

Upcycling of Cereal Byproducts: A Sustainable Opportunity to Valorize Wasted Nutrients and Derive Bioactive Compounds for Humans and Animals Nutrition and Health

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Abstract: With the global population projected to reach close to 10 billion by 2050, the escalating demand for cereals such as wheat, rice, corn, oat, and barley places significant pressure on production systems. These systems are increasingly vulnerable to the adverse impacts of climate change, threatening global food security. This article emphasizes the critical need to address these challenges and explores strategies for sustainable food production, focusing on the opportunities that the upcycling of cereal byproducts offers for human and animal nutrition and health.

Keywords: Cereal byproducts · Circular economy · Health benefits · Nutrition · Upcycling

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1. Introduction

The world's population is expected to reach nearly 10 billion by 2050, and this demographic growth is accompanied by an escalating demand for food, particularly cereals such as corn, wheat, rice, oat, and barley.^[1] This demand places considerable pressures on cereal production systems, which, in turn, are vulnerable to the adverse effects of climate change. Addressing this challenge is crucial for global food security.

Corn, wheat, rice, and barley represent over 90% of the world's production of cereals and are staple resources in both human and animal nutrition.^[2] However, the diverse processes involved in cereal handling and manufacture generate significant quantities of underexploited byproducts. It is estimated that in Europe, Asia, and North America alone, up to 35% of the entire cereal production ends up as processing byproducts.^[3] Due to economic reasons, these are commonly sent to landfills, used as animal feed, turned into fertilizers, or simply discarded as waste. For example,

in the case of brewers' spent grain, the main byproduct of the brewing industry, 70% is used as animal feed and about 20% is landfilled.^[4]

However, cereal byproducts comprise valuable nutrients and physiologically active compounds such as carbohydrates, proteins, phenolics, and vitamins with tremendous potential for widespread applications. The food and feed industries have therefore been exploring alternative approaches to reduce the volume of cereal byproducts and transform them into high-added value products. This not only reduces waste but also promotes sustainability, aligning with the global trend toward more circular and health-oriented practices. This review provides a comprehensive overview of the cereal processing side streams with an emphasis on the current strategies utilized to valorize and capture the full potential of cereal byproducts.

2. Cereal Production for Human and Animal Nutrition

From 1961 to 2021, global cereal production has increased by 250 percent and will continue growing.^[1] Over the next 10 years, a higher share of global cereal production will originate from yield growth, as area expansion is expected to become more limited. Yield improvements will result from several factors such as improved and more widely accessible seed varieties, efficiency gains in the use of inputs, and better agricultural practices. However, certain factors including increased environmental concerns, limited access to new technologies, and a lack of investment could constrain output growth.

Climate change brings about unpredictable weather patterns and extreme events that affect cereal crops. Increased temperatures, changes in rainfall patterns, and the prevalence of pests and diseases disrupt traditional farming practices. Adaptation and mitigation strategies are therefore essential to sustain cereal production and efficient resource utilization is vital in meeting growing population rates.^[5–7]

Assessing the potential impact of extreme weather, scientists have found that in the case of the United States, nearly all its wheat reserves will be depleted after 4 years in both scenarios of a 2 °C and 4 °C temperature increase, while global stocks could drop by 31%.^[8] Additionally, countries such as Argentina, Brazil, and China could be losing 7.9–17.8% of their corn yields with a 2 °C

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temperature increase and 19.4–46.5% loss with a 4 °C temperature increase (Fig. 1).^[9]

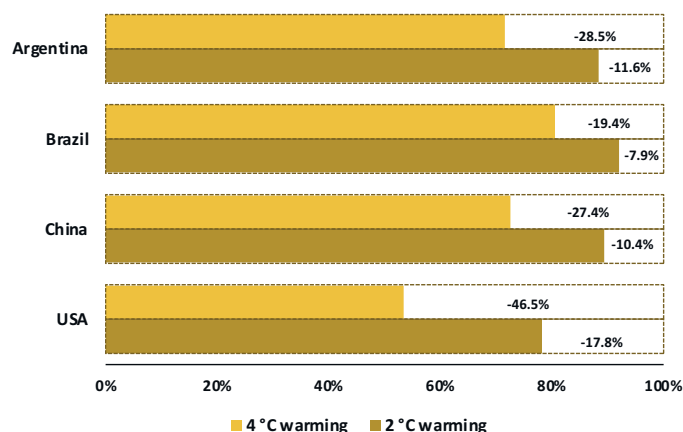


Fig. 1. Corn production projections under different global warming scenarios.

In the coming years, cereal production will continue to be dominated by food demand closely followed by feed use. In 2032, 41% of all cereals will be directly consumed by humans, while 37% will be used for animal feed. Biofuels, among others, are projected to account for the remaining 22%. Increased global consumption of cereals for feed is expected to be dominated by corn (1.3% p.a.), followed by wheat (0.9% p.a.) and other coarse grains (0.6% p.a.) over the next decade. Consumption of cereals for food is expected to increase at a slower rate than in the previous decade.^[10]

To ensure sustainable cereal production, adaptation and mitigation strategies are imperative and should be integrated and implemented, while minimizing the environmental impact. As shown by life cycle assessments, there is a substantial carbon footprint generated by grain production: 0.2–0.7 kg CO₂ equivalent per kg of cereal.^[11] This underscores the urgent need to examine potential solutions and emphasizes the importance of efficient resource utilization, where the whole crop should be used in a more efficient way without compromising health and safety aspects. Valorization of the cereals side streams can also partially offset the CO₂ already generated and minimize land use, while enhancing productivity, sustainability, and resilience for human and animal nutrition.

