Whole Grains in Amelioration of Metabolic Derangements

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Abstract

Daily diet influences whole body metabolism, and intricately linked to the prevention or progression of metabolic diseases including obesity, diabetes and cardiovascular diseases. Several epidemiological and large scale studies have shown that diets enriched with whole grains improves metabolic function and protect from the development of metabolic diseases. Direct impact of whole grain diet can be mediated on several levels of metabolic functions i.e. reduced glycemic index, improved fat oxidation potential, increased cholesterol clearance or decreased cholesterol biosynthesis and modulation of gut microbiome. In this article we reviewed several studies indicating the beneficial effects of whole grain diets on metabolic functions, as well as discussed the potential active phytochemicals present in these whole grain foods to contribute in modulation of metabolic function in our body.

Keywords: Whole Grain; Diabetes; Obesity; Metabolism; Fat; Phytochemicals; Nutrition; Microbiome; Metabolic Diseases;

Introduction

The sharp spike in the prevalence and severity of obesity, type 2 diabetes and metabolic syndrome is a chief concern for society as a whole [1]. Obesity is characterized by the accumulation of excess fat in the adipose tissue. At its core, the obesity epidemic stems from an excess of energy intake compared to energy expenditure [1]. Thus, consumption of “healthy” diet is a critical to curtailing the dual epidemics of obesity and type 2 diabetes. Currently, a tremendous amount of research worldwide explores the beneficial health effects and nutritional composition of foods that are part of our diet. Not only vitamins and minerals are explored for their promised beneficial properties, but also bioactive phytochemicals in functional foods are of great interest in research. Growing evidence asserts potent roles of phytoconstituents of various functional foods in the amelioration of chronic diseases, including diabetes, obesity and the resultant metabolic syndrome [2, 3].

Whole grains were brought to public attention as research around the world to uncover their beneficial health effects. The 1995 USDA Dietary Guidelines did not specifically recommend the intake of whole grains; however, the 2005 and 2010 guidelines suggested consuming at least 3 ounces of whole grains per day, and ensuring 50% of daily grain intakes come from whole grains [4, 5]. Further, a markedly greater number of whole grain products are available to consume in the current market. The most recent examination of the principal sources of whole grains in the American diet was done by Bachman et al. in 2001-2002 [6]. Wheat is the leading grain in the American diet, and oats, corn, barley, rice, rye, millet and spelt are all consumed in varying proportions [6, 7]. These whole grains are present in many types of foods like breads, pastas, baked goods, tortillas, breakfast cereal and several others.

The broad spectrum of foods that constitute whole grains, coupled with varying definitions of a “whole grain” between organizations, studies and databases renders much uncertainty in the estimation of an individual’s whole grain intake. Regardless of the variance, however, the overwhelming majority of studies assert that majority of population with western food habits do not consume adequate amounts of whole grains. Despite the positive steps taken by governmental agencies and industry, the average Americans still does not consume the recommended amount of whole grains per day [8-10].

Whole Grains

According to the FDA and American Association of Cereal Chemists International, a whole grain is defined as “whole grain consists of the intact, ground, cracked or flaked caryopsis, whose principal anatomical components - the starchy endosperm, germ and bran - are present in the same relative proportions as they exist in the intact caryopsis” [11]. A whole grain may either remain intact, or be reconstituted. A reconstituted whole grain is one in which the components of the whole grain are recombined.
to match relative proportions that are present in the naturally occurring kernel [12]. The overwhelming majority of whole grain products commercially distributed fall under the category of reconstituted whole grains.

The outermost layer of a whole grain is the bran, which contains mainly non-digestible carbohydrates (cellulose, arabinoxylan and others). Function of bran is to protect the inner layers from external environmental stresses. The inner layers of the grain – the endosperm and the germ consist of soluble fibers, resistant starch, vitamins, minerals, and various other phytonutrients (polyphenols and others) [11]. Refining whole grains removes the bran and germ, leaving the endosperm to be processed into white flour (Figure 1). The majority of nutrients and phytochemicals, however, are concentrated in the bran and germ portions of the whole grain [13, 14]. Therefore, many of the key nutrients and phytochemicals, including over 75% of the fibers, are physically removed through the process of refining [15]. Overall, whole grains have higher phytonutrient content, leading to higher antioxidant activity, and more beneficial modulation of glucose and energy homeostasis. Refining wheat loses 83% of total phenolic acids, 79% of total flavonoids, 93% of ferulic acid, 78% of total zeaxanthin, 51% of total lutein, and 42% of total β-cryptoxanthin [16]. Table 1 described major macronutrient composition of the most common whole grains (Table 1).

