Science Review of Isolated and Synthetic Non-Digestible Carbohydrates

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Introduction

We are providing a summary of our review of the scientific evidence that we identified for certain isolated or synthetic non-digestible carbohydrates that are not listed as a dietary fiber in 21 CFR 101.9(c)(6)(i). Our review has relied on the draft guidance for industry "Scientific Evaluation of the Evidence on the Beneficial Physiological Effects of Isolated or Synthetic Non-digestible Carbohydrates Submitted as a Citizen Petition (21 CFR 10.30)"[1] to identify those studies from which scientific conclusions could be drawn about a physiological effect that is beneficial to human health.

[1] Available at http://www.fda.gov/Food/GuidanceRegulation/default.htm

Gum Acacia

Background

Gum acacia (gum arabic) is the dried gummy exudate from stems and branches of trees of various species of the genus *Acacia*, family Leguminosae. Gum acacia primarily comes from the tree, *Acacia Senegal*, grown in various countries in Africa. Gum acacia is an ingredient used as a thickener, emulsifier, or stabilizer (21 CFR 172.780; 21 CFR 184.1330). Gum acacia is a nondigestible polysaccharide that is completely fermented in the colon (Ross et al., 1983). Gum acacia is soluble, but it is not viscous (Slavin, 2013).

Blood Cholesterol Levels

We identified eight human studies that evaluated the effect of gum acacia consumption on blood cholesterol levels. Scientific conclusions could not be drawn from seven of these studies: (Campbell et al., 1997; Davidson et al., 1998; Jensen et al., 1993; Jensen et al., 1997; Mee et al., 1997; Ross et al., 1983; Sharma et al. 1985a) because: (1) a mixture of non-digestible carbohydrates, including gum acacia, was provided and therefore the physiological effect of gum acacia *per se* could not be evaluated, (2) an inappropriate control group was used, or (3) evaluating the effect of gum acacia on fasting blood cholesterol levels was not possible because one or more of the test periods was of insufficient duration.

Haskell et al. (1992)

In a randomized, placebo-controlled trial, 42 hypercholesterolemic U.S. men and women were provided either a placebo control (non-fiber carbohydrate) or 15 g/day gum acacia for one month. After the one month period, no significant difference was observed in total or LDL cholesterol levels ($P > 0.05$).

Blood Glucose Levels

We identified two published human studies that evaluated the effect of gum acacia consumption on blood glucose levels. Scientific conclusions could not be drawn from one study (Campbell et al., 1997) because a mixture of non-digestible carbohydrates, including gum acacia, was provided and therefore the physiological effect of acacia gum *per se* could not be evaluated.

Sharma (1985b)

Twelve healthy Indian men participated in a cross-over design study in which the glycemic response was measured after consumption of glucose with or without (control) 20 g gum acacia. The area under the curve was 4,036 mg/min/dL for glucose and 3,420 mg/min/dL when gum acacia was included. This reduction in blood glucose levels with gum acacia was significantly greater compared to the control ($P < 0.05$).

Laxation/Bowel Function

We identified four human studies that evaluated the effect of gum acacia consumption on laxation. Scientific conclusions could not be drawn from three of these studies (Bliss et al., 2001; Bliss et al., 2014; Sunvold et al., 1995) for one or more of the following reasons: (1) a mixture of non-digestible carbohydrates, including gum acacia, was provided and therefore the physiological effect of acacia gum *per se* could not be evaluated, and (2) unhealthy subjects were evaluated (e.g., subjects suffered from fecal incontinence).

Bliss et al. (1996)

Sixteen patients with chronic renal failure participated in a study that tested the effect of acacia gum on laxation to evaluate the fecal excretion of metabolites that are typically retained in such patients. In this cross-over study, the subjects consumed a low protein diet along with either 50 g/day gum acacia or a placebo (1 g/day pectin) for 4 weeks. There was no significant difference in mean daily stool frequency between the placebo group (1.2 stools/day) and the gum acacia group (1.4 stools/day) ($P = 0.48$).

Energy Intake

We identified three publications that evaluated the effect of gum acacia consumption on energy intake. Scientific conclusions could not be drawn from two of these studies (Babiker et al., 2012; Davidson et al., 1998) because: (1) a mixture of non-digestible carbohydrates, including gum acacia, was provided and therefore the physiological effect of gum acacia *per se* could not be evaluated, and (2) statistical comparisons were not conducted between the gum acacia and control group.

Calame et al. (2011)

This publication included two randomized, double-blinded, placebo-controlled cross-over studies conducted in the Netherlands. The first study determined the extent to which high doses (10, 20 and 40 g) of gum acacia dissolved in water might affect subjective scores of satiety and energy intake in 12 healthy men. Energy intake was measured 3 hours after consumption while Visual Analogue Scales (VAS) scores were recorded every 30 minutes after consumption. Compared to the control, there was a significant difference in the VAS score on satiety when 10, 20 or 40 g of gum acacia was consumed. Compared to the control (water), energy intake was significantly lower when consuming 40 g of two types of gum acacia ($P < 0.05$). Energy intake was not significantly different for the other doses (10 and 20 g).

