), demonstrating that the cooking procedure decreased FFA content (Hemery et al., 2010). A further study by Moore et al, examined the effect of combined processing on both FFA and antioxidant capacity but results were unclear (Moore et al., 2009). Given that there were only two studies that examined the effect of combining the three processing methods a clear conclusion about the combined methods is not possible.

4. Discussion

The most effective method of releasing FA from wheat bran based on the studies included in this review was the combination of particle size reduction, pre-hydrolysis thermal processing and bioprocessing. Since FA is mainly covalently bound to the arabinoxylans in the cell walls of wheat and is thus not bioavailable. Milling, thermal processing and bioprocessing are required to facilitate its release. The release of FA will also depend on the TFA content in the starting material. The TFA detected in the studies included in this review varied considerably. This is likely due to the different varieties of wheat used, and the differences in the methods used to determine the TFA content (Mpofu et al., 2006).

4.1. Effect of reducing particle size and debranning

FA content in different parts of the wheat grain varies, decreasing from outer to inner layers. The highest FA content was found in pericarp (8180 $\mu\text{g/g}$), followed by aleurone (8170 $\mu\text{g/g}$), scutellum (3480 $\mu\text{g/g}$), embryonic axis (310 $\mu\text{g/g}$) and endosperm (100 $\mu\text{g/g}$) (Laddomada et al., 2015). Aside from the variation of FA content in different parts of wheat, one might expect that the extent of release of FA is dependent on particle size, with a smaller particle size leading to a higher amount of FFA. This expectation was confirmed by Zaupa et al, whose study reported samples with particle size $< 20 \mu\text{m}$ contained the highest FFA content (Zaupa et al., 2014). Yu et al. also indicated that the particle size of substrates can impact the release of FA during bioprocessing (Yu et al., 2002). Their results demonstrated that when particle size decreased from 1 mm to 250 μm , the amount of FA released increased from 0 to 2.8 % (Yu et al., 2002). Bioaccessibility of FA with smaller particle size is also higher (Hemery et al., 2010). This is potentially because the larger particle size restricts the accessibility of the bonds to be hydrolysed, i.e., the smaller particle size of wheat increases the accessibility of enzyme to the feruloyl groups, which promotes enzyme activity, leading to a higher amount of FFA (Yu et al., 2002). However, the effect of particle size on FA release is limited. As the results of Alzuwaid et al. demonstrated, after a critical point, decreasing particle size cannot increase release (Alzuwaid et al., 2020). This is mainly because the FA is covalently bound to the arabinoxylan, and the ester bond is strong and therefore difficult to break using physical methods. In addition, heat (up to 95 °C) generated during milling by friction (e.g., plate milling) may also impact FFA content (Haridas Rao et al., 1989).

For example, Sapna et al. claimed that heating induced by plate milling decreased FFA content from 45.0 to 39.9 $\mu\text{g/g}$, despite failing to measure the temperature during the process (Sapna et al., 2019). Thus, reducing particle size can increase FFA content to some extent but is not the maximally effective process.

4.2. Effect of thermal processing

The studies in Table 2 suggest that thermal processing is a double-edged sword for releasing FA. On the one hand, cellular constituents can be damaged by high temperature thermal processing, and increase the extraction of intracellular FA (Izidorczyk, 2021). The beneficial effect of thermal processing is not confined to wheat. It has also been demonstrated that FFA content in sweet corn significantly increased after thermal treatment at 121 °C for 25 min (Dewanto et al., 2002). Similar results were also obtained by Sapna et al. in 2019, who demonstrated that FA content in black rice increased 72 % after baking (Sapna et al., 2019). On the other hand, FA is sensitive to thermal degradation to different degrees when exposed to an extremely high temperature for a relatively long period (Samaras et al., 2005). Fiddler et al, showed that the degradation of FA occurred via two steps, the first being decarboxylation at 245 °C, giving the major product 4-vinylguaiaicol (Fiddler et al., 1967). In the second stage, vanillin, acetovanillone, vanillic acid, 4-methyl- and 4-ethylguaiaicols were formed. The first three phenolics only formed in the presence of oxygen, whilst the last two can be formed in both oxygen and oxygen-free environments (Fiddler et al., 1967). They also indicated that decomposition rate was related to oxygen content. (Coghe et al., 2004; Fiddler et al., 1967). For example, Gong et al. demonstrated that FFA is readily degraded under steam explosion, with the highest FFA amount observed at 220 °C (4.0 MPa) (1000 $\mu\text{g/g}$) but it sharply decreased to 200 $\mu\text{g/g}$ at 230 °C (4.0 MPa) (Gong et al., 2012).