Epidemiology: Benefits Of Whole Grains In Diabetes And Metabolic Diseases

The epidemiology demonstrating that consumption of whole grains ameliorates obesity, type II diabetes and their resultant complications is fairly consistent. Over the past decade, many large scale studies have reached the conclusion that there exists a significant inverse association between the intake of whole grains and the incidence of type II diabetes [14] and cardiovascular disease in both sexes [17-19]. Kastorini and Panagiotakos reviewed several broad studies exploring whole grains and diabetes [20] and Priebe et al. compiled numerous cohort studies [21, 22]. Phytochemicals present in whole grains may confer potent anti-diabetic/obesity properties. The succeeding sections of this article will review the important phytochemicals part of whole grains, and their role in amelioration of type 2 diabetes and metabolic derangements. However, as the research exploring the specific effects of phytochemicals isolated from whole grains is relatively young, it is important to keep the findings in context until stronger and more mechanistic studies demonstrate their definite role against metabolic diseases. Furthermore, as it has been shown with phytochemicals from fruits, vegetables and other food groups have synergistic effect of whole grain’s phytochemicals that may be responsible for the significant health benefits derived from whole grains.

Whole Grains And Blood Glucose Regulation

Pioneering studies conducted in 1980’s uncovered the role of whole grains in the regulation of glucose homeostasis. Compared to a high glycemic index diet (GI = 90) of potatoes and white bread, a low glycemic index diet (GI = 67) containing bread with whole grains, parboiled wheat, pasta and legumes demonstrated a significantly decreased blood glucose and circulating insulin levels in both normal and diabetic subjects [23]. And compared with a diet using refined grain flour, one using whole grain flour demonstrated a significantly lowered circulating glucose and insulin levels [24]. In 2004, Slavin thoroughly reviews the subsequent studies that substantiated the evidence of association between whole grain intake and beneficial regulation of glucose homeostasis, and in some cases, amelioration of diabetes mellitus [25]. Overall, they reports that consumption of whole grains is inversely correlated with circulating insulin and glucose levels. Interestingly in 2002, Periera et al. showed that there may be enhancement of insulin sensitivity due to whole grain intake [26].

The research about whole grains and metabolic diseases is young, and relatively few phytochemicals are known to beneficially modulate glucose metabolism. Many anti-nutrients, including phytic acid, amylase inhibitors, saponins, phenolics and lectins have been shown to decrease circulating glucose and insulin [25]. Cyanidin, an anthocyanidin with a characteristic reddish-orange color, has previously been shown to reduce blood glucose levels and improve insulin sensitivity due to the reduction of retinol binding protein 4 expression in type 2 diabetic mice [27]. In addition, Takanori et al discovered that cyanidin glucoside from purple corn extract has a potential to ameliorate diabetic complications [28]. Members of the carotenoids, flavonoids, hydroxycinnamic acids, vitamin E, and other phytochemicals that are part of whole grains have also been shown to play beneficial roles in diabetes. β-Cryptoxanthin is an antioxidant, which may help prevent free radical damage to cells and DNA, as well as to stimulate the repair of oxidative damage to DNA. An increased intake of total β-Cryptoxanthin along with other phytochemicals was associated with a reduced risk to type 2 diabetes [29, 30]. Lutein, an antioxidant that is an essential chemical in ocular function, is also found in whole grains [31]. Arnal et al found that a combined treatment with lutein and insulin prevented the development of cataracts in streptozotocin-induced diabetic...
Table 1: Common whole grains and their approximate phytochemical constituents