The second study was designed to identify a minimum dose (5 or 10 g) of gum acacia required to obtain the satiety effects ($n = 42$ men and women). The gum acacia was consumed in plain water served as the control. Both doses significantly increased the VAS score for satiety ($P < 0.03$). A significant decrease in energy intake ($P < 0.02$) was observed for the two doses compared to the control.

Mineral Absorption

We identified one human study that evaluated the effect of gum acacia consumption on mineral absorption. Scientific conclusions could not be drawn from this study (Sunvold et al., 1995) because a mixture of non-digestible carbohydrates, including gum acacia, was provided and therefore the physiological effect of acacia gum *per se* could not be evaluated.

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Alginate

Background

Alginate is a soluble fiber composed of β-1,4-D-mannuronic acid and α-1,4-L-guluronic acid organized in homopolymeric compounds of either mannuroante or guluronate, or as heteropolymeric compounds, expressed as mannuronic acid to guluronic acid ratio. Alginate is present in the cell walls of brown seaweeds as the calcium, magnesium and sodium salts of alginic acid of various species, (e.g., *Ascophyllum*, *Durvillaea*, *Ecklonia*, *Laminaria*, *Lessonia*, *Macrocystis* and *Sargassum*) (McHugh et al., 2003). Alginate is widely used in the food industry to improve texture of salad dressings, yogurts, and jellies because of its gelling, viscosifying, and stabilizing properties (Jensen et al., 2013).

Blood Cholesterol Levels

We identified three studies that evaluated the relationship between alginate consumption and blood cholesterol levels.

Hall et al. (2012)

Ten overweight English men participated in a randomized, single-blinded, cross-over study and consumed either bread enriched with 4% of *Ascophyllum nodosum* providing 1.15 g of alginate per serving or seaweed-free control bread. There was no significant difference in the area under the curve for post-prandial blood total cholesterol following the consumption of alginate enriched bread compared to control.

Jensen et al. (2012b)

In a double-blind, parallel-intervention study, 96 obese Danish men and women were randomly assigned into two groups who consumed either an energy-restricted diet plus an alginate-based pre-load supplement (15 g) or an energy-restricted diet plus a control pre-load supplement before each of the three main meals of the day over a 12-week period. No significant differences were observed in fasting total cholesterol and LDL cholesterol between the two groups in the intention-to-treat analysis ($P > 0.1$).

Paxman et al. (2008a)

Fourteen healthy English men participated in a randomized, single-blinded, controlled two-way cross-over trial consuming a 100 mL pre-load drink (1.5 g of sodium alginate or control) followed by a lunch. There were no significant differences between the alginate groups compared to the control groups for post-prandial cholesterol ($P = 0.764$) or peak blood cholesterol ($P = 0.075$).

Blood Glucose Levels

We identified nine studies that evaluated the relationship between alginate intake and blood glucose levels. Scientific conclusions could not be drawn from three of the studies (Torsdottir et al., 1991; Williams et al., 2004; Wolf et al., 2002) for one or more of the following reasons: (1) the intervention provided non-digestible carbohydrates, in addition to alginate, and therefore the effect of alginate *per se* could not be evaluated, (2) the study did not evaluate the effect of alginate on attenuation of blood glucose levels in response to consumption of a food and/or beverage but instead measured the glycemic index of alginate, and (3) unhealthy individuals were evaluated (i.e., type 2 diabetics).

Hall et al. (2012)

Ten overweight English men participated in a randomized, single-blinded, cross-over study and consumed either bread enriched with 4% of *Ascophyllum nodosum* providing 1.15 g of alginate per serving or alginate-free control bread. There was no significant difference in the area under the curve for postprandial glucose following the consumption of alginate enriched bread compared to the control ($P > 0.05$).

Harden et al. (2012)

Forty healthy English men participated in a randomized, single-blinded, controlled, parallel trial to determine the glycemic response to a controlled test-lunch following an ionic-gelling alginate (1.5 g of sodium alginate) pre-load drink compared to an acidic-gelling control. There was a 14% lower mean peak post-prandial blood glucose at 90 minutes following the ionic-gelling alginate (6.06 ± 0.59 mmol/L) compared to the acidic-gelling control (6.92 ± 0.70 mmol/L) ($P < 0.05$).

Jensen et al. (2012a)

In a randomized double-blind, placebo-controlled, four way cross-over design study, twenty Danish men and women consumed pre-load beverages at two different volumes, 330 mL-low volume (LV) and 500 mL—high volume (HV) containing alginate (3% alginate concentration equivalent to 9.9 g and 15 g, respectively), and without alginate (LV-control and HV-control). The subjects consumed the pre-load beverages 30 minutes before consuming a standard breakfast and 30 minutes before *ad libitum* lunch was served. The HV-alginate pre-load group resulted in a 40% smaller area under the curve post-prandial glucose response (41.8 ± 10.0 mmol/L) compared to the HV-control group (70.3 ± 11.6 mmol/L) ($P =0.046$).

Jensen et al. (2012b)

In a double-blind, parallel-intervention study, 96 obese Danish men and women were randomly assigned into two groups who consumed either an energy-restricted diet plus an alginate-based pre-load supplement (15 g) or an energy-restricted diet plus a control pre-load supplement before

each of the three main meals of the day over a 12-week period. No differences were observed in fasting blood glucose between the two groups in the intention-to-treat analysis ($P > 0.1$).