The increase in cereal demand is paralleled by a continuous growth in animal farming. Most of the past decades, the sector's growth took place in large-scale, specialized monogastric farms, and this trend can be expected to continue. Importantly, the whole livestock industry is responsible for about 14.5% of global greenhouse gas emissions (e.g. methane and nitrous oxide).^[12] Hence, different approaches aimed at reducing the environmental impact of animal farming and making food systems more circular should be implemented.

Globally, ruminants (e.g. cows and sheep) and monogastric animals (e.g. pigs and poultry) consume on average about 2–3 kg of human-edible feed protein to produce 1 kg of edible animal protein.^[13] At present, most of the compound feed is provided by intact cereal grains (64%), with a limited contribution by intact oil seeds and legume seeds (2%).^[14] Such distribution is critical in the context of animal-human competition and global food security.

Currently, given the global environmental situation and the cost of feed, companies are constrained to re-evaluate and improve feed efficiency. Advancements in raw materials may result in new feedstocks that could change the entire approach to feed

formulation. This is no longer a concern only for monogastric animals. Inexpensive feed options traditionally given to ruminants are limited and the future alternative is a carefully formulated feed aimed for greater efficiency in both monogastrics and ruminants.^[15]

Animal diets addressing circularity should contain much less cereals and soybean meal and include a higher proportion of diverse co-products, residues, and human-inedible ingredients (Table 1). The composition of animal feed would therefore be modified with respect to the characteristics of the available co-products, including a decrease in energy and nutrient density, starch content, and an increase in crude fat, fiber, and phosphorous content. In return, this should have consequences on feed intake, digestive processes, microbiome, and bioavailability of nutrients for the animals. It is imperative to adapt the existing practices to address the possible challenges with modified diets. Introduction of precision nutrition is one of the most promising approaches to achieve desired animal performance without compromising the quality of meat, milk, and overall N-efficiency, even in the case of reduced dietary input.^[16]

With the nutrient requirement not precisely met throughout most of the animal production, a depression in growth (in the case of under supply) or inefficient use of nutrient (in the case of over supply) is probable and costly for the animal industry. Introduction of precision nutrition for broilers, when nutrients are under and over supplied throughout production, showed a great potential to remove the under and over-feeding downsides, which is apparent in standard feeding diets.^[17] Further, a modest reduction in excessive nutrient levels within the diets can significantly reduce the potential for environmental pollution. As an example, a slight decrease of less than 2% in crude protein content in broiler diets resulted in an impressive 18% reduction in litter nitrogen content.^[18] Replacing cereals and soybean meal with human-inedible byproducts in dairy cows demonstrated an increased net food protein production without lowering milk production.^[19] Furthermore, 12% inclusion of wheat bran in dairy cows showed improvement in oxidative status of cows, milk quality, shelf-life, and functional properties of cheese.^[20] However, the potential use of crop processing side streams for monogastrics is much lower due to their limited ability to digest feedstuffs with high fiber contents.

Applying the maximum substitution potential of food-competing feedstuffs with byproducts could free up to 26 million tons of protein for humans, corresponding to 11% of the current global food supply. When also considering crop residues as potential replacement materials, up to 28% of cereal feed use could be replaced. When applying world average yields for the replaced feed crop groups, the replacement would free up to 54 million ha. of cropland. If also considering crop residues as replacement materials, this would free more than 100 million ha. of cropland, corresponding to 7% of the world total arable land use in 2018.^[21]

The adoption of resource-efficient strategies of crops, especially *via* the upcycling of cereal processing side streams is essential in securing sustainable and resilient global food and feed supply chains. These approaches that embrace the principles of circular economy offer a path forward in the multidimensional interplay between food security, climate change, and environmental sustainability.

3. Cereals Composition and Processing Methods

3.1 Cereal Composition

Cereal grains are organized microstructures composed of three main components: the bran, the endosperm, and the germ/embryo (Fig. 2). The endosperm, which is the largest part of the grain (70–85%), is made up of storage cells containing starch granules

Table 1. Main forms of industrial food processing and derived co-products available for use in monogastric animal feed in Europe.^[22]

Industry	Raw Materials	Main Products	Co-products
Grain milling	Cereal grain	White flour	Wheat and rice brans
Sugar production	Sugar beet	Sugar	Pulp, molasses
Starch production	Corn, Wheat	Starch	Corn and wheat gluten feed, gluten meal, germ meal
	Potato	Starch	Potato protein, potato pulp
Ethanol production	Cereal grains	Ethanol	Dried distillers' grains, condensed distillers soluble
Brewing	Barley	Beer	Brewers' spent grain
Fruit processing	Citrus fruit	Juice	Citrus pulp
Industrial fermentation	Sugar, molasses	Alcohol, additives	Microbial biomass, single-cell proteins
Oil crushing	Oil seeds	Vegetable oils, biodiesel	Oil seed meal and cake, e.g., of soybean, rapeseed, sunflower seed, palm kernel, linseed, olives, groundnut
Slaughter and rendering	Animal carcasses	Meat and animal products	Processed animal proteins, feather meal, animal fat
Gelatin production	Hides, bone	Gelatin	Animal fat, dicalcium phosphate
Dairy industry	Milk	Dairy products	Whey products, skimmed milk powder
Food industry	Manufactured food	–	Processed former foods, e.g. bread and biscuit waste

embedded within a matrix of proteins and carbohydrates.^[22] The bran consists of the outer layers of the grain (pericarp, seedcoat, and aleurone) and makes up 10% to 20% of the whole grain. The bran is rich in carbohydrates, mainly non-starch polysaccharides such as cellulose and hemicellulose that are intertwined with lignin and proteins. The germ/embryo, the minor part of the grain (1–4%), contains mainly proteins, lipids, and vitamins.