<table>
<thead>
<tr>
<th>Common Names</th>
<th>Yellow Corn</th>
<th>Brown Rice</th>
<th>Barley</th>
<th>Millets</th>
<th>Sorghum</th>
<th>Teff</th>
<th>Wheat</th>
<th>Oat</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scientific Name</td>
<td>Zea mays</td>
<td>Oryza sativa</td>
<td>Hordeum vulgare L.</td>
<td>Panicum miliaceum L.</td>
<td>Sorghum spp. (Zuccagni) Trotter</td>
<td>Eragrostis tef</td>
<td>Triticum aestivum L.</td>
<td>Avena sativa L.</td>
</tr>
<tr>
<td>Energy (kJ/100 gm)</td>
<td>1527</td>
<td>1548</td>
<td>1481</td>
<td>1582</td>
<td>1418</td>
<td>1536</td>
<td>1423</td>
<td>1628</td>
</tr>
<tr>
<td>Protein (gm/100 gm)</td>
<td>9.42</td>
<td>7.94</td>
<td>12.48</td>
<td>11.02</td>
<td>11.3</td>
<td>13.3</td>
<td>10.69</td>
<td>16.89</td>
</tr>
<tr>
<td>Fat (gm/100 gm)</td>
<td>4.74</td>
<td>2.92</td>
<td>2.3</td>
<td>4.22</td>
<td>3.3</td>
<td>2.38</td>
<td>1.99</td>
<td>6.9</td>
</tr>
<tr>
<td>Carbohydrates (gm/100 gm)</td>
<td>74.26</td>
<td>77.24</td>
<td>73.48</td>
<td>72.85</td>
<td>74.63</td>
<td>73.13</td>
<td>75.36</td>
<td>66.27</td>
</tr>
<tr>
<td>Fiber (gm/100 gm)</td>
<td>7.3</td>
<td>3.5</td>
<td>17.3</td>
<td>8.5</td>
<td>6.3</td>
<td>8</td>
<td>12.7</td>
<td>10.6</td>
</tr>
<tr>
<td>Calcium (mg/100 gm)</td>
<td>7</td>
<td>23</td>
<td>33</td>
<td>8</td>
<td>28</td>
<td>180</td>
<td>34</td>
<td>54</td>
</tr>
<tr>
<td>Iron (mg/100 gm)</td>
<td>2.71</td>
<td>1.47</td>
<td>3.6</td>
<td>3.01</td>
<td>4.4</td>
<td>7.63</td>
<td>5.37</td>
<td>4.72</td>
</tr>
<tr>
<td>Magnesium (mg/100 gm)</td>
<td>127</td>
<td>143</td>
<td>133</td>
<td>114</td>
<td>NR</td>
<td>184</td>
<td>90</td>
<td>177</td>
</tr>
<tr>
<td>Phosphorus (mg/100 gm)</td>
<td>210</td>
<td>333</td>
<td>264</td>
<td>285</td>
<td>287</td>
<td>429</td>
<td>402</td>
<td>523</td>
</tr>
<tr>
<td>Potassium (mg/100 gm)</td>
<td>287</td>
<td>223</td>
<td>452</td>
<td>195</td>
<td>350</td>
<td>427</td>
<td>435</td>
<td>429</td>
</tr>
<tr>
<td>Sodium (mg/100 gm)</td>
<td>35</td>
<td>7</td>
<td>12</td>
<td>5</td>
<td>6</td>
<td>12</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Zinc (mg/100 gm)</td>
<td>2.21</td>
<td>2.02</td>
<td>2.77</td>
<td>1.68</td>
<td>NR</td>
<td>3.63</td>
<td>3.46</td>
<td>3.97</td>
</tr>
<tr>
<td>Selenium (mg/100 gm)</td>
<td>15.5</td>
<td>23.4</td>
<td>37.7</td>
<td>2.7</td>
<td>NR</td>
<td>4.4</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Thiamin (mg/100 gm)</td>
<td>0.385</td>
<td>0.401</td>
<td>0.646</td>
<td>0.421</td>
<td>0.237</td>
<td>0.39</td>
<td>0.41</td>
<td>0.763</td>
</tr>
<tr>
<td>Riboflavin (mg/100 gm)</td>
<td>0.201</td>
<td>0.093</td>
<td>0.285</td>
<td>0.29</td>
<td>0.142</td>
<td>0.27</td>
<td>0.107</td>
<td>0.139</td>
</tr>
<tr>
<td>Nicin (mg/100 gm)</td>
<td>3.63</td>
<td>5.091</td>
<td>4.604</td>
<td>4.72</td>
<td>2.927</td>
<td>3.363</td>
<td>4.766</td>
<td>0.961</td>
</tr>
<tr>
<td>Folate, total (mcg/100 gm)</td>
<td>19</td>
<td>29</td>
<td>19</td>
<td>85</td>
<td>NR</td>
<td>NR</td>
<td>41</td>
<td>56</td>
</tr>
<tr>
<td>beta-Carotene</td>
<td>97</td>
<td>0</td>
<td>13</td>
<td>NR</td>
<td>NR</td>
<td>5</td>
<td>5</td>
<td>NR</td>
</tr>
<tr>
<td>alpha-Carotene</td>
<td>63</td>
<td>0</td>
<td>0</td>
<td>NR</td>
<td>NR</td>
<td>0</td>
<td>0</td>
<td>NR</td>
</tr>
<tr>
<td>Vitamin A (IU)</td>
<td>214</td>
<td>0</td>
<td>22</td>
<td>0</td>
<td>0</td>
<td>9</td>
<td>9</td>
<td>0</td>
</tr>
</tbody>
</table>