Khoury et al. (2014)

Twenty-four healthy Canadian males were randomly provided with the following treatments: (1) chocolate milk (CM), (2) 1.25% alginate CM, (3) 2.5 % alginate CM, and (4) 2.5% alginate solution in a cross-over design study. Sodium alginate was composed of 56% guluorunic and 44% mannuronic residues. *Ad libitum* pizza was served after 120 minutes of each treatment. Blood glucose was measured at pre- (0-120 minutes) and post- (120-260 minutes) meal intervals. In the pre-meal period, 2.5% alginate CM resulted in lower mean blood glucose compared with the CM control ($P < 0.05$). In the post-meal period, all three alginate-enriched pre-loads reduced post-prandial and total glucose responses compared with CM alone ($P < 0.0001$).

Paxman et al. (2008a)

Fourteen healthy English men participated in a randomized, single-blinded, controlled two-way cross-over trial consuming a 100 mL pre-load drink (1.5 g of sodium alginate or control) followed by a lunch. There were no significant differences after alginate compared to the control for post-prandial glucose ($P =0.874$) or peak blood glucose ($P = 0.687$).

Energy Intake

We identified fourteen studies that evaluated the relationship between alginate consumption and satiety and/or energy intake. Scientific conclusions could not be drawn from eight of these studies (Appleton et al., 2004; Hoad et al., 2004; Jensen et al., 2011; Mattes et al., 2007; , Paxman et al., 2008b; Pelkman et al., 2007; Peters et al., 2011; Solah et al. 2010 ,) for one or more of the following reasons: (1) energy/food intake was not measured, (2) an appropriate control was not provided, (3) the intervention provided non-digestible carbohydrates, in addition to alginate, and therefore the effect of alginate *per se* could not be evaluated, or (4) only an abstract was available, which provides insufficient information for evaluating a study.

Hall et al. (2012)

Ten overweight English men participated in a randomized, single-blinded, cross-over study and consumed either bread enriched with 4% of *Ascophyllum nodosum* providing 1.15 g of alginate per serving or seaweed-free control bread. The results showed no significant differences in hunger and fullness between the two groups. Consumption of the alginate enriched bread at breakfast led to 16.4% significant reduction ($P = 0.006$) in energy intake (mean = 914.2 ± 380.2 kcal) compared to the control bread (1092.9 ± 460.7 kcal) from an *ad libitum* test meal four hours later. However, the energy intake during a free-living period of 24-hour post-test meal was not significantly different.

Jensen et al. (2012a)

In a randomized, double-blind, placebo-controlled, four way cross-over design study, twenty Danish men and women consumed pre-load beverages at two different volumes, 330 mL—low volume (LV) and 500 mL—high volume (HV) containing alginate (3% alginate concentration equivalent to 9.9 g and 15 g, respectively), and without alginate (LV-control and HV-control). The pre-load beverages were consumed 30 minutes before a standard breakfast and 30 minutes before *ad libitum* lunch was served. HV-alginate significantly increased satiety feelings (P = 0.038), reduced hunger (P = 0.042), and feeling of prospective food consumption (P = 0.027). Consumption of LV-alginate preload significantly (P = 0.040) reduced the energy intake (8%) at the subsequent lunch meal when compared to the LV-control. The 5.5% reduction in energy intake observed with the HV-alginate was not significant (P = 0.20).

Jensen et al. (2012b)

In a double-blind, parallel-intervention study, 96 obese Danish men and women were randomly assigned into two groups who consumed either an energy-restricted diet plus an alginate-based pre-load supplement (15 g) or an energy-restricted diet plus a control pre-load supplement (maltodextrin) 30 minutes before breakfast, lunch, and dinner, over a 12-week period. The energy intake, as assessed by a food diary, was not significantly different in the alginate group (1608 ± 48 kcal) when compared to the control group (1638 ± 48 kcal) (P = 0.68).

Khoury et al. (2014)

Twenty-four healthy Canadian males were randomly provided with the following treatments: (1) chocolate milk (CM), (2) 1.25% alginate CM, (3) 2.5 % alginate CM, and (4) 2.5% alginate solution in a cross-over design. Sodium alginate was composed of 56% guluronic acid and 44% mannuronic acid. *Ad libitum* pizza was served after 120 minutes of each treatment. The 2.5% alginate CM resulted in lower appetite responses only in the pre-meal phase compared with CM (P < 0.0001), 1.25% alginate CM (P = 0.001), and 2.5% alginate solution (P < 0.0001). However, all treatments resulted in similar food intake, cumulative energy intake, and water intake at the *ad libitum* lunch.

Odunsi et al. (2010)

In a randomized, placebo-controlled study, 48 U.S. overweight or obese women and men, ingested capsules of sodium alginate (405 mg per capsule) or placebo (lactose monohydrate) for a period of two weeks. Three capsules (days 1-7) and six capsules (days 8-10) were ingested 30 minutes prior to the satiation test, which measured the energy intake by the volume of a nutrient drink consumed at constant rate until maximum satiation, followed by an *ad libitum* meal four hours later. There were no significant differences in the total calories (kcal) (P = 0.92) ingested at the free choice buffet meal or the fullness score (P = 0.78) between the placebo and alginate groups.

