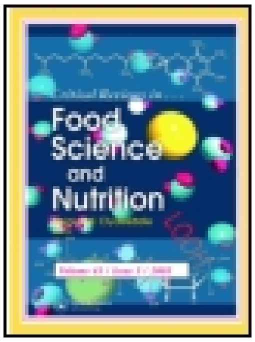

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Obesity and neurological disorders: Dietary perspective of a global menace

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ABSTRACT
Obesity is considered a major public health concern throughout the world among children, adolescents, as well as adults and several therapeutic, preventive and dietary interventions are available. In addition to life style changes and medical interventions, significant milestones have been achieved in the past decades in the development of several functional foods and dietary regimens to reduce this menace. Being a multifactorial phenomenon and related to increased fat mass that adversely affects health, obesity has been associated with the development of several other co-morbidities. A great body of research and strong scientific evidence identifies obesity as an important risk factor for onset and progression of several neurological disorders. Obesity induced dyslipidaemia, metabolic dysfunction, and inflammation are attributable to the development of a variety of effects on central nervous system (CNS). Evidence suggests that neurological diseases such as Parkinson's disease and Alzheimer's disease could be initiated by various metabolic changes, related to CNS damage, caused by obesity. These metabolic changes could alter the synaptic plasticity of the neurons and lead to neural death, affecting the normal physiology of CNS. Dietary intervention in combination with exercise can affect the molecular events involved in energy metabolism and synaptic plasticity and are considered effective non-invasive strategy to counteract cognitive and neurological disorders. The present review gives an overview of the obesity and related neurological disorders and the possible dietary interventions.

KEYWORDS
Obesity; co-morbidities; neurological disorders; management; dietary aspects

1. Introduction

Obesity is recognised as a major public health threat throughout the world in both developed and developing countries (Mazon et al., 2017; Bhurosy and Jeewon 2014). Declared as a global epidemic (Revels et al., 2017), the prevalence of obesity has increased at an alarming rate during the last few decades and about 2.1 billion people (30% of global population) are considered obese or overweight (O'Brien et al., 2017). Considered as the 5th leading cause of human death globally (Mazon et al., 2017; WHO 2016), obesity is held responsible for 2.8 million human deaths annually (5% of world deaths) among adults (EASO 2016). If the increased incidence continues at the current pace, it is predicted that almost half of the world's adult's population will be obese or overweight by 2030 (Tremmel et al., 2017).

Obesity is a metabolic disorder that has reached an epidemic scale in high-income developed countries (O'Brien et al., 2017; Skalny et al., 2016). Over 40% of all Americans are obese or morbidly obese and from 1960 to 2012, the prevalence of obesity has increased by 733% in USA (Revels et al., 2017). Although the increasing incidence of obesity has shown positive indications of plateauing in high-income developed countries, the changing lifestyle in developing countries is contributing to the global burden (Ng et al., 2014). The prevalence of obesity has tripled in developing countries over the last two decades (Imes and Burke 2014) and two-thirds (62%) of the world's obese people now live in developing countries (Ng et al., 2014). Nearly half of the 41 million children under 5 who were overweight or obese in 2014 lived in Asia (WHO 2016). It is also worth mentioning that while an increased rate of obesity was observed in general population; there was a significant decline in the rate of weight counselling in the subjects of obesity and obesity-related pathologies (Kraschnewski et al., 2013).

Recent reports documented significant differences in the prevalence of obesity due to gender as it is more commonly observed in women (Behl and Misra 2017; Skalny et al., 2016). In a study involving 68 countries, it was demonstrated that there were three obese women for every two obese men (Wells et al., 2012). The prevalence of obesity has also increased in children and adolescents in epic proportions and more than 40 million children (<5 years), 30 million in developing countries and 10 million in developed countries, are considered obese in the world (Rouxinol-Diasa et al., 2016). The prevalence of obesity is very high in children in Europe and range from 6.0 to 26.6% among boys and from 4.6 to 17.3% among girls with the highest level of obesity observed in southern European countries (EASO 2016).

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2. Causes of obesity

The World Health Organization (WHO) has defined obesity as excessive or abnormal body fat accumulation due to a positive energy balance that may impair health. Defined as a ratio of an individual's weight in kilograms to their squared height in meters, body mass index (BMI) is a criterion used by WHO to diagnose obesity. It is a screening tool used to classify obesity and overweight and to evaluate the relative risk of disease in comparison to normal weight. It does not diagnose health status and is not without flaws. As per the BMI criteria, <18.5 kg/m^2 BMI is classified as underweight, 18.5 to 24.9 kg/m^2 BMI is classified as normal weight, 25 to 29.9 kg/m^2 BMI is classified as overweight, 30 to 34.9 kg/m^2 BMI is classified as class I obesity (1st degree obesity), 35 to 39.9 kg/m^2 BMI is classified as class II obesity (2nd degree obesity), 40 to 49.9 kg/m^2 BMI is classified as class III obesity (3rd degree obesity), 50 to 59.9 kg/m^2 BMI is classified as super-obesity and >60 kg/m^2 BMI is classified as super-super-obesity. Besides BMI, body fat distribution is another important factor to assess obesity and gives more information about the health risk as different fat compartments are associated with different metabolic risk (McShea 2017; Rouxinol-Diasa et al., 2016).

Genetics may predispose certain ethnicities and individuals to develop obesity (Grarup et al., 2014), however, there are certain factors, such as overconsumption of energy-dense foods (positive energy balance) and sedentary life-style, which are mainly responsible for gaining weight. Genetic, environmental, neural, and endocrine factors and even infectious agents contribute to obesity (Rouxinol-Diasa et al., 2016). Excessive storage of triacylglycerol in cells during positive energy imbalance results in hypertrophy (cell enlargement) or hyperplasia (cell proliferation) of adipocytes, or both, leading to expansion and accumulation of adipose tissue to store the surplus calories. Several factors have been held responsible for childhood obesity, which include but are not limited to, the amount and energy density of foods consumed, environmental factors, parental health, physical activity and amount of sleep (Ministry of Health-NZ 2017).

Some specific lifestyle and dietary factors have been associated with obesity and weight gain, however, the role of dietary behaviours in the development of obesity is not clearly understood (Sares-Jäske et al., 2017). Numerous studies have examined the relationships between diet and obesity that focused on individual nutrients or foods (Kim et al., 2017; You and Henneberg 2016; Nicklas et al., 2015). However, the conclusions of such studies were not supported by epidemiological data due to the complexity of human diets having a large number of candidate foods and complex interactions between various food components that might influence their digestion and absorption behaviour within the gut. Recently, diet has been considered as a single entity and emphasis have been on the effects of quality of the overall diet in the development of obesity, rather than on individual nutrients or foods (Sares-Jäske et al., 2017).

3. Impact of obesity

The impact of obesity is huge on a social level and it has a significant economic burden as it has been linked to serious medical issues and significant healthcare expenditures globally and in particular in the USA. As much as 10 percent of all healthcare expenditures are spent on BMI-related medical issues (Revels et al., 2017). The global economic impact of obesity in 2014 was estimated to be 2.0 trillion US dollars, equivalent to 2.8 percent of global gross domestic product (Tremmel et al., 2017). Obesity has been associated with a 77 percent increase in medications and 36 percent increase in outpatient and inpatient spending (Revels et al., 2017). The annual healthcare costs attributable to obesity in USA alone range from 147 billion to 210 billion US dollars (Trust for America's Health 2017; Cawley and Meyerhoefer 2012) and that may double every decade to reach 860.7 to 956.9 billion US dollars by 2030 (Revels et al., 2017). The direct spending on the healthcare for obese and severely or morbidly obese adults is 42 percent and 81 percent higher, respectively than for healthy weight subjects (Trust for America's Health 2017).

4. Co-morbidities and neurological disorders

Obesity is a high risk factor for the development of various chronic and neurodegenerative diseases such as cardiovascular disease, type 2 diabetes, certain cancers (kidney, uterine, breast, prostate, pancreatic, and colon), hypertension, sleep apnea, dyslipidemia, hypercoagulability causing blood clots, musculoskeletal disorders, pseudotumor cerebri, non-alcoholic fatty liver disease, gastric reflux, gallbladder disease, cerebrovascular accident, infertility, and psychological problems (McShea et al., 2017; Behl and Misra 2017; Revels et al., 2017; Jabir et al., 2017a, b; Davis et al., 2014). The high incidences of oxidative stress (Bondia-Pons et al., 2012), inflammation (Milanski et al., 2009) and mitochondrial dysfunction (Sivitz 2010) associated with obesity impacts on the development of neurodegenerative diseases (Procaccini et al., 2016) and may impair cognitive function (Miller and Spencer 2014). The current rising trend of cardio-vascular diseases and type-2 diabetes is closely associated with the increased prevalence of excessive visceral obesity (Revels et al., 2017).