Acute consumption of barley β-glucan, but not resistant starch, in muffins was effective in reducing glucose and insulin responses in men who were mildly insulin-resistant [36-38].

Dietary intake of β-glucans has been shown to help with control of blood glucose level and lipids; and reduction of hypertension [39]. Kobori et al asserted that quercetin (a flavonol found in many fruits, vegetables, leaves and grains) reduced blood glucose level and improved plasma insulin levels in streptozotocin-induced diabetic rats [40]. Another study concluded that quercetin may have a pharmacological application in treating cardiovascular disease in diabetic patients via its antioxidant and anti-inflammatory potential [41, 42]. Yang et al showed that quercetin combined with resveratrol can inhibit fat cell differentiation and development [43].

Ohnishi et al found that dietary ferulic acid can alleviate oxidative stress and attenuated hyperglycemic associated response in diabetes [44]. Balasubashini et al showed that ferulic acid enhances antioxidant capacity thus alleviating diabetes [45].

In another study, it has been shown that saponin (a common phytochemical found in grains) from Tribulus terrestris could significantly reduce the level of serum glucose [46], but it was not clear that saponin from whole grain sources has the same effects on blood glucose levels. Lower β-tocopherol (vitamin E) concentration is known to be associated with impaired insulin sensitivity [47, 48], and treatment of vitamin E exerts a protective role against diabetes-induced peripheral muscle dysfunction and renal function [49-51], as well as reduced risk of type 2 diabetes [30]. Kushad et al showed that tocotrienol can prevent diabetes associated cognitive deficits [52], and reduced risk of type 2 diabetes have been associated with increased tocotrienol [30]. Mice on diets with greater phytic acid (a common anti-nutrient in grains) intake displayed lower blood glucose levels after glucose tolerance tests [53, 54], and also known to lower blood glucose response by reducing the rate of starch digestion and slowing the gastric emptying [55]. Gamma-oryzanol or rice bran oil (an oil extracted from the hard outer brown layer of rice after chaff / rice husk) increased insulin sensitivity in diabetic mice [56].

many hypotheses (e.g. the fiber hypothesis) float around, but it is critical that future research explores the beneficial effects of whole grains in blood sugar metabolism at a mechanistic level. Further, as many believe that the mechanism by which whole grains regulate glucose metabolism is largely based on the botanical structure of the grain and its phytochemicals; detailed analyses of structural interactions are warranted. Overall, it is critical to further elucidate the role of whole grain phytochemicals in ameliorating the pathogenesis of type 2 diabetes.

Antioxidant Activity Of Whole Grains

Antioxidant activity is a potent mechanism by which whole grains deliver their beneficial health effects against several human diseases including obesity and diabetes. At core, the function of antioxidants is to react with free radicals to protect against free radical or Reactive Oxygen Species (ROS) attack on self-lipids, protein and DNA [57]. Free radical attack is established to be a critical initiator of several chronic diseases, including type 2 diabetes [58]. Whole grains contain a mass of antioxidant compounds, which have been shown to possess potent antioxidant activity [59]. Many soluble antioxidant compounds, including phenolic acids, tocopherols and flavonoids, are present in whole grains [60]. The highest phenolic acid content is present in corn (265 mg gallic acid equivalents/100 g), followed by wheat (135 mg), oats (111 mg) and rice (95 mg) [61]. Ferulic acid, one of the most well studied phenolic acids, is shown to be a strong antioxidant by donating hydrogen atoms to free radicals [61, 62]. Carotenoids in whole grains include lutein, alpha-carotene, beta-carotene and beta-cyproxanthin, are found in the bran and germ layers of whole grains, can also serve as antioxidants [63]. Further, antioxidant capacity is inherent in insoluble grain fibers [64, 65]. Phytic acid is common phytochemical in many whole grains, and is well known as an antioxidant that represses iron-catalyzed redox reactions [66, 67].