Wanders et al. (2013)

In a randomized, cross-over design study, 121 Dutch men and women consumed *ad libitum* cookies containing 2.5 g or 5 g of alginate per 100 g of test products. Energy intake was 22% lower for the product containing 5 g of alginate per 100g of the test product (3.1 ± 1.6 MJ) compared to the control group (4 ± 2.2 MJ) (P <0.001).

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Apple Fiber

Background

Apple fiber is extracted from apples. Apple fiber is added to baked goods and beverages. Some manufacturers claim that it provides fruit specific flavors to food products.

Blood Cholesterol Levels

We identified two human studies evaluated the effect of apple fiber consumption on blood cholesterol levels. Scientific conclusions could not be drawn from one study because a mixture of nondigestible carbohydrates, including apple fiber, was provided and therefore the effect of apple fiber *per se* could not be evaluated (Mee and Gee, 1997).

Mayne et al. (1982)

Twelve Irish men and women with type 2 diabetes and hypercholesterolemia ingested 15 g/day of apple fiber for seven weeks. The apple fiber was added to their usual diet. The apple fiber was composed of 17% pectin and 62% cellulose/hemicellulose/lignin. Compared to the baseline blood total cholesterol which represented the usual intake without apple fiber and served as the control, there was no significant difference ($P > 0.05$) when compared to the addition of apple fiber.

Blood Glucose Levels

We identified one human study that evaluated the effect of apple fiber consumption on blood glucose levels. Scientific conclusions could not be drawn from the study because it was conducted in individuals with type 2 diabetes (Mayne et al.,1982).

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Bamboo Fiber

Background

Bamboo fiber is isolated from the fiber rich parts of the bamboo plant. Manufacturers add bamboo fiber to increase freshness of meat and fish products as well as to increase dough yield of baked goods. Some manufacturers also claim that bamboo fiber reduces breakage in baked products.

While we identified one study that evaluated the effect of bamboo shoot consumption on lipid profiles and bowel function, it did not specifically evaluate the effect of isolated bamboo fiber on these endpoints (Park et al., 2009).

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Carboxymethyl Cellulose (Cellulose Gum)

Background

Carboxymethyl cellulose (CMC) is a cellulose derivative with carboxymethyl groups (-CH_2-COOH) bound to some of the hydroxyl groups of the glucopyranose monomers that make up the cellulose backbone (Latif et al., 2007). CMC is often extracted from wood pulp and pure cotton cellulose. The polar (organic acid) carboxyl groups render the cellulose soluble and viscous. The functional properties of CMC depend on the degree of substitution of the cellulose structure (i.e., number hydroxyl groups that have taken part in the substitution reaction), as well as the chain length of the cellulose backbone structure and the degree of clustering of the carboxymethyl substituents. CMC provides multiple technical effects to foods (e.g., adds texture, stabilizes proteins, retains moisture, and forms oil-resistant films in variety of food products).

Blood Cholesterol Levels

We identified two human studies that evaluated the effect of CMC consumption on blood cholesterol levels. Scientific conclusions could not be drawn from one of the studies (Zhu et al., 2010) because of the lack of an appropriate control.

Behall et al. (1984)

Twelve U.S. men were provided with a low-fiber basal diet, followed by a diet with added CMC (0.75 g/100 calories, or 19 to 27 g/day) for four weeks. Consumption of CMC significantly reduced total cholesterol levels (164 mg/dL) compared to the basal diet (196 mg/dL), as well as LDL cholesterol levels (131 *versus* 107 mg/dL) ($P < 0.05$).

Blood Glucose Levels

We identified three human studies that evaluated the effect of CMC consumption on blood glucose levels. Scientific conclusions could not be drawn from one of the studies (Zhu et al., 2010) because of the lack of an appropriate control and because it was conducted in individuals with type 2 diabetes.

Behall et al. (1984)

Twelve U.S. men with normal blood cholesterol levels were provided a low-fiber, basal diet (control), followed by a diet with added CMC (0.75 g/100 calories, or 19 to 27 g/day) for four weeks. Fasting glucose (insulin) levels were not significantly different between the control and CMC diet groups after four weeks. Post-prandial glucose (and insulin) levels also were not significantly different between the two diets.

Brenelli et al. (1997)

Ten Brazilian men and women took part in a short-term intervention study. After an overnight fast, meals were consumed that contained 75 g glucose with or without (control) 11.6 g CMC. Post-prandial glucose (and insulin) levels were significantly lower than the control groups at 30 minutes ($P < 0.01$), 45 minutes ($P < 0.02$), and 60 minutes ($P < 0.002$) after CMC ingestion. The three hour area under the curve, however, was not statistically significant less than the control.