Obesity and overweight are considered as high-risk factors for the development of several mental health disorders and neurodegenerative diseases such as anxiety, depression, body image disorders, Alzheimer's and Parkinson's disease (Mazon et al., 2017; McShea et al., 2017; Procaccini et al., 2016; Davis et al., 2014). Metabolic changes induced by obesity could cause damage to the central nervous system (CNS) and affect cognition through different mechanisms (Miller and Spencer 2014). The dyslipidaemia, metabolic dysfunction, and inflammation induced by obesity could contribute to a wide variety of effects and disorders on the nervous system (O'Brien et al., 2017). Both the CNS and peripheral nervous system, which are quite distinct in form and function, are susceptible to the effects of obesity. The effects of obesity are initially observed in the peripheral systems and organs where it induces changes in the autonomic nervous system by causing imbalances in sympathetic-parasympathetic activity (O'Brien et al., 2017). Later, obesity causes abnormalities in the hypothalamus in CNS (Kälin et al., 2015; Williams 2012) and induces atrophy in the hippocampus (Cherbuin et al., 2015) and alterations in the cerebral frontal cortex (Souza et al., 2007). Mild changes induced by obesity in the structure and function of the hippocampus, which is associated with cognition, memory, learning, and emotions, could initiate mild cognitive impairment in some individuals. Similarly, alterations in hypothalamic function and subsequent changes in whole-body energy balance might be early events that influence weight gain and contribute to the development of obesity.

The fact that metabolic disorder and obesity are associated with chronic low-grade inflammation (O'Brien et al., 2017) has changed the insight to the underlying etiology and progression of obesity. Insulin resistance and chronic hyperglycemia, which induce a state of oxidation and inflammatory response, are risk factors for triggering neuronal death and causing cognitive decline (Treviño et al., 2015). Changes in hormones, such as insulin and leptin, have a significant role in the regulation of neuronal injury and various neurodegenerative processes (Procaccini et al., 2016). Insulin resistance, hyperglycemia and leptin, are all associated with obesity. Insulin resistance, which plays a fundamental role in the development of dementia (Hazar et al., 2016), could be attributed to the increase in free fatty acids associated with obesity (Schneeberger et al., 2014). There is also a decreased activity of leptin (leptin resistance), a hormone that has a role in energy expenditure, food intake and possibly cognitive functions, in obese people (Lee 2011).

Fig. 1 shows how obesity is associated with some of the potential factors for Parkinson's and Alzheimer's disease. Obesity has been reported to have an impact on the development of neurodegenerative diseases (Mazon et al., 2017; Jellinger 2009) as it is related to the presence of inflammation (Milanski et al., 2009), oxidative stress (Bondia-Pons et al., 2012), and mitochondrial dysfunction (Sivitz 2010). Parkinson's disease has been suggested to occur due to a complex interaction between environmental and genetic factors, including mitochondrial dysfunction (Hu and Wang 2016; Xu et al., 2014), oxidative stress (Gaki and Papavassiliou 2014), neuroinflammation (Wang et al., 2015), and excitotoxicity and iron deposition (Licker et al., 2009), which may lead to dopaminergic system degeneration in the CNS (Barreto et al., 2014). Free radicals generated through oxidation, nitrosylation and peroxidation, which are directly associated with neuronal injury, may result in additional damage to macromolecules and organelles (Barreto et al., 2014).

Alzheimer's disease is characterized by the pathological accumulation of Aβ proteins (beta-amyloid peptides) and the presence of the TAU protein (Mazon et al., 2017). Other neurodegenerative mechanisms, such as genetic and environmental causes, oxidative damage, mitochondrial dysfunction, energy metabolism failures, proinflammatory responses, and dysfunctions in various neurotransmission systems (Islam and Tabrez 2017; Islam et al., 2017; Jabir et al., 2015; Ferrer 2012; Chu 2012; Cai et al., 2011), have been proposed and are associated with the disease (Alves et al., 2012). Oxidative stress is known as one of the major factors that contribute to the Aβ formation and has been identified as the disease-triggering mechanism (Finder 2010). The interaction between neuroinflammation and oxidative stress has been reported by several studies as a leading cause of Aβ formation (Simpson et al., 2010; Agostinho et al., 2010). Several cytokines have been implicated in the pathophysiology of Alzheimer's disease involving proinflammatory cytokines, which contribute to the

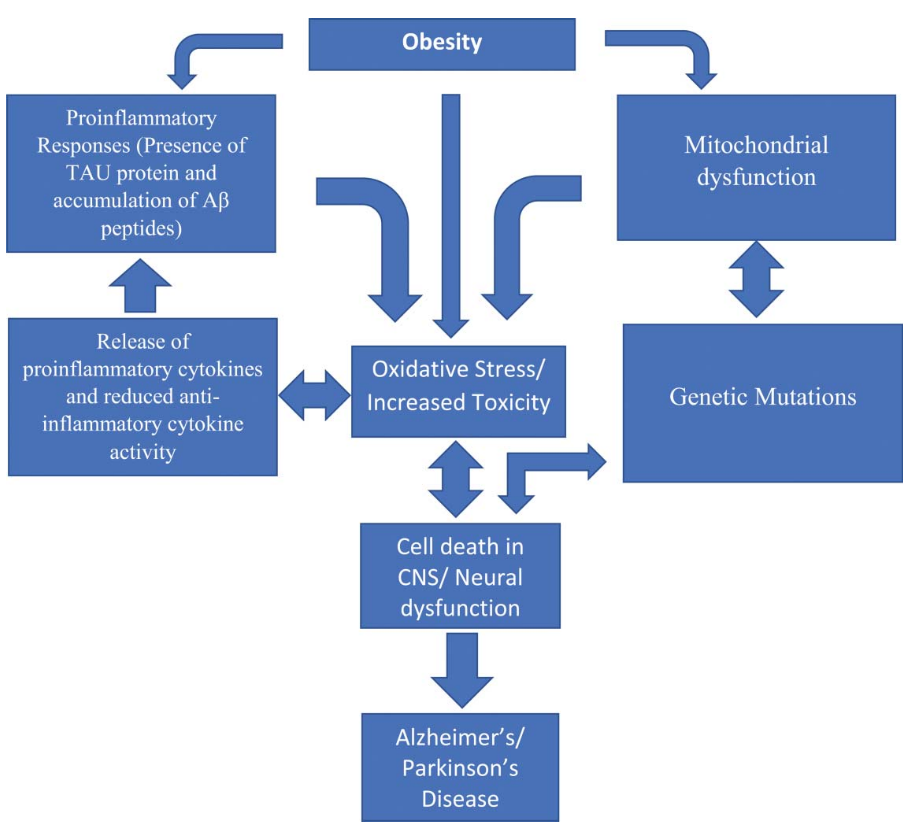

Figure 1. Potential factors for Parkinson's and Alzheimer's disease (adapted from Mazon et al. 2017).

disease progression (Bossù et al., 2007). There is also a decrease in the activity of anti-inflammatory cytokines in addition to an increase in proinflammatory cytokines. Proinflammatory cytokines such as interleukin-4, interleukin-10 and interleukin-13 serve to reduce inflammation (Szczepanik et al., 2001; Fujita et al., 2006).

5. Management of obesity

Change in lifestyle, through healthy dietary options and increased physical activity, has been recommended as a preferred approach to reduce obesity and the health risks associated with it, although, pharmacologically active drugs and bariatric surgery are the other promising options for obese people.

5.1. Exercise

Increased physical activity improves weight loss and helps to maintain it. Recommending an appropriate exercise regimen after assessing the physical activity of the subjects is essential while keeping the other factors like age, health status and physical conditioning in mind. Usually a combination of muscle-strengthening and aerobic exercises is beneficial. A daily target of 60 minutes of workout or weekly ≥300 minutes of moderate intensity exercise is generally an effective strategy for weight loss (Behl and Misra 2017).

5.2. Pharmacotherapy

Pharmacological interventions could also be added to the exercise regimen and lifestyle changes to further improve weight loss. If the subjects are on drugs, such as antidepressant's or antiepileptic drugs (e.g. gabapentin, pregabalin, and valproic acid), which are associated with weight gain, the drugs may be identified and immediately substituted with the possible options that are weight neutral (e.g. lamotrigine, levetiracetam, and phenytoin) or associated with weight loss (e.g. felbamate, topiramate, and zonisamide) (Ben-Menachem 2007). Weight loss pharmacotherapy is suggested on a case-to-case basis after evaluating the health status of the patients and the drugs need to be taken on a regular basis for long term to achieve effective and meaningful results. Some of the weight loss drugs approved by United States Federal Drug Administration include liraglutide, orlistat, lorcaserin, bupropion-naltrexone combination and phentermine-topiramate combination. Patients who do not show a weight loss of 5% in three months should be taken off these medications (Behl and Misra 2017).