4.3. Effect of bioprocessing

4.3.1. Enzyme addition

Bioprocessing, on its own, could be predicted to be the most efficient single method of releasing FA because enzymes directly hydrolyse the bond between FA and arabinoxylan. For example, FFA content was increased significantly after treatment with a mixture of cellulase, xylanase, β -glucanase, α -amylase and FAE (Mateo Anson et al., 2009). Bioprocessing was shown to increase the FFA content 6-fold in comparison to no bioprocessing (Villalva et al., 2018). Sancho et al. showed FA release with use of barley esterase extracts and *Trichoderma* varied xylanase (Sancho et al., 2001). It was theorized that this is because of the production of FAE and decarboxylase during the metabolism of bacteria, which could hydrolyse the bond between FA and other compounds, especially the FAE, which specifically targets the ester bond between FA and arabinoxylan and therefore releases the FA (Coghe et al., 2004). Although other enzymes cannot directly hydrolyse the bond between FA and arabinoxylan, they can break the arabinoxylan backbone into lower molecular weight oligosaccharides by targeting the β -1, 4 glycosidic bonds, to increase the accessibility of FAE, making the ester bond between FA and other polysaccharides readily accessible (Wu et al., 2017). Therefore, enzyme addition represents a direct method of increasing FA release.

4.3.2. Fermentation

The other bioprocessing method included in this review, fermentation, also increased FFA content in wheat (Table 3). This is because the metabolism of microorganisms used produced exogenous enzymes capable of hydrolysing polysaccharides. However, the effect of fermentation was highly associated with the microbial species used and the fermentation time. During fermentation, depolymerizing enzymes were produced by the microorganisms, the preference of these depolymerizing enzymes for poly α -1, 4-D-methyl galacturonic acid are

different (Heerd et al., 2012). In addition, these enzymes act as exo- or endo-enzymes and randomly attack the poly α -1, 4-D-methyl galacturonic acid link, generating different galacturonic acid oligomers, resulting in the different amounts of FFA after fermentation (Heerd et al., 2012). The negative effect of overlong fermentation time is probably because other active enzymes transform the FFA into compounds such as di-ferulate or other antioxidants, leading to a decrease in FFA content.

4.3.3. Fermentation and enzyme

The combination of enzyme and fermentation is more effective than any single process (Mateo Anson et al., 2009; Villalva et al., 2018). Fermentation with enzyme treatment produced a threefold increase in FFA content compared to fermentation alone in one study (773.3 % vs 250.0 % respectively) (Mateo Anson et al., 2009). Villalva et al. demonstrated that FFA content in enzymatically treated fermentation samples was $28.4 \pm 0.19 \mu\text{g/g}$, which was higher than the fermentation only sample ($24.9 \pm 0.68 \mu\text{g/g}$) (Anson, van den Berg, et al., 2009; Villalva et al., 2018). The reason that the combined approach led to a higher release of FFA is due to the synergistic effect of not only the enzyme added but also the enzymes produced by fermentation targeting the glycosidic bond. Other types of enzymes shorten oligosaccharides and therefore increase contact opportunity for FAE. The difference in the increase of FFA content in the studies above is likely due to the composition of the enzyme mixtures used. Anson et al. used cellulase xylanase, β -glucanase, α -amylase and FAE while Villalva et al. only used xylanase, which cannot specifically target the bond between FA and arabinoxylan (Anson, van den Berg, et al., 2009; Villalva et al., 2018). Therefore, the type of enzymes and ratios are important and merit further detailed investigation.