Laxation/Bowel Function

We identified three human studies that evaluated the effect of CMC consumption on laxation. Scientific conclusions could not be drawn from two of the studies (Bliss et al., 2014; Sunvold et al., 1995) for one or more of the following reasons: (1) a mixture of non-digestible carbohydrates, including CMC, was provided to the subjects and therefore the physiological effect of CMC *per se* could not be evaluated, and (2) CMC was evaluated using diseased subjects (e.g., subjects suffering from fecal incontinence).

Behall et al. (1987)

Eleven U.S. men consumed a basal diet with and without (control) 7.5 g CMC/1,000 calories for four weeks each. There was no significant difference in oro-fecal transit times between the two groups (26.7 for the control group *versus* 23.8 hours for the CMC group) ($P > 0.05$). The average number of defecations over an eight day period, however, was significantly higher for the CMC diet group (12.2) compared to the control group (7.4).

Mineral Absorption

We identified one human study that evaluated the effect of CMC consumption on mineral absorption. Scientific conclusions could not be drawn from this study (Sunvold et al., 1995) because a mixture of non-digestible carbohydrates, including CMC, was provided and therefore the physiological effect of CMC *per se* could not be evaluated.

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Corn Hull Fiber (Corn fiber, Insoluble Corn fiber, Corn Bran Fiber)

Background

Corn Hull Fiber (CHF) is extracted from corn bran, the tough fibrous outer layer or hull of the corn kernel. CHF is a lignocellulose ingredient with cellulose being the major component (approximately 50%) (FDA GRAS notification No. 427). CHF is considered an insoluble non-digestible carbohydrate because of its composition. Manufacturers claim that CHF has multiple technical effects. It is used as a bulking agent, as a moisture retention agent, and for freeze/thawing stability purposes.

We identified two studies that evaluated the effects of insoluble corn fiber (Cherbut et al., 1997; Sugawara et al., 1991). However, it was not clear if the non-digestible carbohydrates that were the subject of these studies were similar to or the same as CHF as we have described it in the preceding paragraph.

Blood Glucose Levels

We identified one study that evaluated the effect of CHF on blood glucose levels. Scientific conclusions could not be drawn from this study (Hallfrisch et al., 2002) because the test product included a mixture of nondigestible carbohydrates in addition to CHF and therefore the effect of CHF *per se* on blood glucose levels could not be evaluated.

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Cottonseed Fiber

Background

Cottonseed fiber is used as a bulking agent. It consists primarily of water-insoluble fiber with low viscosity (Madar et al., 1988).

Blood Cholesterol Levels

We identified one human study that evaluated the effect of cottonseed fiber consumption on blood cholesterol levels.

Madar et al. (1988)

Twelve Israeli men and women with type 2 diabetes and high blood cholesterol levels consumed diets with or without cotton seed dietary fiber (16.5g) in pita twice a day for one month. The cottonseed fiber contained 24% cellulose and 32% lignin. Fasting cholesterol levels were measured after one month. There was no significant difference between total cholesterol levels between the test subjects who consumed cottonseed dietary fiber (212 mg/dL) and those who did not (293 mg/dL).

Blood Glucose Levels

We identified one human study that evaluated the effect of cottonseed fiber consumption on blood glucose levels (Madar et al., 1988). Scientific conclusions could not be drawn from this study because it was conducted only in individuals who had diabetes.

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Galactooligosaccharides (GOS)

Background

GOS is produced by the enzymatic treatment of lactose to produce oligosaccharides of varying lengths (typically between 2 and 8 saccharide units) with one saccharide unit being a terminal glucose and the remaining saccharide units being galactose (Macfarlane et al., 2008). The enzymatic production of GOS has transgalactosylation activities that result in the formation of a mixture that includes GOS. GOS is used to improve the texture of foods and as a bulking agent.

Blood Glucose Levels

We identified one human study that evaluated the effect of GOS consumption on blood glucose levels.

Vulevic et al. (2013)

Forty-five overweight English men and women participated in a double-blind, randomized, placebo-controlled, cross-over study. The study subjects randomly consumed a diet that included a placebo (5.5.g/day maltodextrin) or 5.5 g/day GOS in water for 12 weeks each. Dietary nutrient intake did not differ between the two test periods. There was no significant difference in fasting blood glucose levels between the two diets ($P > 0.005$).

Blood Cholesterol Levels

We identified two human studies that evaluated the effect of GOS consumption on blood cholesterol levels.

Vulevic et al. (2008)

In a double-blind, placebo-controlled, cross-over study, 44 elderly English volunteers received either a placebo (maltodextrin) or GOS (5.5.g/day) in random order for 10 weeks each. Information was not provided on the study subjects' dietary energy and nutrient intake during the two study periods. This study showed that there was no significant difference in total cholesterol levels between the placebo and GOS diet ($P > 0.05$).

Vulevic et al. (2013)

Forty-five overweight English men and women participated in a double-blind, randomized, placebo-controlled, cross-over study. The study subjects randomly consumed a diet that included a placebo (5.5.g/day maltodextrin) or 5.5 g/day GOS in water for 12 weeks each. Dietary energy and nutrient intake did not differ between the two test periods. While there was no significant difference in LDL cholesterol levels between the two diets, total cholesterol levels were significantly lower after consuming the GOS diet ($P < 0.0001$).