5.3. Bariatric surgery

Surgical options are also available for obesity management and some commonly performed surgical procedures include laparoscopic sleeve gastrectomy, laparoscopic adjustable gastric banding, biliopancreatic diversion with duodenal switch and laparoscopic Roux-en-Y gastric bypass. Although there are frequent medical complications and some patients regain weight, surgical procedures, like Roux-en-Y gastric bypass, are highly effective for morbidly obese subjects (Sjostrom et al., 2012). The patients have been reported to show profound improvements in cognitive functions and metabolic homoeostasis after the surgery (Miller et al., 2013). Other benefits observed in postoperative subjects are improvement in dyslipidemia, hypertension, osteoarthritis and obstructive sleep apnea (Vander Naalt et al., 2014; Sjostrom et al., 2012).

5.4. Dietary approach

Based on the postprandial blood glucose levels, carbohydrate based foods can be classified by their glycemic indices, a ranking system on a scale of 0 to 100, into low (≤55), medium (56–69) and high (≥70) (Pinhero et al., 2016; Wolever 2006). Glycemic index is used to rank the foods based on their potential to liberate glucose towards blood. Long term intake of diets with high glycemic index has been reported to increase the risk of several chronic diseases including obesity, type-2 diabetes and cardiovascular diseases (Shumoy and Raes 2017; Pinhero et al., 2016; Ferng et al., 2016; Youn et al., 2012; Marques et al., 2007). Similarly, diets with low glycemic response have been reported to reduce the risk of metabolic diseases (Ferng et al., 2016; Brand-Miller 2007; Jenkins 2007). A low glycemic load diet helps in maintaining better cognitive function during the aging process (Garber et al., 2017). By altering the glycemic index of ingested carbohydrates, it is of considerable interest to control obesity and improve control of diabetic patients (Agama-Acevedo et al., 2012). Table 1 shows the effect of different dietary ingredients on *in vivo* glycemic response, weight loss and neurological symptoms in various animal and human trials. A study was conducted by Lobos et al., (2017) to investigate the impact of low and high glycemic index breakfasts on postprandial metabolic parameters in subjects with type 2 diabetes mellitus. Low glycemic index meal generated a significantly lower glycemic response with 46% decrease in the area under the curve of glucose and in mean glycemia analysed at 30, 60 and 120 min. Silva et al., (2016), however, did not find any association between the glycemic index or glycemic load with overweight and adiposity in children of five years of age.

Chew and Brownlee (2017) evaluated the impact of supplementation with dietary fibres in various forms (i.e. as pills, capsules and powder mix formats) on the weight loss in overweight adults. Dietary fibre supplements previously linked to improved weight management were used i.e. pectin, alginate, guar gum, psyllium, glucomannan, inulin, polydextrose, β-glucan, gum, wheat dextrin, bran, lignin, and chitosan. Significant increases were observed in weight loss in treatment groups for chitosan compared to control groups. Breymeyer et al., (2016) studied the effect of high-and low-glycemic load experimental diets on the mood and energy levels of healthy weight and overweight/obese, but otherwise healthy, adults. In comparison to a low-glycemic load diet, high-glycemic load diet was associated with higher depression symptoms, total mood disturbance, and fatigue particularly in overweight/obese adults. Compared to the low-glycemic load diet, consumption of high-glycemic load diet resulted in 38% higher score for depressive symptoms ($P = 0.002$) as well as 55% higher score for total mood disturbance ($P = 0.05$) and 26% higher score for fatigue ($P = 0.04$). Perez-Cornago et al., (2014b) examined the effects of a weight loss intervention on anxiety symptoms in subjects with

Table 1. Effect of different dietary ingredients/dietary supplementations on *in vivo* glycemic response, weight loss and neurological symptoms in animal and human trials.

Treatment/Dietary Supplementation	Results Obtained	Reference
A controlled, crossover and single-blind clinical trial was developed to evaluate the effect of low glycemic index breakfast on subjects of type 2 diabetes mellitus [high GI breakfast (GI of 80) included half-fat liquid milk, low-fat white bread, jam and an apple whereas low GI breakfast (GI of 45) included a diet yoghurt smoothie, an apple and a pear]	Lowered glycemic response	Lobos et al. (2017)
A meta-analysis was done to quantify the efficacy of barley β-glucan on postprandial glycemic response in healthy humans. The interventions included β-glucan extract, barley flour, and barley kernels incorporated into different products including pasta, muffins, crackers, cookies, bread, porridge, and soup. The dose of β-glucan ranged from 1.4 to 12 g in the test meals, while the dose of available carbohydrate in the test meal ranged from 25 to 84 g	β-glucan from barley significantly reduced glucose area under the curve, glycemic index, insulin area under the curve and insulin index	AbuMweis et al. (2017)
Blinded, randomised-controlled trials were used to evaluate the effect of dietary fiber supplementation in various forms (i.e. as pills, capsules or powder mix formats). Dietary fibers previously linked to improved weight management were used i.e. pectin, alginate, guar gum, psyllium, glucomannan, inulin, polydextrose, β-glucan, gum, wheat dextrin, bran, lignin, and chitosan	Meta-analysis of statistically pooled data for chitosan found significant increases in weight loss in treatment groups in comparison to control groups	Chew and Brownlee (2017)
Addition of oat β-glucan to steamed bread substituting wheat flour from 0 g/100 g to 5 g/100 g levels	No change in *in vivo* glycemic response	Wang et al. (2017)
Effect of low glycemic load diets in metabolic syndrome and type 2 diabetes mellitus in male Nile rats (aged 3 weeks to 15 months). Dietary exposures varied in glycemic index (GI, 36–88), glycemic load (GLoad, 102–305/2000 kcal), and cumulative glycemic load (Cum GLoad = days $\times$ GLoad, 181–537g total glucose)	Lentil diets with low GLoads (102, 202) prevented, delayed, reduced and even reversed the progress of metabolic syndrome and type 2 diabetes mellitus	Bolsinger et al. (2017)
Effect of soy flour fortified whole wheat meal consumed with *Talinum triangulare* soup on the glycemic index of the test human subjects. 50 g of D-glucose was dissolved in 100 ml of water for each of the control subjects	Lowered glycemic index with respect to D-glucose group	Emaleku et al. (2017)
Potential of green tea polyphenols to alleviate metabolic syndrome and prevent memory impairment in mice (three months old). 2 g/L green tea polyphenols [>98% purity; gallic acid (67.0 $\pm$ 2.2 mg/g), epi-gallocatechin (84.6 $\pm$ 0.3 mg/g), epigallocatechin-3-gallate (431.0 $\pm$ 2.2 mg/g), and epicatechin-3-gallate (394.3 $\pm$ 4.0 mg/g)] was fed through drinking water for 8 weeks	Tea polyphenols helps in management of obesity, metabolic syndrome and cognitive disorder through circadian clock related mechanisms	Qi et al. (2017)
Effect of (−)-epigallocatechin-3-gallate (EGCG) on diet-induced metabolic syndrome in mice (3 months old). 2 g/L EGCG (>98% purity) was fed through drinking water for 16 weeks	Decreased lipid accumulation and attenuated insulin resistance	Mi et al. (2017)
Effect of mulberry (*Morus alba L.*) leaf extract on starch digestion and absorption in healthy human subjects. Subjects were randomized to receive corn flakes (50 g corn flakes + 100 ml low fat milk) either with the mulberry leaf extract (36 mg of active component-1-deoxynojirimycin) or the placebo for one week and each subject received opposite preparation one week later	Decreased starch digestion and absorption	Józefczuk et al. (2017)
Effect of blackcurrant and apple polyphenol-rich drinks to postprandial glucose response in healthy men and women. Subjects consumed a placebo drink and 2 polyphenol-rich drinks containing fruit extracts: either 1200 mg apple polyphenols, or 600 mg apple polyphenols + 600 mg blackcurrant anthocyanins, in random order with a starch and sucrose meal	Decreased postprandial glucose, insulin and incretin response	Castro-Acosta et al. (2017)
Effects of *Phaseolus vulgaris L.* seed coat and *Vaccinium myrtillus L.* leaf extracts in diabetes-induced Wistar rats (140 to 150 g body weight). Rats were fed with or without *Phaseolus vulgaris L.* seed coat or *Vaccinium myrtillus L.* leaf extracts for 50 days in place of water ad libitum	*Vaccinium myrtillus L.* leaf extract reduced hyperglycemia and both extracts exhibited lipid-lowering properties	Sidorova et al. (2017)
Examining the association between glycemic index or glycemic load and overweight or adiposity in children of five years of age	No association found between glycemic index or glycemic load and overweight or adiposity	Silva et al. (2016)
Effect of high-glycemic load (HGL) and low-glycemic load (LGL) diets on mood and energy levels of healthy weight and overweight/obese adults. The intervention diets were isocaloric for the two arms, HGL and LGL, with the same target macronutrient composition for both diets (55% energy carbohydrate, 30% energy fat, and 15% energy protein)	High-glycemic load diet was associated with higher depression symptoms, total mood disturbance, and fatigue, particularly in overweight/obese adults	Breymeyer et al. (2016)
Premeal consumption of a soy protein isolate (0 g, 20 g and 40 g) on post-meal glycemic profile of healthy young subjects	Decreased incremental area under the curve and peak blood glucose response for preload of 40 g	Kashima et al. (2016)
Effect of polyphenol-enriched bread on glycemic response and postprandial insulin in healthy human subjects. Subjects consumed 50 g of available carbohydrate from a control white bread, white bread with green tea extract (GTE, 0.4%), or white bread with baobab fruit extract (BAO, 1.88%), and 250 mL of still water. This equated to 103.61 g control bread, 104.16 g GTE bread with a total of 96.33 mg added polyphenols, and 106.97 g BAO bread with 61.24 mg total added polyphenols	Baobab fruit extract increased postprandial insulin economy as it reduced the total and segmental insulin area under the curve	Coe and Ryan (2016)
A single-blind randomized controlled clinical trial was carried out to evaluate the effect of chamomile tea consumption on antioxidant status and glycemic control in human patients with type 2 diabetes mellitus. Subjects consumed chamomile tea (3 g/150 mL hot water) 3 times per day immediately after meals for 8 weeks	Short term intake of chamomile tea had beneficial effects on glycemic control and antioxidant status	Zemestani et al. (2016)
Effect of cinnamon supplementation on glycemic control in type 2 diabetes subjects. Studies ranged from 4 to 16 weeks in duration and doses of cinnamon ranged from 120 to 6,000 mg/day	Modest effects on fasting plasma glucose	Costello et al. (2016)
Effects of a weight loss intervention on anxiety symptoms in subjects with metabolic syndrome	Significant decline (−28.3%) in the anxiety symptoms	Perez-Cornago et al. (2014b)