Whole grains are rich in both soluble and insoluble fibers (60–80%) including cellulose, arabinoxylans, β -glucans, proteins (5–7%), lipids (0.5–5%), vitamins (niacin, riboflavin, vitamin A, E and K) and minerals (calcium, magnesium, potassium, and iron) (Fig. 3).^[23–26] In most cereals, the content of cellulose (30–45%) in straws and husks is higher than that of hemicellulose (10–35%). In contrast, the content of hemicellulose (>30%) in most cereal brans is more than double that of cellulose, making cereal brans an excellent raw material for hemicellulose valorization (mainly arabinoxylans and β -glucans).^[27] A high hemicellulose content is also found in corn cob, corn stover, barley husk, and barley straw.

3.2 Cereal Processing Methods

Cereals are commonly processed using a range of operating techniques aimed at enhancing grain digestibility and maximizing the bio-accessibility and absorption of nutrients. As a result, a wide range of residues (e.g. straw, corn stover and silk, bran, germ, husk, and hull) is generated.^[28,29] The structure and composition of these byproducts are contingent on the specific grain cultivar, the degree of refinement, and the type of processing utilized. The most prevalent processing techniques are cleaning, dry and wet milling, pearling, and malting.

Cereals are first cleaned prior to processing the grains to remove the impurities and immature grains. Dry and wet milling, which include successive grinding and sieving operations, enable the isolation of the starchy endosperm from the germ and the outer

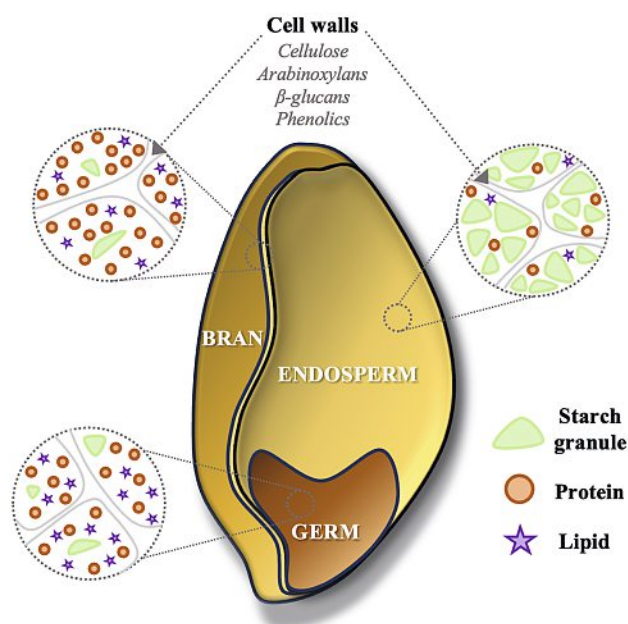


Fig. 2. Schematic representation of the structure and composition of a cereal grain.

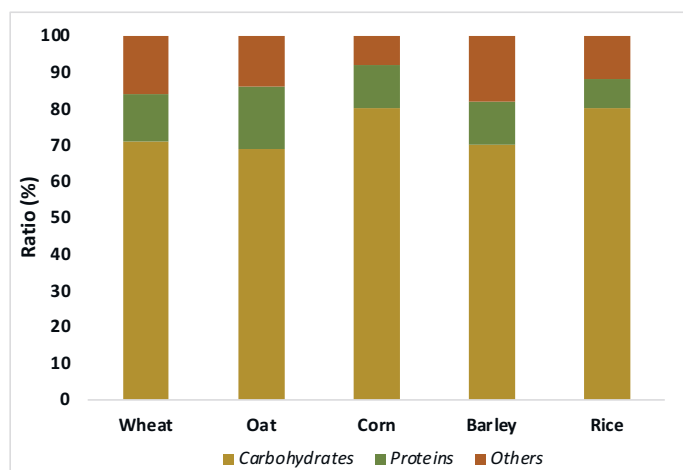


Fig. 3. Average composition of the main cereal grains produced worldwide. Others refer to lignin, lipids, phenolics, vitamins, and minerals.^[24–26]

layers of the grain. Pearling involves the removal of the germ and seedcoat to obtain polished and refined grains. Malting comprises steeping, germination, and kilning steps, during which the fermentable saccharides are hydrolyzed by specialized enzymes, generating spent grains as a byproduct.