Laxation

We identified seven human studies that evaluated the effect of GOS consumption on laxation. Conclusions could not be drawn from four of the studies because: (1) a mixture of non-digestible carbohydrates, including GOS, was provided and therefore the physiological effect of GOS *per se* could not be evaluated, (2) dietary information was not collected in the parallel design study to determine whether nutrient intake was similar between the study groups, or (3) the subjects had irritable bowel syndrome (Drakoularakou et al., 2010; Hughes et al., 2011; Shadid et al., 2007; Silk et al., 2009).

Davis et al. (2010)

In a single-blinded study, 18 U.S. subjects consumed chocolate chews that contained GOS at four sequential dosage levels: 0 g/day (control); 2.5 g/day; 5.0 g/day; and 10.0 g/day for three weeks each. The study did not provide information on the study subjects' dietary energy and nutrient intake for the different doses of the study. This study showed that there was no significant difference in the average daily number of bowel movements between the different doses ($P > 0.05$).

Ito et al. (1990)

Twelve healthy Japanese men participated in a single-blinded cross-over study in which 0 g/day (control), 2.5 g/day, 5.0 g/day, or 10 g/day of GOS in apple juice was provided for seven days each with a minimum seven day wash-out period. Stool samples were collected on days five through seven. Information was not provided on the study subjects' dietary energy and nutrient intake for the different doses of the study. This study observed no significant difference in stool frequency between the control group (7.5 stools per week) and the GOS diet group (7.3 – 7.8 stools per week).

Walton et al. (2012)

In a randomized, double-blind, placebo-controlled, cross-over study, 37 English men and women consumed diets that included juice that contained 0 g/day (control) or 8 g/day GOS. Each diet was consumed for three weeks. The study subjects' dietary intake during the study was estimated. Information was not provided on the study subjects' dietary energy and nutrient intake for the two phases of the study. There was no significant difference in stool frequency between the two diets ($P > 0.05$).

Calcium Absorption

We identified two human studies that evaluated the effect of GOS consumption on calcium absorption.

van den Heuvel et al. (1998)

In a randomized, cross-over design study, twelve Dutch men received a basal diet that provided 0 g/day (control) or 15 g/day GOS for 21 days. Intestinal absorption was measured using stable isotopically labeled calcium (and iron). Compared to the control diet, GOS had no significant effect on calcium (and iron) absorption ($P > 0.05$).

van den Heuvel et al. (2000)

In a cross-over design study to assess the effect of GOS intake on calcium absorption, 12 Dutch subjects drank a yogurt beverage twice a day that provided either 20 g/day GOS or sucrose (control) for nine days each. Calcium absorption was measured using stable isotopically labeled calcium. GOS significantly increased calcium absorption compared to the control ($P = 0.04$).

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Inulin/Oligofructose/Synthetic Short Chain Fructooligosaccharides

Background

Inulin is a naturally occurring polysaccharide that is a heterogenous collection of fructose polymers and belongs to a class of carbohydrates known as fructans (IOM, 2001). Individual fructan products may be distinguished by their source, method of production, or degree of polymerization (DP), that is, the number of fructose or glucose residues in the chain. The degree of polymerization varies from 3 to 60 DP, with the longer chain being predominant (approximately 70%). Inulin is not digested by human enzymes in the gastrointestinal tract because of the β (2,1) linkages, but rather is fermented by microorganisms in the colon. While inulin is a soluble fiber, it does not possess the typical physical effects of soluble viscous dietary fibers, such as viscosity (Schneeman, 1999). Inulin is present in plant products, many of which typically are not consumed as part of the U.S. diet (e.g., chicory roots and Jerusalem artichokes). Inulin is used as a bulking agent in foods (FDA GRAS Notification No. 118). Inulin that is present in food products is often listed as "chicory root extract."

Oligofructose (OF) is a shorter chain inulin that is extracted from chicory roots. OF refers to fructans what have a DP of < 10 and it accounts for approximately 30% of total inulin present in chicory root extract. Inulin can be enzymatically hydrolyzed to produce OF (Niness, 1999). OF is not digested by human enzymes in the gastrointestinal tract because of its β (2,1) linkages, but rather is fermented by microorganisms in the colon.

Short chain frutctooligosaccharides (FOS) can be manufactured from sucrose and fructose by an enzymatic process (FDA GRAS notification No.44). The number of fructose units varies from two to four.

Blood Cholesterol Levels

We identified forty-one studies that evaluated the effect of inulin, and/or OF, or synthetic short chain FOS consumption on blood cholesterol levels. Scientific conclusions could not be drawn from nineteen of these studies (Alles et al., 1999; Campbell et al., 1997; Cicek et al., 2009; Gomez-Reyes et al., 2010; Kaminskas et al., 2013; Kietsiriroje et al., 2015; Kruse et al., 1999; Lee et al., 2004; de Luis et al., 2013; Olesen & Gudmand-Hoyer, 2000; Montano-Hernandez et al., 2013; Morales et al., 2016; Moroti et al., 2012; Parnell et al., 2009; Pourghassem et al., 2013a; Pourghassem et al., 2013b; Rave et al., 2007; Wong et al., 2010; Yamashita et al., 1984) for one or more of the following reasons: (1) a mixture of non-digestible carbohydrates, including inulin, probiotics, or nutrients, or other foods, known to affect blood cholesterol levels was provided and therefore the physiological effect of the treatment *per se* could not be evaluated, (2) there were significant differences in weight loss between the treatment and control group and therefore the physiological effect of the treatment *per se* could not be evaluated, (3) an appropriate control was not provided, (4) statistical analysis was not conducted between the control and treatment group, (5) studies were not published in English, (6) unhealthy individuals were included in the studies (i.e., ischemic heart disease and irritable bowel syndrome without reporting cholesterol values), and (7) only an abstract was available, which provides insufficient information for evaluating a study.