(*Continued on next page*)

Table 1. (*Continued*)

Treatment/Dietary Supplementation	Results Obtained	Reference
Effect of a hypocaloric diet during a weight loss intervention on self-perceived depression in subjects of metabolic syndrome	Reduced malondialdehyde plasma levels and a higher intake of folate were related to improvements in manifestations of depression	Perez-Cornago et al. (2014a)
A randomized, single-blind, repeated-measures design for evaluating the effect of Baobab extract on the glycemic response in humans was done. Baobab extract was consumed in solution at a low-dose (18.5 g) and a high-dose (37 g) aqueous drink in 250 mL of water along with white bread	Reduced glycemic response at both high and low doses	Coe et al. (2013)
A randomized, controlled, double-blind cross-over study design was used to measure the effect of blackcurrant juice and crowberry–fortified blackcurrant juice (polyphenol content of 159 and 293 mg/100 mL, respectively) on postprandial glycemic control in healthy subjects. Subjects consumed 300 mL of the juice and the fortified juice was prepared by adding crowberry powder 100 g/L in the basic juice.	Improved postprandial glycemic control	Törrönen et al. (2012)

metabolic syndrome. A significant decline (−28.3%) was observed in the anxiety symptoms after a weight loss treatment which paralleled a greater decrease in body weight and anthropometric markers. Perez-Cornago et al., (2014a) examined the association between a hypocaloric diet during a weight loss intervention and self-perceived depression in subjects of metabolic syndrome and the potential involvement of dietary components and oxidative stress changes. A decline in malondialdehyde plasma levels and a higher intake of folate were related to improvements in manifestations of depression. Bolsinger et al., (2017) studied the role of dietary modification (low glycemic load diets) in the management of metabolic syndrome and type 2 diabetes mellitus in male Nile rats. Evaluated by the blood glucose and plasma lipid parameters and necropsy findings (kidney and liver pathology plus adipose reserves), diets with low glycemic loads prevented, delayed, reduced and even reversed the progress of metabolic syndrome and type 2 diabetes mellitus.

Over the years, there has been a nutritional trend to increase the proportion of resistant or indigestible carbohydrates and reduce the level of high glycemic carbohydrates in food products (Agama-Acevedo et al., 2012). Reducing the intake of high GI foods and adhering to low glycemic index diets has been a major strategy to control body weight during obesity management (Shumoy and Raes 2017; Karl et al., 2015). While clinical assessment of glycemic index is expensive, other methods such as *in vitro* starch digestibility models provide an effective, quick and low-cost alternative (Pinhero et al., 2016; Ek et al., 2014). The rate of digestion of the food starch during *in vitro* digestibility trials depends on several factors including the physicochemical structure such as molecular weight, chain length and distribution (Tian et al., 2016), botanical origin, which influence the shape and structure of starch granules and amylose content (Frei et al., 2003), factors which influence the gelatinization like processing and moisture content (Sasaki et al., 2016) and presence of dietary fibre that restricts starch gelatinization by influencing the microstructure and water availability (Cleary and Brennan 2006). One of the important health benefits of dietary fibres is postprandial control of blood glucose levels following ingestion of carbohydrate rich meals (Goff et al., 2017). Some of the soluble dietary fibres (such as pectin, psyllium, and oat gum), known as cardiovascular health-promoting dietary fibres, form viscous solutions and can lower serum blood glucose and cholesterol levels (McRorie and McKeown 2017; Russell et al., 2016). Both soluble and insoluble dietary fibres could contribute to postprandial control of blood glucose through several mechanisms such as reduction of amylase activity and slowed starch hydrolysis, reduction in gastric emptying, changes in release of hormones related to digestion and fermentation, and modifications in the absorption process in the small intestine (Goff et al., 2017).

5.4.1. Addition of fibre

One of the methods for reducing the glycemic index of food products is the addition of fibre that reduces the energy density through dilution and interaction with other ingredients in the food matrix, affecting the microstructure, digestibility and absorption of nutrients. Dietary fibre helps in regulating the carbohydrate metabolism by reducing the rate of glucose breakdown and its absorption, thereby preventing excess glucose build up (Pinhero et al., 2016). Both the types of fibres i.e. soluble fibre, such as gums, β-glucans, pectin, arabinoxylans, and mucilage, and insoluble fibre, such as cellulose, lignin, and hemicellulose, have been used to reduce the caloric content and glycemic response (Salgado-Cruz et al., 2017; Fendri et al., 2016). Soluble fibre, that could be obtained from almost all cereals, fruits and seeds, has been mostly associated with the glycemic response (Salgado-Cruz et al., 2017). Presence of soluble fibres, such as inulin and glucan, has been reported to lower the glycemic index by reducing the enzymatic vulnerability and impeding the gelatinisation of starch (Schuchardt et al., 2016). Table 2 shows the effect of different fibre ingredients on *in vitro* digestibility and estimated glycemic index of different foods.

Liu et al., (2018) studied the effect of different soluble fibres (hydrocolloids) viz. carboxymethylcellulose, hydroxypropylmethylcellulose, xanthan gum and apple pectin on *in vitro* starch digestibility and glycemic index of gluten-free potato steamed bread. A significant decrease was observed in the rapidly digestible starch content and estimated glycemic index (eGI) of the bread with added soluble fibres. Addition of soluble fibre was suggested to restrict the hydration and gelatinization of starch, causing the retardation of starch hydrolysis by the enzyme (Sui et al., 2016). Limited gelatinization of the starch granules and the amorphous starch regions in the starch granular structure reduce the susceptibility of starch granules to hydrolysis by the enzyme alpha amylase (Liu et al., 2018). Understanding the relationships between molecular structure and functionality of dietary fibres is essential to deliver more fibre-enriched

Table 2. Effect of addition of different fiber-based ingredients on *in vitro* digestibility and estimated glycemic index of different foods.