Different byproducts are generated at various stages of processing, depending on the variety of cereal and the intended use for which they are being processed.^[28] For instance, milling is commonly used to extract the starchy endosperm fraction from corn, which is then used for flour production. Besides corn bran and gluten meal side products, corn germ meal is also produced as secondary byproduct of the oil extraction process from corn germ. In the same vein, due to its high lipid content, rice bran is used for oil production, which generates defatted rice bran as secondary side stream. Brewers' spent grain (BSG), which comprises the hull of the barley grain, the seedcoat layers, and endosperm residuals, is the main byproduct of the brewing industry, accounting for over 85% of the total brewing waste generated.^[30]

The common removal of the starchy endosperm from grains alters the compositional profiles of the generated byproducts (Fig. 4).^[27,31–34] While carbohydrates remain the dominant components (>40% in most cereal bran and up to 70% in corn cob), these are mainly made of cellulose and hemicellulosic compounds (arabinoxylans and β -glucans), while starch is a minor component. The content of proteins varies significantly depending on the cereal processing side products, where proteins as low as ~3% in corn cob and as high as ~25% in BSG are measured.^[27,31,33,34] The content of phytochemicals (*e.g.* lipids, lignans, phenolic acids, vitamins, *etc.*) is usually higher compared to the whole grain, reaching up to ~41% in rice bran.

4. Nutritional Value and Health Benefits of Upcycled Cereal Byproducts

4.1 Carbohydrates

In an effort to minimize processing wastes, the food and feed industries have explored various means of improving the overall nutritional value of food and feedstuffs, primarily by increasing their dietary fiber content. Dietary fibers refer to non-starch polysaccharides (cellulose, arabinoxylans, and β -glucans) that are slowly or undigested by the endogenous enzymes in the small intestine of humans and animals.^[35] This leads to an enhancement of digestive health through the regulation of gut microflora. In this context, leftover materials from cereal processing are often directly repurposed to provide additional dietary fiber in the feed industry for animals like pets and livestock (*e.g.* cattle, sheep,

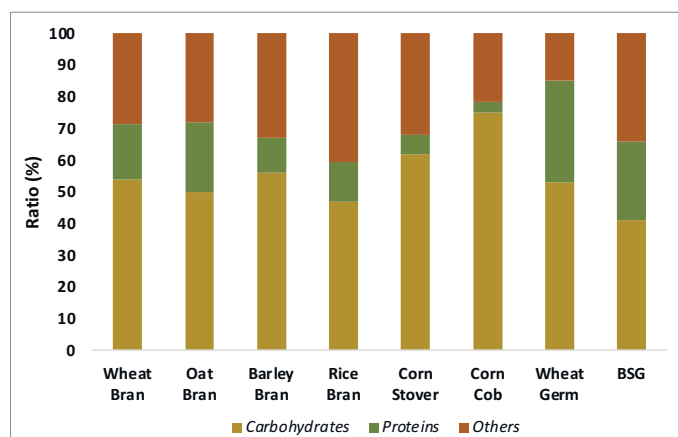


Fig. 4. Average composition of common cereal processing byproducts. Others refer to lignin, lipids, phenolics, vitamins, and minerals.^[27,31–34]

pigs, and chickens).^[36] Companies such as Purina and RiceBran Technologies exemplify this practice by incorporating nutrient-dense components like rice bran and germ into their livestock and pet feed. Nature's Best Organic Feed relies on cereal brans and meals as a nutritional foundation for livestock feed, while Portland Pet Food Company repurposes cereal byproducts to produce pet treats.

Leftover materials from cereal processing can also find versatile applications as ingredients in the food industry by being incorporated in breakfast cereals, snacks, pasta, and baked goods.^[34,36,37] This enriches the nutritional profile of these products by adding fibers, proteins, vitamins, and minerals. Corporations including Quakers, Kellogg's, and General Mills reuse cereal brans from oat, wheat, and rice to create breakfast cereals fortified with dietary fibers, potentially conferring health benefits such as reduced risk of heart disease. Healthy Valley and Oatwell specialize in producing oat bran flakes, while Nature's Path incorporates oat and wheat brans in the production of snacks. Rise Products, BiaSol, Grainstone, Grain4Grain, and Susgrainable, among others, focus on transforming leftover BSG into high-fiber (30–46%) and protein-rich (18–30%) flours. ReGrained and Brewbee repurpose BSG into nutritious snacks, while Canvas upcycles BSG to craft beverages enriched with dietary fibers and proteins. Nevertheless, it is noteworthy that the physicochemical properties of cereal byproducts, such as particle size, swelling capacity, and viscosity can affect the sensorial characteristics and technofunctional properties of the food preparations such as protein solubility, emulsifying capacity, and foaming properties.^[38] Consequently, this may restrict the extent to which these byproducts can be included in the food formulations. For example, surpassing 10% inclusion of BSG in bread or 30% of cereal bran in pasta can negatively alter their textures and flavors, reducing their sensory appeal and overall consumer approval of these products.^[36]

As an alternative approach with higher-added value, essential nutrients can be extracted and isolated from cereal byproducts to generate food and feed supplements that can exert significant health benefits. Arabinoxylans, found abundantly in most cereal byproducts (up to 40% in corn bran), have gained substantial recognition for their nutritional and physiological benefits.^[39] Arabinoxylans consist of β -(1,4)-linked D-xylose backbones, which are monosubstituted and/or disubstituted at the C(O)-3 and/or the C(O)-2 positions with monomeric α -L-arabinose side chains. The arabinoxylans structures can substantially differ depending on the nature of the grain and the location of the cell tissues. Corn and rice have more complex arabinoxylans structures than wheat and barley grains, where additional xylose, galactose and glucuronic acid are bound to the primary arabinoxylans.^[40]