Aliasgharzadeh et al. (2015)

In a randomized, placebo-controlled, parallel study, Iranian women with type 2 diabetes received either inulin and OF (n = 27) or a placebo (n = 25) for eight weeks (10 g/day). Total and LDL cholesterol were significantly lower in the inulin and OF treatment group compared with the control group ($P < 0.05$).

Brighenti et al. (1999)

Twelve healthy normocholesterolemic young Italian men were provided with a rice-based, ready-to-eat cereal (control) and the same cereal containing 18% inulin for four weeks in a sequential design study. There was no significant difference in total or LDL cholesterol concentration between the inulin and the control diet ($P > 0.05$).

Causey et al. (2000)

Twelve U.S. men with mild hypercholesterolemia participated in a randomized, double blind, cross-over study in which they consumed a study diet containing 20g/day of inulin and a control diet (no inulin) each for three weeks. There was no difference in total ($P = 0.14$) or LDL ($P = 0.36$) cholesterol levels between the two diets.

Clarke et al. (2016)

Twenty healthy Canadian adults participated in a randomized, double-blind, placebo-controlled, cross-over study, which consisted of two 28-day periods separated by a 14-day washout period. Participants consumed 15 g/day of inulin and OF during the treatment period. There were no significant differences in total and LDL cholesterol levels ($P > 0.05$).

Daubioul et al. (2005)

The effect of daily ingestion of OF on blood cholesterol levels in seven Belgian men with non-alcoholic steatohepatitis (NASH) and normal blood cholesterol levels was evaluated in a randomized, double-blind, cross-over study. NASH is asymptomatic and identified through elevated liver enzyme activity. The study subjects were fed 16 g/day OF or maltodextrin (control) for eight weeks. There was no significant difference in total or LDL cholesterol levels ($P > 0.05$).

Daud et al. (2014)

In a parallel, single-blind, placebo-controlled study, 22 healthy overweight or obese English men and women received 30 g/day of OF or cellulose (control) for six weeks. There was no significant difference in total cholesterol levels between the OF and control groups ($P > 0.05$).

Davidson et al. (1998) & Davidson and Maki (1999)

In a randomized, double-blind, cross-over study with two six week periods, 21 U.S. hypercholesterolemic men and women were provided food products that contained either 18 g/day or no (control) inulin. Both total and LDL cholesterol levels were significantly lower when the inulin-containing diet was consumed compared to the control diet ($P < 0.05$).

Dehghan et al. (2013)

Iranian women with type 2 diabetes, some of whom had high blood cholesterol levels, were provided with either a control diet with 10 g/day maltodextrin (n=25) or a diet containing 10 g/day inulin (n= 24) for eight weeks. There was no significant difference between the total or LDL cholesterol levels between the control and inulin groups ($P < 0.05$).

Dehghan et al. (2016)

Forty-six Iranian women with type 2 diabetes were randomized to 10 g/day of inulin and OF (n = 27) or placebo (n = 22) groups for two months. There was a significant decrease in total and LDL cholesterol in the inulin and OF group compared to the placebo group ($P < 0.05$).

Dewulf et al. (2013)

In a randomized, double-blind, placebo-controlled study, 30 obese women consumed inulin and OF (16 g/day) or a placebo (maltodextrin) for three months. There was no significant difference between the inulin and OF group and the placebo group for total and LDL cholesterol ($P > 0.05$).

van Dokkum et al. (1999)

Twelve healthy Dutch men, some of whom were hypercholesterolemic, participated in a randomized, double-blind, cross-over study in which they were provided with a diet containing either 15 g/day of inulin or OF, or a diet that contained no inulin or OF (control) for three weeks. There was no significant difference in total and LDL cholesterol concentration between the three diets ($P < 0.05$).

Forcheron and Beylot (2007)

Seventeen healthy French men and women were provided daily with either a placebo or 10 g of a mixture of inulin and OF along with their usual diets for six months. Nutrient intake was similar between the two groups. There was no significant difference in total and LDL cholesterol levels between the placebo and inulin and OF groups ($P < 0.3$).

Francois et al. (2014)

In a randomized, placebo-controlled, cross-over study, 20 healthy Belgian adults consumed OF (15 g/day in the first week and 30 g/day in the second week) and placebo for two weeks each.

There was a two week run-in period before the first treatment period and two week washout period between treatments. There was no significant differences in total and LDL cholesterol levels between the OF diets and the control diet ($P > 0.05$).