Source of Fiber	Food Material	Results Obtained	Reference
Carboxymethylcellulose, hydroxypropylmethylcellulose, xanthan gum and apple pectin at the level of 0.5%, 1.0%, and 2.0% (flour basis)	Gluten-free potato steamed bread	Decreased rapidly digestible starch content and glycemic index	Liu et al. (2018)
Alfalfa seed flour at different substitution levels to common rice flour (0%, 15%, 30% and 45% w/w)	Gluten-free rice cookies	Decreased starch hydrolysis index and increased crude protein, total dietary fibre and resistant starch content	Giuberti et al. (2018)
Hulless barley bran. Refined wheat flour (670 g) was mixed with 230 g of ground barley bran to yield a wheat-barley composite flour with a 90% extraction rate	Chapattis, an Indian flatbread	Increased slowly digestible and resistant starches and lowered retrogradation	Gujral et al. (2018)
Fenugreek gum, yellow mustard mucilage and flaxseed mucilage at concentration of 5.9 g (1.18 wt%), 15.5 g (3.10 wt%), and 11.4 g (2.28 wt%), respectively, per 500 mL of treatment mixture	Puddings	Reduced peak glucose and plasma insulin concentration	Kay et al. (2017)
Flaxseed hull (1–5%)	Wheat bread	Decreased protein digestibility	Sęczyk et al. (2017)
Chia mucilage (2 g per 98 g of wheat flour)	Pita bread	Increased slowly digestible starch fraction and lowered glycemic index in crust section	Salgado-Cruz et al. (2017)
Guar gum (5%)	Chapatti and idli, steamed and fermented product	Reduced glycemic index	Giri et al. (2017)
High amylose starch (>60% amylose)- 20%	Gluten free bread and cookies	Increased resistant starch content and lowered glycemic index	Giuberti and Gallo (2017)
Oat β-glucan (substituting wheat flour from 0 g/100 g to 5 g/100 g levels)	Steamed bread	Up to 5 g/100 g of oat β-glucan lowered glycemic index	Wang et al. (2017)
Lentinus edodes β-glucan (replaced wheat starch at 0%, 2.5%, 5%, 10%, 15% and 20% by weight)	Wheat starch gel	Increased slowly digestible starch content and reduced rate of starch digestion. Predicted glycemic index was reduced at 20% level	Zhuang et al. (2017)
Native form of β-glucan (15.6%)	Oat starch	Decreased starch digestion rate and postprandial glycemia	Zhang et al. (2017)
Oat β-glucans (3.5% β-glucans, wet weight basis)	Wheat bread	Reduced glycemic index and glucose iPeak	Ekström et al. (2017)
Dietary fiber from apples (replaced wheat flour at 10, 20, 30 and 40% by weight)	Wheat flour gel	Reduced glycemic index when wheat flour was replaced with equal blend of soluble (SDF) and insoluble dietary fibers (IDF) at 20% level. At 30% level and above, eGI was independent of ratio of SDF and IDF	Bae et al. (2016)
Dry Jerusalem artichoke (buckwheat flour and 0% or 30% or 60% or 80% artichoke)	Extruded food products	Lowered glycemic index and increased total dietary fiber and inulin. Samples containing 80% artichoke were considered as low GI food and samples containing 30% and 60% as medium GI foods	Radovanovic et al. (2015)
Banana pseudo-stem flour (replaced wheat flour at 10% w/w) and hydrocolloids (xanthan gum or sodium carboxy-methyl cellulose at 0.8%)	Bread	Reduced hydrolysis and glycemic index	Ho et al. (2015)
Fiber-enriched material obtained from apple peels (3 g and 6 g per 100 grams)	Cake	Lowered glycemic index	Jun et al. (2014)
Agave fiber (*Agave tequilana*) (sugar was replaced at 50, 62.5, 75, 87.5 and 100 g/100 g by native agave fructans)	Granola bars	Increased soluble dietary fiber and decreased glycemic index (moderate GI foods)	Zamora-Gasga et al. (2014)
Unripe banana flour (replaced wheat flour at 0%, 15%, 30% and 50%)	Cookies	Decreased hydrolysis percentage and predicted glycemic index. Increased slowly digestible starch	Agama-Acevedo et al. (2012)
Barley β-glucan (0%, 2%, 4%, 6%, 8%, and 10%)	Spaghetti	Lowered IAUC (incremental areas under the curve) values and decreased glycemic index at 10% level	Chillo et al. (2011)

functional food products for glycemic control (Goff et al., 2017). To increase the nutritional value of gluten-free cereal-based foods, Giuberti et al., (2018) incorporated alfalfa seed flour (0%, 15%, 30% and 45% w/w) in cookies substituting rice flour in the formulation. A significant increase was observed in the crude protein, total dietary fibre and total polyunsaturated fatty acid content of alfalfa-incorporated cookies. The starch hydrolysis index decreased whereas the resistant starch content increased linearly with increasing levels of incorporation. The reduced accessibility of amylase to hydrolyse the starch was attributed to the increased amount of protein and dietary fibre that acted as a physical barrier and/or increased viscosity (López-Barón et al., 2017). Kay et al., (2017) studied the effect of the addition of three soluble dietary fibres viz. fenugreek gum, yellow mustard mucilage and flaxseed mucilage on post-prandial glycemic response of puddings. The fibres were matched for apparent viscosity under simulated small intestinal conditions rather than concentration. All the soluble dietary fibres reduced the peak glucose and plasma insulin concentration significantly in comparison to control. Sęczyk et al., (2017) studied the effect of fortification with flaxseed hull (1–5%) on *in vitro* digestibility and glycemic index of wheat bread. Addition of flaxseed decreased the relative protein digestibility up to 8%, however, no significant influence of fortification was observed on slowly and rapidly digestible starch, *in vitro* starch digestibility and values of the expected glycemic index.

Salgado-Cruz et al., (2017) studied the effect of chia mucilage on the glycemic index and microscopic characterisation of pita bread. The presence of fibre in the bread affected the degree of gelatinisation and glycemic index. In addition to a higher glycemic index, a large proportion of gelatinised starch was observed in the crumb of the bread incorporated with chia mucilage in comparison to control bread. Addition of chia mucilage decreased the glycemic index in the crust section and increased the slowly digestible starch fraction of the bread. Menga et al., (2017) also reported an increase in the slowly digestible starch fraction of gluten-free pasta with chia (*Salvia hispanica* L.) as a thickening agent. Giri et al., (2017) attempted to modify the glycemic index of chapatti, an unleavened Indian flatbread, and idli, a steamed product prepared from fermented rice and black gram batter, by using unmodified and modified guar gum. Addition of 5% unmodified and modified guar gum, separately, reduced the glycemic index of chapatti from 62.56 to 51.25 and 53.45 while that of idli was reduced from 71.28 to 60.00 and 61.63, respectively. Texture and sensory attributes of both the types of products were acceptable. In order to overcome the nutritional imbalance of gluten free foods, which have relatively higher glycemic index and lower resistant starch content, Giuberti and Gallo (2017) suggested that at least 20% replacement of the total flours with high amylose starch (>60% amylose) was required to increase the resistant starch content and lower the glycemic index of gluten free bread and cookies.

Bae et al., (2016) studied the effect of two dietary fibre enriched materials obtained from apples on *in vitro* starch digestibility using a wheat flour gel model. Replacing wheat flour with an equal blend of soluble and insoluble dietary fibres at 20% level resulted in a noticeable reduction of predicted glycemic index (pGI) values. While studying the glycemic impact of different potato varieties, Pinhero et al., (2016) observed a strong positive correlation between glycemic index (eGI) and rapidly digestible starch and a strong negative correlation between glycemic index (eGI) and resistant starch content. Radovanovic et al., (2015) evaluated the use of dry Jerusalem artichoke, high in soluble fibre particularly inulin, as a functional ingredient for the development of extruded food products with low glycemic index. A significant ($P<0.05$) increase was observed in total dietary fibre and inulin levels of extruded food products upon the addition of artichoke. The samples with 30% and 60% artichoke fulfilled the criteria for medium GI foods and the samples containing 80% artichoke met the criteria for low GI foods. Zamora-Gasga et al., (2014) used agave fibre (*Agave tequilana*), a by-product from fructan production, for the development of granola bars. The bars containing agave dietary ingredients contained a high soluble dietary fibre (23.35 g/100 g) with *in vitro* starch hydrolysis and estimated glycemic index values of 74% and 72%, respectively, fulfilling the criteria for moderate GI foods. Addition of unripe banana has also been reported to affect the starch digestibility and glycemic index of cookies (Agama-Acevedo et al., 2012). Addition of unripe banana decreased the hydrolysis percentage and predicted glycemic index of the cookies by increasing the slowly digestible starch and reducing rapidly digestible starch. While studying the *in vitro* digestibility of unripe banana flour and its derived autoclaved/debranched powder, Liao and Hung (2015) reported that resistant starch had an obvious impact on the glycemic response and estimated glycemic index. Ho et al., (2015) studied the *in vitro* starch digestibility of bread with banana pseudo-stem flour and hydrocolloids. A significant reduction of hydrolysis index and estimated glycemic index was observed for the composite breads. A lower predicted glycemic index was also observed by Jun et al., (2014) for the cake samples prepared with fibre-enriched materials.