Processing affects the biological activities of food and their ingredients, and most of grains and their food products go through very exhaustive food processing route [66, 68-70]. Vitamin E, is another common ingredient of whole grains is a potent antioxidant that protects cell membranes and inhibits the formation of nitrosamines [72, 73], but it is almost wholly removed during the refining process of whole grains [71]. In addition, the toasting process that many whole grains undergo (e.g. toasting whole wheat bread) increases the antioxidant activity compared to the raw materials, and actually develops a similar activity as that of many fruits and vegetables [74]. However, it is important to note that although many potent antioxidant compounds have been identified in whole grains, and their individual effects have been reported, but studies elucidating which compounds provide the most potent and specific effects in the context of whole grains is not done very comprehensively.

Anti-Obesity Effects

Epidemiologically, whole grains have been shown to beneficially alter critical measures of obesity, such as weight, Body Mass Index (BMI) and waist circumference [75]. Jonnalagadda et al. reviewed the prospective studies that utilize diverse patient databases to conclude that consumption of whole grains is inversely correlated with weight, BMI and waist circumference [14]. Further, visceral adipose tissue volume is negatively correlated with intake of whole grains (3 ounce-equivalent servings per day) in both men and women [76]. Overall, reduction in weight gain has been the central benchmark for many of the clinical studies conducted on whole grains and obesity [14], with the trend heading towards examining the role of whole grains in decreasing visceral adiposity. The recent evidences also suggest that in addition to the marked decreases in body weight are associated with whole grain intake and suggested that, whole grains may contribute to the redistribution of fats within the body [76]. Intervention studies, however, report the inconsistent results of beneficial effects of whole grains in reducing overweight and obesity [14]. Therefore, it is more critical to place the emphasis on placing refined grains versus whole grains as a central tenant in many of these studies, as therein lies the challenge for society as a whole.

Overall, however, the vast majority of clinical studies – both epidemiological and mechanistic – are conducted in the Caucasian population. Studies exploring similar benefits in other populations both within the United States and around the world are warranted in more comprehensive manner and considering parallel comparison to existing studies designs.

The mechanisms by which phytochemicals present in whole grains directly affect various conditions of obesity have been minimally explored. One mechanism suggests that whole grains act to increase satiety, and consequently render those who consume whole grains to desire less food intake [77, 78]. Indeed, several studies have reported an increased feeling of fullness with the addition of whole grain to the diet [77, 78]. These reductions in hunger caused by intake of whole grains may be due to a differential profile of gut hormones, as whole grains have been shown to influence ghrelin, peptide YY, glucagon-like peptide 1, cholecystokinin levels [14]. Although variability in changes in hunger versus satiety feelings in several studies have been reported, and acknowledged the subjects do not demonstrate a decrease in energy intake [14]. However, in some studies, whole grains have been clearly observed to reduce energy intake [79]. This calls for further research elucidating the mechanisms by which whole grains may alter satiety and food intake signals, a critical player in the delicate balance between energy intake and expenditure.

Beneficial Effects on Cholesterol Metabolism

Imbalance in cholesterol metabolism and elevated cholesterol levels are common conditions in obese and diabetic subjects, and tightly correlated with increased incidence of cardiovascular diseases [80, 81]. Phytosterols from whole grains have been shown to displace cholesterol from micelles, in turn reducing cholesterol absorption, increasing excretion, and ultimately decrease serum cholesterol in hypercholesterolemic men and women [82-84]. Linoleic acid and palmitate, both part of the unsaturated fatty acids that are highly present in whole grain fats, and whole grain derived these fatty acids have been...
## Table 2: Whole grain phytochemicals associated with diabetes and obesity