Further, higher degree of substitution of arabinose to the xylose backbone has been reported for the wheat endosperm compared to the bran tissues. These structural differences are of paramount importance, where both the molecular weight and degree of arabinose substitution to the xylose backbone are key characteristics that direct arabinoxylans bioactivity.^[39] Indeed, high molecular weight arabinoxylans can induce antinutritional effects due to their viscous nature, hindering the optimal digestion and absorption of nutrients in the gastrointestinal tract.^[41] Chemical and enzymatic hydrolysis of arabinoxylans can mitigate these antinutritional effects by producing shorter chains known as arabinoxylan-oligosaccharides (AXOS) and non-substituted xylo-oligosaccharides (XOS), which can confer prebiotic benefits to the host.^[39,42]

Prebiotics are non-digestible ingredients in the small intestine that beneficially impact the host by selectively stimulating the activity and/or growth of bacteria in the colon, thereby improving the host health. Supplementation from 20 mg to 1 g per kg of body weight per day for up to 42 days of (A)XOS with low degree of polymerization (usually between 2 to 10 units) has been shown to modulate the composition of the colonic and cecal microbiota by promoting beneficial bacterial populations such as *Bifidobacterium* and/or *Lactobacillus* species (Table 2).^[39] Both *in vitro* and *in vivo* studies have demonstrated that fermentation of (A)XOS by these beneficial bacteria gives rise to the production of short chain fatty acids (SCFA) including acetate, propionate, and butyrate. These are metabolites involved in the regulation of the intestinal transit, the good function of the colonic epithelial cells, the inhibition of pathogenic bacteria, and overall contribute to welfare of humans and animals. Due to its high content of arabinoxylans (>30%), corn cob is often the preferred raw material

to produce XOS by companies such as Heagreen, Suntory, and Shandong Longlive BioTechnology.

Prebiotics are of particular interest as feed additives for livestock, since they play a pivotal role in maintaining a balanced gut microbiome, which is crucial for managing digestive stresses and disorders.^[39,42] Simultaneously, they enhance the absorption of essential nutrients, resulting in improved feed efficiency. This leads to reduced feed costs and overall boosts productivity. Prebiotics can also bolster the immune functions by diminishing the likelihood of infections and diseases caused by pathogens, which consequently reduces the dependence on antibiotics.

In addition to arabinoxylans, the technological prospects and health benefits of β -glucans have also attracted considerable attention. β -glucans are made of β -D-glucopyranosyl units bound by β -(1 \rightarrow 4) and β -(1 \rightarrow 3) linkages and are mainly found in the oat and barley bran fractions (5–20%).^[37] High viscosity is a hallmark of β -glucans, making them an effective thickening agent and a valuable source of dietary fiber in the formulations of beverages, dairy products, and baked goods.^[43] Their physiological properties have also been linked to numerous health benefits such as regulation of the glycemic index and reduction of the LDL cholesterol levels.^[44–48] In particular, due to their gel forming ability with gastrointestinal fluids, β -glucans can delay digestion by endogenous enzymes and absorption of sugars in the bloodstream, enabling a more gradual release and uptake of glucose and a lower insulin response.^[44,47,48]

The mechanism by which β -glucans decrease the LDL cholesterol levels is linked to the regulation of the bile acid metabolism.^[45,46,48] Viscous β -glucans can entrap bile acids, which are then excreted in feces, thus preventing their re-absorption in the small intestine. This promotes the synthesis of new bile acids

Table 2. Physiological effects on humans and animals of bioactive ingredients extracted from cereal byproducts.^[40,48,51,52,55]

Target Compounds	Raw Feedstocks	Structural Features	Hosts	Dose/Period	Physiological Effects and Properties
Arabinoxylans	Corn bran and husk, wheat bran, BSG	Ratio arabinose/xylose \approx 0.6–0.8	Humans, rats, and mice	Dose: \approx 50 to 200 mg per kg of body weight per day Time: 1 to 42 days	Increased fecal frequency, reduced ammonia levels in feces, prebiotic effects, reduced serum glucose and cholesterol levels, anticarcinogenic effects
(A)XOS	Corn cob, wheat bran, BSG	DP2 to DP61 Ratio arabinose/xylose \approx 0.1–0.7	Humans, rats, and chicken	Dose: \approx 20 to 820 mg per kg of body weight per day Time: 1 to 42 days	Reduced ammonia levels in caecum, <i>p</i> -cresol levels in feces, serum glucose and triglycerides levels, lipid peroxidation in serum and liver, increased antioxidant capacity in liver, prebiotic effects
β -glucans	Oat bran, barley bran	MW \approx 10 ² kDa–10 ³ kDa	Humans and mice	Dose \approx 40 to 170 mg per kg of body weight per day Time: 2 to 12 weeks	Hypoglycemic and hypocholesterolemic activities, prebiotic effects
Protein hydrolysates/Peptides	Rice bran, wheat bran, BSG	Dipeptides to pentapeptides Protein hydrolysates with MW \approx 3 kDa–50 kDa	<i>In vitro</i> trials	N.A.	Antioxidant, anti-inflammatory, anticarcinogenic, hypoglycemic and ACE inhibitory effects, inhibition of α -glucosidase, and α -amylase activities
Phytochemicals	Rice bran	Ferulic acid, γ -oryzanol, tocotrienols, and tocopherol	Humans, rats, and mice	Dose: \approx 0.5 to 10 mg per kg of body weight per day Time: 5 weeks	Anticarcinogenic and hypocholesterolemic effects

in the liver from cholesterol, leading to a reduction in its overall levels. Research studies have also shown that β -glucans can interfere with the absorption of lipids, slowing down and/or diminishing the processes involved in serum lipid hydrolysis and metabolism.