5.4.2. Cereal β-glucan

European Food Safety Authority (EFSA) in 2011 officially recognized the potential of cereal β-glucan, a kind of indigestible polysaccharide, to lower postprandial glycaemic responses (EFSA 2011). Gujral et al., (2018) studied the effect of hulless barley bran from 9 different cultivars on the functionality and digestibility of chapattis, Indian flat bread. The composite flours contained up to three fold more β-glucan and the chapattis prepared from it had significantly more slowly digestible and resistant starches and lowered starch retrogradation. Wang et al., (2017) evaluated the effects of incorporation of oat β-glucan on the glycemic response of steamed bread. Oat β-glucan was added at 0 to 5 g/100 g levels replacing wheat flour in the formulation. Products with 1 g/100 g and 3 g/100 g oat β-glucan were sensorially acceptable. Although, oat β-glucan lowered the *in vitro* predicted glycemic index, no significant change was observed on *in vivo* glycemic response. Zhuang et al., (2017) studied the effect of *Lentinus edodes* β-glucan on *in vitro* starch digestibility of wheat starch gel. *Lentinus edodes* β-glucans increased the amount of slowly digestible starch and significantly reduced the rate of starch digestion and predicted glycemic index when added at 20% (w/w) level. Zhang et al., (2017) studied the impact of the native form of β-glucan (15.6%) on starch digestion and postprandial glycemia. A significant decrease in starch digestion rate and postprandial glycemia was observed in comparison to gelatinized oat starch. The microscopic studies revealed a network-like native structure of β-glucan with encapsulated protein and starch that might have reduced the enzyme accessibility and thereby reducing the rate of digestion. Maintaining the native form of β-glucan in oat grains was suggested as a better way to modulate the postprandial glycemia of oat-based whole grain foods.

Ekström et al., (2017) studied the effect of oat β-glucans on starch digestion and glycemic profile of bread. In comparison to white wheat reference bread, a significant reduction (by 32–37%) was observed in the glycemic index and glucose iPeak of oat β-glucan-enriched bread, suggesting the potential of oat β-glucan for tailoring the glycemic profile of bread products. AbuMweis et al., (2017) studied the effect of barley β-glucan on the postprandial glycemic response in healthy human population. Consumption of β-glucan containing foods significantly reduced the glycemic index, insulin area under the curve (by 2577 min × pmol/L) and insulin index (−33.8). Gamel et al., (2017) studied the impact of various proteases, amylases and lipase on the solubility and resulting viscosity of β-glucan extracted from oat bran cereals. The viscosity of β-glucan was reported to influence its ability to lower serum cholesterol and postprandial blood glucose levels.

Kim and White (2012) studied the *in vitro* digestion rate and glycemic index of different oat flours containing different levels of β-glucan content. The presence of soluble fibre (β-glucan) slowed the starch digestion as the rate of digestion was negatively correlated with the β-glucan content. The glycemic index was also reported to decrease with increasing level of β-glucan, suggesting its importance in the development of new products with low GI. Chillo et al., (2011) studied the effect of incorporation of two β-glucan barley concentrates (Glucagel and Barley Balance) on the glycemic index and postprandial glycemic response of spaghetti. The IAUC (incremental areas under the curve) values of the spaghetti incorporated with Barley Balance were lower than control spaghetti (without β-glucan) with lowest values (52%) observed for the products incorporated with 10% Barley Balance. The glycemic index of the spaghetti decreased with increasing levels of Barley Balance and the products incorporated with 10% Barley Balance showed a 54% lower GI than control.

5.4.3. Role of proteins

Recent studies have indicated the significance of dietary proteins in satiety, weight loss and obesity management. After a period of energy restriction and weight loss, a diet characterized by a moderately higher protein and slightly lower glycemic index was reported to be more efficient in counteracting weight gain (Larsen et al., 2010). In the children of overweight parents, *ad lib* consumption of protein diets has been reported to improve metabolic risk markers (Damsgaard et al., 2013). Dairy proteins have an advantageous effect on metabolic health due to their muscle promoting and satiety improving abilities (McGregor and Poppitt 2013) and have been reported to attenuate the markers of inflammatory and oxidative stress in metabolic syndrome patients (Stancliffe et al., 2011). Whey proteins, in particular, have beneficial effects on risk factors associated with the metabolic syndrome (Pal and Ellis 2010). The co-ingested proteins may also influence the postprandial glycemia through glucose regulatory properties and should be considered in addition to the GI characteristics of carbohydrates in foods.

Presence of some proteins and amino acids has been reported to reduce the postprandial glycemia to composite meals or glucose in healthy subjects (Augustin et al., 2015). Whey proteins, in particular, have been reported to reduce postprandial glycemia by stimulating insulin response (Nilsson et al., 2004). Ingestion of whey has been reported to promote higher levels of five amino acids in the blood viz. threonine, lysine, valine, leucine and isoleucine. The oral ingestion of a protein mixture of these five amino acids in a similar ratio as that in postprandial blood after ingestion of whey protein has been reported to mimic the effects of whey on insulinaemia and glycemia following a carbohydrate challenge (Nilsson et al., 2007). Several other studies have also reported similar effects of whey protein on insulinaemia and glycemia in healthy subjects following an oral glucose challenge (Augustin et al., 2015; Lan-Pidhainy et al., 2010). A dose-response relationship measured by Gunnerud et al., (2013) showed a decrease of 3.8 mmol min/L in blood glucose incremental area under the curve (0–120 min) for each gram of added whey protein.

Coda et al., (2017) studied the effect of faba bean flour and sourdough on the protein quality of wheat bread. Protein content was increased from 11.60% to 16.50% by addition of 30% faba bean flour. The predicted glycemic index was lowest whereas the protein chemical score, free amino acid profile, biological value index and protein digestibility were highest for faba bean sourdough bread. Maetens et al., (2017) used germinated soybeans for the development of healthy snack chips. Addition of germinated soybeans increased the protein content and reduced the estimated glycemic index. Ng et al., (2017) studied the effect of grey oyster mushroom (*Pleurotus sajor-caju*) powder on the microstructure, *in vitro* starch digestibility, *in vivo* glycemic index and sensorial properties of biscuits. Incorporation of up to 8% powder was found acceptable for production of high-protein/high-fibre biscuits without adversely affecting the sensorial characteristics of the products. Addition of the powder affected the integrity of starch granules inducing uneven spherical shapes and reducing the size of the starchy granules that resulted in reduced susceptibility of starch to digestive enzymes. The reduced rate of hydrolysis markedly reduced the glycemic index of the biscuits. Lorusso et al., (2017) studied the effect of substitution of semolina with fermented quinoa flour (20%) on the nutritional quality and *in vitro* starch digestibility of pasta. Pasta enriched with quinoa flour, high in protein and amino acids, showed highest *in vitro* protein digestibility, protein nutritional indices (biological value, essential amino acid index, protein efficiency ratio, and nutritional index) and lowest predicted glycemic index.

Emaleku et al., (2017) studied the effect of soy flour fortified whole wheat meal on the glycemic index and lipid profiles of the test human subjects. A significantly lower glycemic index was observed for soy flour fortified whole wheat meal in comparison to D-glucose. Kashima et al., (2016) studied the effect of premeal consumption of different amounts of a soy protein isolate (0 g, 20 g and 40 g) on the post-meal glycemic profile of healthy young subjects. A significant decrease was observed in the incremental area under the curve and peak blood glucose response for preload of 40 g. In addition to exaggerated insulin response to the soy protein preload, glycemic control appeared to be attributable to non-insulin dependent mechanisms, such as delayed gastric emptying. Pineli et al., (2015) developed quinoa milk with high protein content and low glycemic index using an adaptation of a process for rice milk. Replacement of water by acidified saline solution during cooking and inclusion of a soaking step resulted in about 3 times more protein and a low glycemic index. Yonga et al., (2011) studied the effect of mixtures of wheat starch and whey protein isolate (20% and 50%), as a model high-protein-low carbohydrate food, on the glycemic index of extruded foods. Addition of whey reduced the rate of digestion and glycemic load, however, it increased the glycemic index and rapidly digested starch.