4.4. Effect of combination processing

Among the three combination approaches to processing (bioprocessing & thermal processing, thermal processing & milling, bioprocessing, milling & thermal processing) examined in this review, the only combination that demonstrated a significant positive effect on FFA was the combination of bioprocessing and thermal processing, which led to the highest FFA content ($3835.34 \pm 119.78 \mu\text{g/g}$) among all methods (Bautista-Expósito et al., 2020). In the study of Bautista-Expósito et al., autoclave treatment was applied as a pre-treatment before enzyme addition (Bautista-Expósito et al., 2020). This procedure broke open wheat cell walls allowing access of the FAE to the substrates and increasing the release of FFA. However, Konopka et al. observed that, in bread, the FFA in the crust was lower than in the crumb (Konopka et al., 2014). This was likely due to the high temperature in the crust leading to the degradation of FFA. Therefore, although the combination of thermal processing and bioprocessing can increase the FFA content significantly, the effect was strongly associated with processing conditions (e.g., temperature, time) and sequence of steps (e.g., thermal processing as pre-treatment or bioprocessing as pre-treatment).

The two other combinations (thermal processing & milling, bioprocessing, milling & thermal processing) showed no effect or negative effects on FFA content. This was mainly because the removal of the outer layers by debranning removed most of FA although bioprocessing and thermal processing helped FA release.

4.5. Antioxidant capacity of wheat following processing

Ferulic acid has a high antioxidant capacity, while the antioxidant properties of wheat depend not only on FA but also on other antioxidants. An increase in FFA content after treatment was frequently correlated with an increase in antioxidant capacity in most of the included studies. FA is one of the most abundant phenolic compounds in wheat, and the antioxidant activity of FA is mainly from the free form, which could account for most of the increase of antioxidant capacity. For example, Chen et al. found that the antioxidant capacity of FFA doubled

that of vanillic acid and P-coumaric acid (Chen et al., 2013). However, some studies demonstrated that when FFA content was constant or decreased, antioxidant capacity was increased (Podio et al., 2019). This is mainly because the di-ferulic acids sharply increased after thermal processing. For example, Podio et al. found that although there were no significant differences in trans-FA before and after cooking, FA derivatives increased significantly, which in turn led to a significant rise in antioxidant capacity. (Podio et al., 2019). Another potential explanation is the impact of the Maillard reaction. The end products of the Maillard reaction are melanoidins, which are known for their antioxidant capacity (Çelik & Gökmen, 2020). This suggestion is supported by Lu et al, who showed that after bread baking, the antioxidant capacity of bread increased, especially in the upper crust of bread, which showed the most significant antiproliferative effects (antiproliferative Activity in HT-29 Human Colon Cancer Cells) compared to the crumb and the dough (Lu et al., 2015).

5. Conclusions

The FFA content of wheat is largely determined by the TFA content, the degree of covalent bond (FA to arabinoxylan) hydrolysis and the extent to which FFA is degraded or converted to other compounds (e.g., vanillic acid). This most efficient method of releasing FA in this review is the combination of pre-hydrolysis thermal processing and bioprocessing. However, both of these treatments, particularly thermal processing, have the potential to degrade FFA, which may lead to a reduction of FFA. Debranning decreased the FFA content significantly because of the removal of the outer layers which contain most of the FA. Although the effect is limited, FA release from wheat bran can be increased by reducing particle size. Therefore, the greatest potential method of releasing FA is the combination of particle size reduction, pre-hydrolysis thermal processing and bioprocessing. Developing or refining processing methods to increase FA release is important because the antioxidant capacity of FA is limited to its free form. Future work should, therefore, focus on how best to combine processing methods to maximise FA release in order to improve the health benefits of wheat.

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

Data will be made available on request.

Acknowledgement

This research did not receive any specific grant from funding agencies in the public, commercial, or not for profit sectors.

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