Similar to (A)XOS, β -glucans can also elicit prebiotic effects that improve intestinal barrier functions, boost the immune system, and lower intestinal inflammations, all factors which are able to minimize the risk of developing metabolic diseases (e.g. diabetes, cardiovascular diseases, and colon cancer).^[49] The physicochemical properties (i.e. molecular weight and solubility) of β -glucans govern their bioactivity since they directly influence the digesta viscosity. It is generally concluded that high molecular weight β -glucans are more likely to elicit greater beneficial health effects due to their higher gelatinization capacity. The potential of β -glucans is harnessed by Nurture, who commercially prepares the extracts from oat and barley brans with amounts of up to 54% that are destined to dietary supplements, functional foods, and nutraceuticals.

4.2 Proteins

Aside from carbohydrates, cereal byproducts are abundant in proteins (up to 25%), which are essential nutrients that play a key role in regulating various physiological functions in humans and animals.^[50,51] The proteins present in cereal processing side streams are efficiently metabolized and can be a valuable source of added essential amino acids in food and feed formulations. For example, BSG proteins contains up to 30% of essential amino acids, with lysine being one of the most abundant (~14%).^[50] Rice bran proteins are made of up to 40% essential amino acids and their distinctive hypoallergenic nature renders them suitable for dietary support in the context of food restrictions and allergies.^[51] In addition to their nutritional benefits, proteins derived from cereal byproducts also possess important technofunctional attributes such as emulsification and foaming capabilities, solubility, turbidity, and water absorption capacity.^[50] These characteristics play a pivotal role in formulating diverse products in the food industry.

Cereal byproducts are also a reservoir for bioactive proteins and peptides with significant potential for a wide range of health benefits.^[51,52] The key factors influencing their effectiveness include the specific grain cultivar and their structural features, where the degree of hydrolysis, molecular size, and amino acid profiles are intimately linked to their biological functions. Notably, a growing body of work has focused on bioactive peptides derived from rice bran proteins, where the hydrolysis of albumin generates peptides with enhanced immune functions.^[51] Considering that the content of albumin in the bran is six times higher than that in the refined rice, this highlights the tremendous potential of cereal byproducts as a valuable source of physiologically active compounds. Protein hydrolysates and peptides extracted from BSG further demonstrate these prospects, where they possess antimicrobial and antioxidant properties, which can have the potential to alleviate health disorders linked to the production of free radicals such as diabetes, cancers, and cardiovascular disorders, among others.^[50-52] The mode of action lies in their ability to reduce or even eliminate free radicals by directly scavenging reactive oxygen radicals, inhibiting lipid peroxidation, or chelating metal ions.

Bioactive peptides can also elicit antihypertensive effects, owing to their ability to inhibit the angiotensin converting enzyme (ACE), which can relax constricted blood vessels and lower blood pressure.^[51] It is noteworthy that *in vivo* trials conducted on rats showed that peptides isolated from rice bran displayed the same ACE inhibitory effect than the synthetic captopril drug, while exhibiting no cytotoxicity to the hosts. ACE inhibitor peptides have therefore the potential to be safe alternative therapeutics for the prevention and treatment of hypertension.

Protein hydrolysates can also help with diabetes management by limiting the enzymatic breakdown of dietary starch by α -amylase and α -glucosidase.^[50-52] The inhibition and/or diminution of the activity of these enzymes hampers the glucose release in the bloodstream. Further, *in vitro* studies have also demonstrated the remarkable potential of cereal bran peptides to combat diverse cancers by displaying inhibitory activity against the proliferation of more than 80% of colon, liver, and breast cancer cells.^[51]

4.3 Phytochemicals

Cereal byproducts contain essential phytochemicals such as tocopherols, phytosterols, carotenoids, polyunsaturated fatty acids, phenolics, vitamins, and minerals, among others.^[28,53] Most phytochemicals have antioxidant capacity and have the potential to mitigate oxidative stress and inflammation. Among the array of phytochemicals, phenolics have captured substantial interest due to their antioxidant, anti-inflammatory, antimicrobial, and anticarcinogenic properties.^[28] It should be emphasized that the majority (>70%) of phenolics are concentrated in the outer layers of cereal grains such as the bran, further underscoring the prospects of upcycling cereal processing side streams. The most common phenolic compounds in cereal byproducts are phenolic acids, which include hydroxybenzoic (e.g. gallic acid and vanillic acid) and hydroxycinnamic acids (e.g. ferulic acid, sinapic acid and coumaric acid).^[28] Other phenolic compounds present in cereal byproducts comprise flavonoids (e.g. catechin) and lignans. Phenolics including ferulic acid and caffeic acid present in rice and wheat brans have demonstrated promising antiproliferative activities against colon and breast cancer cells.^[51] Phenolics extracted from BSG have also shown anticarcinogenic effects in addition to immunomodulatory and anti-inflammatory activities.^[54] Wheat bran phenolics can elicit antibacterial activities against pathogenic strains.^[28] It is also worth noting that the lipid fraction of rice bran is also rich in antioxidants such as tocotrienols, γ -oryzanol, and tocopherols.^[28] Swanson is a company that commercializes supplements rich in phytochemicals sourced from antioxidant-rich rice bran oils and a proprietary blend of modified rice bran to regulate and support the immune system.