5.4.4. Polyphenols and flavonoids

Plant foods that are rich in polyphenols and flavonoids have been reported to inhibit postprandial glycemic responses to meals (Castro-Acosta et al., 2017). Table 3 shows the effect of different protein-based and polyphenol-based ingredients on *in vitro* digestibility and estimated glycemic index of different foods. Qi et al., (2017) reported that tea polyphenols have the potential to alleviate metabolic syndrome and prevent memory impairment through circadian clock-related mechanisms, suggesting tea polyphenols supplementation as future strategies to combat obesity, metabolic syndrome and cognitive disorder. A similar finding was also reported by Mi et al., (2017) who observed that (−)-Epigallocatechin-3-gallate, an important

Table 3. Effect of addition of different protein-based and polyphenol-based ingredients on *in vitro* digestibility and estimated glycemic index of different foods.

Source of Protein/ Polyphenols	Food Material	Results Obtained	Reference
Faba bean flour (replaced wheat flour at 0% and 30%) and sourdough	Wheat bread	Lowered glycemic index and increased protein chemical score, free amino acid profile, biological value index and protein digestibility	Coda et al. (2017)
Germinated soybeans flour	Snack chips	Increased protein content and lowered glycemic index	Maetens et al. (2017)
Grey oyster mushroom (*Pleurotus sajor-caju*) at 0, 4, 8 and 12% level	Biscuits	Reduced rate of hydrolysis and glycemic index (≥8%) and increased protein content	Ng et al. (2017)
Quinoa flour (replaced 20% semolina)	Pasta	Lowered glycemic index and increased *in vitro* protein digestibility and protein nutritional indices (biological value, essential amino acid index, protein efficiency ratio and nutritional index)	Lorusso et al. (2017)
Pomelo fruit (*Citrus maxima*): fresh pomelo fruit segments (0%, 10%, 20% and 30%) and dried pomelo fruit segments (0%, 2.5%, 5% and 7.5%)	Breads	Lowered glycemic index and increased resistant starch fractions	Reshmi et al. (2017)
Blue maize flour (anthocyanin-rich)	Cooked maize	Inhibited α-amylase, Negative correlation between phenolic content and starch digestion	Camelo-Méndez et al. (2017)
Black rice extract (anthocyanin-rich) at 1%, 2%, and 4% level	Bread	Reduced digestion rate by 12.8%, 14.1%, and 20.5% for bread with 1%, 2%, and 4% extract, respectively	Sui et al. (2016)
Carob flour (*Ceratonia siliqua* L.) (1% to 5%)	Durum wheat pasta	Proportional increase in glycemic index with substitution level and increased phenolics content, antiradical activity and reducing power	Sęczyk et al. (2016)
Baobab fruit (*Adansonia digitata* L.): A low-dose (18.5 g) and a high-dose (37 g) aqueous drink in 250 mL of water along with white bread containing 1.88% of Baobab fruit	White bread and aqueous drink	1.88% Baobab fruit significantly reduced rapidly digestible starch content of white bread. Reduced glycemic index	Coe et al. (2013)
Whey proteins isolate (20% and 50%)	Extruded foods	Reduced rate of digestion and glycemic load. Increased glycemic index and rapidly digested starch	Yonga et al. (2011)

constituent of tea, has the potential to decrease the lipid accumulation and attenuate insulin resistance triggered by circadian misalignment. Mulberry (*Morus alba L.*) leaf extract was also reported to decrease significantly the starch digestion and absorption in healthy subjects, suggesting the importance of mulberry leaf tea that has recently received much attention as a dietary supplement (Józefczuk et al., 2017; Banu et al., 2015). A significant decrease in postprandial glucose, insulin and incretin response to a high-carbohydrate meal was reported by Castro-Acosta et al., (2017) in healthy men and women who consumed blackcurrant and apple polyphenol-rich drinks relative to a placebo drink. The decrease in postprandial glycemia was partly related to inhibition of intestinal glucose transport. Sidorova et al., (2017) examined the hypoglycemic and hypolipidemic effects of *Phaseolus vulgaris L.* seed coat and *Vaccinium myrtillus L.* leaf extracts, containing polyphenolic compounds, on carbohydrate and lipid metabolism in diabetes-induced Wistar rats. The results obtained suggested lipid-lowering and antioxidant action related to the administration of *Phaseolus vulgaris L.* seed coat and *Vaccinium myrtillus L.* leaf extracts in Wistar rats. *Vaccinium myrtillus L.* leaf extract was also reported to reduce hyperglycemia in diabetic animals. While studying the glycemic index and antioxidant properties of red and white basmati rice, Prasantha et al., (2017) found a significant negative correlation between glycemic index values and total anthocyanin content, total phenolic content and antioxidant activity.

Reshmi et al., (2017) studied the effect of pomelo fruit (*Citrus maxima*), a citrus fruit belonging to the family *Rutaceae*, on the starch digestibility and predicted glycemic index in bread. Bread incorporated with the citrus fruit showed low predicted glycemic index (62.97–53.13%) and higher levels of resistant starch fractions (3.87–10.96%) compared to the control bread. Bread with 5% dry and 20% fresh pomelo fruit was found to be sensorily acceptable. The reduction in glycemic index was attributed to the inhibition of carbohydrate hydrolyzing enzyme activity by naringin, a well-known flavanone glycoside, present in pomelo fruit. Naringin has been reported to possess anti-oxidant, anti-inflammatory and anti-diabetic activity (Cui et al., 2012). Chinedum et al., (2017) studied the effect of processing on predicted glycemic indices, starch digestibility and α-amylase inhibitory properties of breadfruit (*Treculia africana*) and beans (*Phaseolis vulgaris*). Higher hydrolysis curves were observed for raw and processed breadfruit than raw and processed beans. Raw and fried breadfruit had high glycemic indices; boiled beans and breadfruit had intermediate glycemic indices whereas raw beans had a low glycemic index. Phenolic compounds in the legumes were suggested to contribute to their α-amylase inhibitory properties. Camelo-Méndez et al., (2017) observed a similar finding while studying the functional properties of blue maize flour. Blue maize, having high total anthocyanins content and high antioxidant activity, exerted inhibitory effect against α-amylase. A negative correlation was observed between phenolic content and starch digestion. Both cooked and uncooked matrices of blue maize had moderate predicted glycemic indexes. Sui et al., (2016) studied the effect of anthocyanin-rich black rice extract powder on quality and *in vitro* digestibility of bread. The quality and acceptability of bread with 2% extract was same as that of control. Addition of extract significantly reduced the digestion rate of the bread, indicating the significance of anthocyanins in the development of functional foods.

Coe et al., (2016) studied the effect of polyphenol-enriched (green tea extract, Baobab fruit extract, grape seed extract, and resveratrol) bread on glycemic response and postprandial insulin in healthy human subjects. Although no significant effect of polyphenol enrichment was observed on glycemic response or hunger, Baobab fruit extract increased postprandial insulin economy in healthy participants as it reduced significantly ($P<0.05$) the total (0–180 minutes) and segmental insulin area under the curve at 0 to 90, 0 to 120, and 0 to 150 minutes. Coe et al., (2013) studied the effect of polyphenol-rich baobab fruit (*Adansonia digitata* L.) on starch digestion and glycemic response in humans. Baobab fruit extract was added to white bread and was consumed in solution at a low-dose (18.5 g) and a high-dose (37 g) aqueous drink in 250 mL of water along with white bread. Addition of Baobab fruit extract at 1.88% significantly ($P<0.05$) reduced rapidly digestible starch of white bread and reduced the glycemic index significantly ($P<0.05$) at both low and high doses. Zemestani et al., (2016) studied the effects of chamomile tea consumption on antioxidant status and glycemic control in subjects with type 2 diabetes mellitus. Short-term intake of chamomile tea was reported to have beneficial effects on glycemic control and antioxidant status in patients with type 2 diabetes mellitus.

Costello et al., (2016) reviewed the effect of cinnamon supplementation on glycemic control in type 2 diabetes subjects using eleven randomized controlled trials. Cinnamon, a rich source of bioactive compounds such as cinnamaldehyde, eugenol, trans-cinnamic acid, phenolic compounds, catechins, proanthocyanidins, monoterpenes, and sesquiterpenes, was reported to have modest effects on fasting plasma glucose and haemoglobin A1c. Sęczyk et al., (2016) evaluated the effect of carob flour (*Ceratonia siliqua* L.) on the antioxidant potential and *in vitro* digestibility of fortified durum wheat pasta. In comparison to control, pasta fortified with 5% carob flour exhibited 2-fold, 18-fold and 3-fold increase in phenolics content, antiradical activity and reducing power, respectively. A proportional increase was observed in expected glycemic index value with the substitution level and ranged between 72.2 and 83.9 for 1–5% substitution, respectively. Törrönen et al., (2012) studied the effect of fortification of blackcurrant juice with crowberry on polyphenol content and postprandial glycemic control in healthy subjects. Fortification of blackcurrant juice with crowberry doubled the polyphenol content and improved postprandial glycemic control in healthy subjects.