<table>
<thead>
<tr>
<th>Family</th>
<th>Phytochemical</th>
<th>Molecular Weight, Formula</th>
<th>Description</th>
<th>Effects/Benefits</th>
<th>Food Sources</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anthocyanidin</td>
<td>Cyanidin</td>
<td>MW: 286 g/mol, Formula: C_{15}H_{10}O_{6}</td>
<td>It has a characteristic reddish-orange color. Cyanidin glycosides are easily absorbed into the plasma. It has antioxidant and radical-scavenging effects.</td>
<td>Cyanidin reduces blood glucose level and improves insulin sensitivity due to the reduction of retinol binding protein 4 expression in type 2 diabetic mice [37]. Takanori et al discovered that cyanidin glucoside from purple corn extract could be used to help treat diabetes and obesity [38].</td>
<td>Purple Corn and various whole grains.</td>
</tr>
<tr>
<td>Carotenoids</td>
<td>Beta-Cryptoxanthin</td>
<td>MW: 552.85 g/mol, Formula: C_{40}H_{56}O</td>
<td>Beta-cryptoxanthin is an antioxidant and may help prevent free radical damage to cells and DNA, as well as stimulate the repair of oxidative damage to DNA.</td>
<td>An increased intake of total beta-cryptoxanthin along with other phytochemicals was associated with a reduced risk of type 2 diabetes [39].</td>
<td>Various whole grains.</td>
</tr>
<tr>
<td></td>
<td>Lutein</td>
<td>MW: 568.87 g/mol, Formula: C_{40}H_{56}O_{2}</td>
<td>Lutein is an antioxidant which is believed to be an essential nutrient for normal vision. It is dominant in the peripheral retina. Lutein is fat soluble, so a deficiency may occur if fat digestion is impaired.</td>
<td>Muriach et al discovered that lutein can be a potential candidate for the reduction of susceptibility to infections of diabetic patients [40]. Arnal et al found that a combined treatment with lutein and insulin prevented the development of cataracts in streptozotocin-induced diabetic rats by inhibiting lipid peroxidation in the diabetic lens [41].</td>
<td>Various whole grains.</td>
</tr>
<tr>
<td></td>
<td>Zeaxanthin</td>
<td>MW: 568.88 g/mol, Formula: C_{40}H_{56}O_{2}</td>
<td>Zeaxanthin is an antioxidant and dominant within the central macula of the eye. It is also fat soluble with similar characteristics to lutein.</td>
<td>Zeaxanthin treatment can potentially inhibit the development of retinopathy in diabetic patients [42].</td>
<td>Various whole grains.</td>
</tr>
<tr>
<td>Dietary Fiber</td>
<td>Lignin, Hemicellulose, Cellulose</td>
<td></td>
<td>Major components of dietary fiber. Lignin fills in the space between cellulose and hemicellulose components of the plant cell wall.</td>
<td>Consumption of dietary fiber has been associated with reduced risk of type 2 diabetes and obesity [43].</td>
<td>Various whole grains for insoluble fiber and beans, oat bran for soluble fiber.</td>
</tr>
<tr>
<td></td>
<td>Beta-glucan</td>
<td></td>
<td>Major component of dietary fiber. It is a polysaccharide that has only glucose as a structural component.</td>
<td>Acute consumption of barley beta-glucan, but not resistant starch, in muffins was effective in reducing glucose and insulin responses in men who were mildly insulin-resistant [44]. Dietary intake of beta-glucans has been shown to help with control of blood glucose level and lipids; and reduction of hypertension [45].</td>
<td>Barley and oats. When extracted from whole grains, it is both soluble and insoluble.</td>
</tr>
</tbody>
</table>
### Flavonoids

<table>
<thead>
<tr>
<th>Compound</th>
<th>Molecular Weight</th>
<th>Formula</th>
<th>Description</th>
<th>Sources</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quercetin</td>
<td>302.24 g/mol</td>
<td>C_{15}H_{10}O_{7}</td>
<td>Quercetin is the most abundant of the flavonoids. It is also a building block for other flavonoids. Quercetin occurs in food as a glycone (attached to a sugar molecule). It is an antioxidant and free radical scavenger.</td>
<td>Buckwheat and various whole grains.</td>
</tr>
</tbody>
</table>

### Hydroxycinnamic Acids

<table>
<thead>
<tr>
<th>Compound</th>
<th>Molecular Weight</th>
<th>Formula</th>
<th>Description</th>
<th>Sources</th>
</tr>
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<tbody>
<tr>
<td>Ferulic Acid</td>
<td>194.18 g/mol</td>
<td>C_{10}H_{10}O_{4}</td>
<td>It is the most abundant phenolic acid in grains. Ferulic acid is an antioxidant which neutralizes free radicals that could cause oxidative damage of cell membranes and DNA. It helps to prevent damage to our cells caused by UV light.</td>
<td>Rye bran, wheat bran, and rice bran.</td>
</tr>
</tbody>
</table>