5. Extraction and Isolation Methods

In cereal byproducts, cellulose, hemicellulose, proteins, lignin, and phenolics form a complex intertwined structure linked together *via* glycosidic, ester, and hydrogen bonds that is often recalcitrant to aqueous extraction (Table 3).^[27,40,56] Hydrothermal extractions at mild temperatures (<100 °C) can preserve the native state of the extracted hemicellulose compounds (arabinoxylans and β -glucans) and proteins but is unable to break the chemical cross-linkages between lignocellulose materials, leading to low extraction yields even at prolonged processing times. Higher operating temperatures (>100 °C) enable more efficient and rapid extraction kinetics and therefore result in increased yields. The higher the temperature and pressure of the hydrothermal treatment are, the easier water molecules can penetrate biomasses to hydrate and depolymerize the lignocellulosic and protein matrix. Despite being environmentally safe, hydrothermal treatments are poorly specific, leading to mixtures of various compounds, low control over the molecular weight of the extracts, the degree of branching, and can also lead to poor quality proteins due to their denaturation and/or aggregation.^[56]

An alternative extraction strategy is to use chemical reactions either in alkali (e.g. NaOH, KOH, Ba(OH)₂, Na₂CO₃, and NH₄OH) or acid (e.g. HCl, H₂SO₄, acetic and formic acid) solutions.^[27,40,56] Under alkali conditions, hydroxyl ions (OH⁻) disrupt the hydrogen bonds between lignocellulosic components and proteins, thus promoting solubilization. Acids hydrolyze the covalent bonds (peptide and glycosidic bonds), which results in depolymerization of the biomasses to smaller molecular weight compounds

Table 3. Extraction methods and conditions applied to various cereal byproducts to extract target molecules.^[27,40,56]

Extraction Methods	Raw Feedstocks	Targeted Compounds	Extraction Conditions
Hydrothermal	Corn cobs, wheat straw and bran, barley straw, rice husks, BSG	(A)XOS, proteins, phenolics	Medium: water Temperature: 25 °C–190 °C Time: 20 min–48 h
Alkaline	BSG, corn bran, rice bran, wheat bran	Phenolics, (A)XOS, hemicellulosic compounds	Medium: NaOH, Na ₂ CO ₃ , NH ₄ OH Temperature: 20 °C–120 °C Time: 90 min–24 h
Acid	Wheat bran, corn bran, and corn silk	Phenolics, hemicellulosic compounds	Medium: H ₂ SO ₄ , HCl Temperature: 85 °C–100 °C Time: 80 min–20 h
Solvent	BSG, corn bran, rice bran, wheat bran, defatted oat bran	Phenolics, hemicellulosic compounds	Medium: Methanol, Ethanol, Acetone, hexane, ethyl acetate, water Temperature: 20 °C–80 °C Time: 1 min–several hours
Enzyme	Rye bran, rice bran, corn husk and corn cob, BSG, wheat bran	Phenolics, lignans, proteins, peptides arabinoxylans, dietary fiber, fatty acids	Medium: Water Enzymes: xylanase; amylase, cellulase, alcalase, trypsin, papain, flavourzyme, neutrase, protamex, feruloyl esterase, Temperature: 37 °C–50 °C Time: 15 min–4 h
Supercritical fluid	Rice bran, oat bran, rye bran, wheat bran and germ, corn cob and germ, BSG	Phenolics, vitamins	Medium: CO ₂ Temperature: 35 °C–90 °C Pressure: 100 bars–550 bars Time: 10 min–4 h
Ultrasounds	Wheat bran and germ, defatted oat bran, rice bran, BSG	Phenolics, β-glucans, proteins, peptides	Medium: Water, ethanol, NaOH Temperature: 20 °C–80 °C Time: 5 min–2 h Power: 24–600 W
Microwaves	Wheat bran, germ, and straw, corn germ and bran, rice husk, BSG	Phenolics, lignin, (A)XOS	Medium: Water, methanol, ethanol, NaOH or H ₂ SO ₄ Temperature: 60 °C–210 °C Time: 30 sec–40 min

(oligosaccharides, monomeric sugars, (poly)peptides, and amino acids). Though this approach is straightforward, harsh conditions using strong acids or bases can degrade saccharides and amino acids and generate toxic chemical residues (*e.g.* HMF and furfural) or undesirable side reactions (*e.g.* Maillard reactions), which ultimately can affect the nutritional quality and application potential of the extracts.

Enzyme based hydrolyses are more environmentally benign than the chemical approaches for extraction, where they are conducted in aqueous solution at mild temperatures (<70 °C).^[56] Importantly, the enzymes are substrate specific, leading to the targeted solubilization and enzymolysis of the compounds of interest without generating toxic side reactions and with minimal side products. For these advantageous reasons, enzymatic treatments of cereal byproducts with various carbohydrases (*e.g.* cellulases, xylanases, arabinofuranosidases, glucanases, and amylases), proteases (*e.g.* alcalase, flavourzyme, trypsin, neutrase, and protamex), and esterases (*e.g.* feruloyl esterase) are commonly used for hydrolyzing carbohydrates, proteins, and phenolics to produce bioactive oligosaccharides (*e.g.* (A)XOS and β-glucans), (poly)peptides, and phenolic compounds.