5.4.5. Other ingredients and factors

The glycemic response of carbohydrate-rich foods also depend on several other factors like processing methods, additives, and storage environment (Ferng et al., 2016; Chiu and Stewart 2013; Rosen et al., 2011). Table 4 shows the effect of different processing methods, additives and storage conditions on *in vitro* digestibility and estimated glycemic index of different foods. Giuberti et al., (2017) studied the effect of three different resistant starch (RS) ingredients on the glycemic index of gluten-free rice cookies. Cookies were formulated by substituting 50% of rice flour with debranched, annealed or acid and heat-moisture treated waxy rice starch (RS_a, RS_b and RS_c, respectively) and compared with control (100% rice flour). RS_a was reported to have highest resistant starch content and total dietary fibre. A reduction in glycemic index was observed upon addition of RS ingredients with the lowest value estimated for RS_a cookies. The estimated RS loss caused by the baking process followed the order of $RS_a < RS_c < RS_b$. Phimolsiripol et al., (2017) studied the effect of crude malva nut gum (0%, 2.5%, 5%, 7.5% and 10% w/w) on the glycemic index of white bread. Both *in vitro* starch digestion kinetics as well as *in vivo* human testing showed a reduction in the glycemic index with the addition of the malva nut gum, suggesting its potential for the development of low GI foods. Ferng et al., (2016) studied the effect of different commercially available rice flours (*japonica, indica* and *glutinous*) on the glycemic response of chiffon cakes. Based on Granfeldt and Goni models with white bread as a reference, results of *in vitro* method indicated that *indica* rice cakes satisfied the low glycemic index criteria whereas *glutinous* and *japonica* rice cakes met the medium glycemic index requirement. *In vivo* test with glucose as a reference food

Table 4. Effect of different processing methods, additives and storage environment on *in vitro* digestibility and estimated glycemic index of different foods.

Additive/Processing Step/Storage	Food Material	Results Obtained	Reference
Decreased dough hydration	White bread	Increased slowly digestible starch	Martínez et al. (2018)
Debranched, annealed or acid and heat-moisture treated waxy rice starch	Gluten-free rice cookies	Reduced glycemic index and increased resistant starch and total dietary fiber	Giuberti et al. (2017)
Carob (*Ceratonia siliqua*)	Snacks	Reduced glycemic index and the feeling of hunger	Papakonstantinou et al. (2017)
Malva nut gum (0% to 10% w/w)	White bread	Reduced glycemic index	Phimolsiripol et al. (2017)
Carbonation	Glucose-based beverages	No affect on glycemic response and gastric emptying	Lau et al. (2017)
Physical modifications (annealed and heat-moisture treated rice starches)	Rice starches	Increased resistant starch content after annealing, reduced glycemic index after both treatments	Hung et al. (2016)
Freezing and frozen storage (-40°C and -18°C)	Foxtail millet-derived products (millet steamed bread and millet pancake)	No effect on glycemic index	Ren et al. (2016)
Drying methods (hot air-drying at 60°C and freeze-drying)	Yam	Decreased amylose content after hot air-drying, Increased resistant starch and decreased rapidly digestible starch after freeze-drying	Chen et al. (2016)
Sprouting and postharvest storage	Green pea, lentil and young mung bean	Increased starch digestibility and glycemic index with postharvest storage	Świeca and Gawlik-Dziki (2015)
Nixtamalisation processes (traditional with lime, classic with ashes and ecological with Ca salts)	Corn tortillas	Nixtamalisation processes improved resistant starch content and reduced glycemic index	Moreno et al. (2015)
Replacement of water by acidified saline solution during cooking and inclusion of a soaking step	Quinoa milk	Lowered glycemic index and increased protein content	Pineli et al. (2015)
Yellow pepper flour	Bread	Highest glycemic index observed for the bread with highest water content	Danza et al. (2014)
Addition of sourdough (*Lactobacillus fermentum*)	Gluten-free bread	Decreased glycemic index and increased fiber and inulin	Novotni et al. (2012)

indicated that rice cakes fulfilled the low glycemic index criteria, clarifying the misunderstanding of them being a high glycemic index food. Papakonstantinou et al., (2017) determined the glycemic index of Carob based snack in comparison to chocolate cookies containing equal amounts of available carbohydrates. Carob (*Ceratonia siliqua*) is a natural sweetener that could be used as a cocoa powder substitute (Durazzo et al., 2014). Carob snack met the criteria for low GI foods and its consumption reduced the feeling of hunger and the glycemic index following a meal. Lau et al., (2017) observed that carbonation of glucose-based beverages does not affect their glycemic response and gastric emptying. The glycemic response of both noncarbonated and carbonated beverages was reported to depend solely on the carbohydrate content of the beverages.

Martínez et al., (2018) studied the effect of hydration depletion on *in vitro* starch digestibility in white bread. Decreasing dough hydration from 75% to 45% increased the slowly digestible starch to 96.81%. Hung et al., (2016) studied the effect of physical modifications on *in vitro* digestibility and *in vivo* glucose response of rice starches. The resistant starch content increased to 19.5–26.9% after annealing treatment and to 18.5–23.9% after heat-moisture treatment. Both these treatments significantly reduced glycemic index values of the rice starches. The glycemic index values of annealed, heat-moisture treated, and native rice starches ranged in 21.2–43.9, 61.2–88.9 and 68.9–100, respectively. No correlation was observed between amylose contents and the resistant starch contents or glycemic index values whereas a strong negative correlation was observed between resistant starch contents and glycemic index values. Ren et al., (2016) studied the effect of freezing and frozen storage (-40 °C and -18 °C) on *in vitro* starch digestibility and estimated glycemic index of foxtail millet-derived products (millet steamed bread and millet pancake). No significant change was observed in the glycemic index of the products during the freezing process and frozen storage within the whole study period. Chen et al., (2016) studied the effect of different drying methods on *in vitro* digestibility of starch from yam. While a significant decrease was observed in amylose content in the starch obtained by hot air-drying at 60 °C, high levels of resistant starch and low levels of rapidly digestible starch and glucose were found in the starch obtained from freeze-dried yam.

Święca and Gawlik-Dziki (2015) studied the effect of sprouting and postharvest storage on *in vitro* starch digestion and the glycemic index of green pea, lentil and young mung bean sprouts. A significant increase was observed in the starch digestibility and values of the expected glycemic index (eGI) with postharvest storage. Moreno et al., (2015) studied the effect of different nixtamalization processes, including traditional with lime (TNP), classic with ashes (CNP) and ecological with Ca salts (ENP), on the glycemic index of corn tortillas. Overall the nixtamalization processes improved the resistant starch content and the tortillas made from ENP 1% ash CNP and ENP Ca propionate met the criteria for low GI foods. Danza et al., (2014) studied the effect of the addition of yellow pepper flour on the glycemic index of bread. The highest glycemic index was observed for the bread with highest water content. Novotni et al., (2012) studied the effect of addition of the sourdough to gluten-free bread on the glycemic index *in vivo*. A commercially available starter, *Lactobacillus fermentum*, was used to ferment the sourdough and was added at different levels (7.5%, 15%, 22.5% and 30%) to bread batter. All the samples were high in fibre (>6 g/100 g) and inulin. Addition of sourdough caused a decrease in glycemic index and bread with 15% and 22.5% had lower glycemic index than control.

6. Conclusions

The rising prevalence of obesity is an important public health concern at national and global levels with serious social and economic ramifications. A great body of research has shown a strong correlation between the development of several neurological disorders and obesity. Diet-induced metabolic dysfunctions can aggravate the already existing neurological disorders. Several pharmacological, surgical, lifestyle and dietary interventions are available to address this menace in order to mitigate the incidence of associated neurological disorders and substantial financial burden. Neurological disorders are a growing health concern and have a great impact on the quality of patients' life. Although much of the research related to specific health attributes is lacking, interest in the glycemic index has increased over the years with increasing number of claims regarding its effectiveness. Several of already existing products have been successfully modified and a large number of new products with low glycemic index have been developed and much more are in the development process.

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