### Saponins

<table>
<thead>
<tr>
<th>Compound</th>
<th>Description</th>
<th>Sources</th>
</tr>
</thead>
<tbody>
<tr>
<td>Saponins</td>
<td>Saponins are glucosides with foaming characteristics. They consist of a polycyclic aglycone attached to one or more sugar side chains.</td>
<td>Quinoa, oats. Most beans, vegetables, and herbs</td>
</tr>
</tbody>
</table>

### Vitamin E

<table>
<thead>
<tr>
<th>Compound</th>
<th>Molecular Weight</th>
<th>Formula</th>
<th>Description</th>
<th>Sources</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alpha-Tocopherol</td>
<td>430.71 g/mol</td>
<td>C_{29}H_{50}O_{2}</td>
<td>Main component of vitamin E family (there are 4 tocopherols in vitamin E). It is a fat soluble antioxidant that stops the production of reactive oxygen species.</td>
<td>Wheat germ oil, sunflower oil, vegetable oils, soybean oil, nuts, seeds, whole grains</td>
</tr>
<tr>
<td>Tocotrienol</td>
<td>660.03 g/mol</td>
<td>C_{6}H_{18}O_{24}P_{6}</td>
<td>Main component of Vitamin E family (there are 4 tocotrienols in vitamin E). Only occurs in very low levels in nature and has different forms. It is a fat soluble antioxidant.</td>
<td>Wheat germ, barley, whole grains, nuts, rice bran oil, vegetable oils</td>
</tr>
</tbody>
</table>

### Others

<table>
<thead>
<tr>
<th>Compound</th>
<th>Description</th>
<th>Sources</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phytic Acid</td>
<td>Phytic acid is a natural plant antioxidant. It is the major store of phosphate in plants. It represses iron-catalyzed redox reactions.</td>
<td>Found in most grains, seeds and beans. Rich sources of phytic acid are wheat bran and flaxseed</td>
</tr>
</tbody>
</table>
Gamma-oryzanol increased insulin sensitivity in diabetic mice [59].

There are many flavonoids in whole grains that need to be studied specifically.

**Gamma-Oryzanol**

- MW: 602.89 g/mol
- Formula: C₄₀H₅₈O₄
- Gamma oryzanol is a naturally occurring mixture of plant chemicals called sterols and ferulic acid esters. It is an antioxidant.

**Figure 2:** Beneficial potential of whole grains and their ingredients against metabolic diseases.
sensitivity and other metabolic measures in mice models [105]. Whole-grain barley feeding known to decrease the high fat diet-induced inflammation that is possibly related to formation of short chain fatty acids i.e. propionate, butyrate and changes in microbiota composition [106]. In addition, in this study authors found that high β-glucan content in the diet reduced plasma cholesterol levels [106]. Food processing is always a factor in whole grain induced changes in gut microbiome, as recent study showed that processing of whole-grain barley to barley malt have significant impact on gut microbiota and metabolites in rats fed high-fat diets [107]. As the mechanisms by which whole grains improve characteristics of overweight and obesity are for the most part obscure, it is critical for research to specifically explore the roles of phytochemicals and other constituents.

Conclusions

Whole grains contain a host of bioactive phyto-consituents i.e. fibers, alkaloids, flavonoids, saponins and other phytochemicals, vitamins, antioxidants and immune modulators, with known health benefits, including amelioration of chronic diseases (such as obesity and diabetes). These bioactive phytochemicals, both in isolation and in combination, appear to be key players in the improvement of glucose metabolism in different metabolic organs i.e. liver, pancreas, skeletal muscles, adipose tissue, gastrointestinal tract, immune cells and brain directly or indirectly via influencing gut microbiome, gut hormones, gut-brain axis and inflammatory response as well as oxidative stress and cholesterol profiles (Figure 2). However, the phytochemicals reviewed here warrant further in depth research. In current literature rarely any phytochemicals from whole grains are reported and discussed directly to influence metabolic function with Comprehensive and defined mechanism(s) of action. In summary, whole grains possess evident anti-diabetic and anti-obese properties, but research must seek to further elucidate the role of both specific phytochemicals and establish mechanistic explanations for these effects. Further, there are unique subsets of phytochemicals in whole grains that are poorly characterized and purified. Therefore, chemical research is also essential to discover all of the bioactive components in whole grains, as each may have potnet abilities to improve the pathophysiology of diabetes, obesity, and the resultant metabolic complications.

References

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Whole Grains in Amelioration of Metabolic Derangements


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