In order to increase the processing efficiency and specificity of the extracts, the conventional hydrothermal, chemical, and enzymatic extraction methods can be used in conjunction with mechanical techniques such as milling or more elaborate processes including pressurized liquid, supercritical fluid, microwaves, and ultrasound-assisted extractions.^[56] Most of these procedures cause physical and/or chemical breakdown of the recalcitrant molecular linkages within biomasses. This facilitates the impregna-

tion of water/organic solvents, promotes enzyme accessibility to the target molecules, and amplifies the rate of diffusion and mass transfer during the extraction processes. They also shorten the reaction times and lower the amount of solvents required.

Besides the target molecule(s), other compounds are often co-extracted due to their inherent interconnected nature within the raw biomasses. Therefore, there is often a need for purification steps to ensure the removal of impurities, contaminants, and undesired side products.^[27,55] This is a crucial step as these can alter the potency of the extracts and may render them ineffective or even harmful for their intended applications. Moreover, purification enhances the consistency and reliability of the final products, which is key for applications where precise dosage and quality control are imperative.

Isolation of the target hemicellulosic and phenolic compounds relies on fractionations and purifications procedures, often using precipitation with organic solvents (*e.g.* ethanol, methanol, and acetone) or membrane-based methods.^[40] Purification of bioactive proteins and peptides can be achieved by various techniques, including salting out, solvent extraction, ultrafiltration, reversed-phase chromatography, gel filtration techniques, size exclusion chromatography, and ion-exchange chromatography.^[55]

6. Bottlenecks and Perspectives of Upcycling Cereal Byproducts

With the escalating quantities of yearly-generated cereal agro-industrial wastes, there is an urgent need for their reuse and revalorization. Discarded cereal byproducts represent an important loss

of valuable nutrients and significantly contribute to the production of greenhouse gas emissions. For example, each ton of BSG alone used as landfill material or animal feed releases over 500 kg of CO₂ equivalent.^[57] With the heightened societal awareness of the importance of sustainability and circular economy, upcycling cereal byproducts holds great promises for alleviating the issues related to the waste management of the processing side streams.^[2] Corporations are recognizing and capitalizing on this emerging opportunity by developing innovative strategies designed to extract the functional and bioactive ingredients locked in cereal byproducts to generate high-added value products. Moreover, companies are also placing greater emphasis on evaluating the environmental impact and conducting life cycle assessments of their upcycling strategies as part of their marketing endeavors. For example, ReGrained promotes the nutritional benefits of their products derived from BSG, while also highlighting their eco-conscious production process that reduces CO₂ emissions and conserves water.

While upcycling biomasses to generate functional ingredients holds great potential for widespread applications, their industrial implementation remains challenging. Although essential for isolating bioactive compounds with high purity, conventional extraction and purification procedures have several drawbacks. They are often tedious, time-consuming, and entail the use of costly, and at times, volatile or even toxic reagents.^[56] Given these demanding aspects in terms of time and cost, it becomes imperative to invest greater efforts in developing more efficient, sustainable, and eco-conscious extraction and purification technologies. This is crucial to establish scalable and cost-effective procedures that can make the valorization of cereal byproducts more practical and viable for industrial applications.^[2]

Importantly, the single ingredient extraction strategy often generates low yield products and invariably creates side streams that are not revalorized. In addition, the costs associated with such approach can be higher than simply resorting to the landfill or animal feed repurposing of cereal byproducts and the extraction and isolation procedures can be more environmentally impacting than those based on conventional reuse options.^[58] As an alternative solution, there is a valuable opportunity in adopting a non-targeted approach that exploits the intrinsic multicomponent nature of cereal byproducts. Combining the diverse bioactive components within biomasses could lead to the generation of products that elicit complementary or even synergistic nutritional and/or biological benefits. This approach, therefore, would enable maximizing the revalorization potential of the nutritional and health promoting ingredients of cereal byproducts, and would reduce the downstream processing requirement (e.g. separation and purifications steps) and generation of byproducts to a minimum. As an example, the amalgamation of phenolics and hemicellulose derived compounds has demonstrated the ability to hold both prebiotic and antioxidant properties in both *in vitro* and *in vivo* settings.^[59,60] Embion Technologies is a Swiss biotech startup founded in 2016 that has developed a breakthrough biomass hydrolysis platform to upcycle agricultural and food industry by-products into high-value functional ingredients. Embion's proprietary ionic polymer catalysts unlock the nutritional value of non-edible biomasses through precision hydrolysis, converting waste streams into sustainable ingredients with superior performance.^[61] The first product, Prembion™, transforms brewers' spent grains into a prebiotic animal feed ingredient that improves gut health and feed efficiency in livestock. Extensive field trials have demonstrated its efficacy as a natural alternative to antibiotics. With patent-protected IP and regulatory approval for the EU, Embion is now launching Prembion in the European animal feed market through established industry partners. Trials on animals have demonstrated the potential of using these bioactive ingredients to efficiently boost animal productivity, while supporting the

immune system, gut health, and overall improving the welfare of animals.

7. Conclusions

Incorporation of cereal processing byproducts into the food and feed supply chains represents a significant opportunity within the framework of circular economy. In particular, the extraction of valuable nutrients and bioactive compounds from these byproducts holds great promise for catalyzing innovation across various industrial sectors. It is imperative to prioritize the design and development of versatile, sustainable, scalable, and economically viable processing technologies for upcycling cereal byproducts. This will ensure food security in a world where resource optimization has become paramount to meet the ever-increasing global food and feed demands.

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