Giacco et al. (2004)

In a randomized, double-blind cross-over study, 30 Italian men and women who were mildly hypercholesterolemic consumed daily diets containing either 10.6 g of short chain FOS or 15 g of maltodextrin (control) with tea or coffee for two months each. No significant difference was observed for plasma total or LDL cholesterol levels between the FOS and control diets ($P = 0.73$).

Jackson et al. (1999)

In this parallel design study, 54 English men and women consumed a placebo or inulin (10 g/day) that was added to various beverages and foods for eight weeks. Total and LDL cholesterol levels were measured at 4, 8 and 12 weeks after the start of the intervention. No significant difference in LDL or total cholesterol levels was observed between the inulin and placebo groups for the various time points ($P > 0.05$).

Letexier et al. (2003)

Eight normocholesterolemic French men and women participated in a double-blind, randomized, placebo-controlled, cross-over study in which they consumed controlled diets that included either 10g/day of inulin or no inulin (control). After three weeks, there was no significant difference in total cholesterol levels between the control and inulin groups ($P > 0.05$).

Luo et al. (1996)

Twelve French men with normal blood cholesterol levels received either 20 g/day FOS or sucrose (control) in a cookie as part of a low fiber diet for four weeks in a double-blind cross-over study. There was no significant difference in total cholesterol levels between the control and FOS groups ($P < 0.05$).

Mahendra and Sheth (2013)

Sixty Indian diabetic men and women with high blood cholesterol levels were supplemented with either 0 g/day (control) or 10 g/day of OF added to water that was consumed at lunch for eight weeks. A significant reduction was observed at the end of the study for total cholesterol levels with OF intake ($P < 0.05$). A significant difference, however, was not observed for LDL cholesterol levels ($P > 0.05$).

Nishimura et al. (2015)

Forty-seven healthy adults consumed a daily beverage (300 mL) containing either 10 g of

chicory root extract (0.75 g inulin/300 mL) or a placebo for four weeks in a randomized, double-blind, parallel study. No significant differences in total and LDL cholesterol levels between the chicory root extract and placebo groups was observed ($P > 0.05$).

Pedersen et al. (1997)

In a randomized, double-blind, cross-over study, a low-fat spread that contained either no inulin (control) or 14 g of inulin was provided daily to 64 normocholesterolemic Dutch women. After four weeks of consumption, no significant difference in blood total and LDL cholesterol levels was observed between the inulin and control intervention groups ($P > 0.1$).

Russo et al. (2008, 2010)

In a randomized, double-blind, cross-over study, twenty-two Italian men with normal blood cholesterol levels were provided a diet that included pasta that contained 11% inulin and pasta that contained no inulin (control). The study provided the subjects with each diet for five weeks, and the subjects' dietary nutrient intake was similar during both periods. There was no significant difference ($P > 0.05$) in total or LDL cholesterol levels between the two diets.

Tovar et al. (2012)

In a randomized trial, 144 Mexican women with normal or slightly elevated blood cholesterol levels consumed for three months dietary supplements, as a partial meal replacement, that contained either 10 g/day (two doses per day, each containing 5 g of inulin) or no inulin (control). There was no significant difference ($P > 0.05$) in total or LDL cholesterol levels between the treatment and control groups.

Blood Glucose Levels

We identified thirty-one studies that evaluated the effect of inulin and/or OF or synthetic short chain FOS consumption on blood glucose levels. Scientific conclusions could not be drawn from fifteen of these studies (Adolphi et al. 2009; Alles et al., 1999; Campbell et al., 1997; Cicek et al., 2009; Dehgnan et al., 2013; Dehghan et al., 2014a; Dehghan, 2014b; Gargari et al., 2013; Jackson et al., 1999; de Luis et al., 2013; Rave et al., 2007; Rumessen et al., 1990; Rumessen and Gudmand-Hoyer, 1998; Sorensen and Johansen, 2010; Yamashita et al., 1984) for one or more of the following reasons: (1) a mixture non-digestible carbohydrates, including inulin, and therefore the physiological effect of inulin *per se* could not be evaluated, (2) appropriate control was not provided, (3) statistical analysis was not conducted between the treatment and control group, (4) the study did not evaluate the effect of inulin or OF/FOS on attenuation of blood glucose levels after the consumption of foods or beverages, but instead measured the glycemic index of inulin, and (5) unhealthy individuals were evaluated (i.e., type 2 diabetics).

Brighenti et al. (1999)

Twelve healthy young Italian men were provided with a rice-based ready-to-eat cereal (control) and the same cereal containing 18% inulin for four weeks in a cross-over design study. The inclusion of inulin in the diet resulted in a similar glycemic response compared to the control diet ($P > 0.05$).

Cani et al. (2009)

In a randomized, double-blind, parallel study, ten healthy Dutch men and women received either a placebo (16 g/day dextrin maltose) or 16 g/day inulin and OF for two weeks. The area-under-the curve for post-prandial blood glucose was significantly lower with the inulin and OF group compared to the placebo group ($P < 0.05$) after the subjects consumed a breakfast.

Capriles and Arêas (2013)

Ten healthy Brazilian men and women were provided gluten-free bread without (control) and with inulin and OF (12%; 4 g inulin/50 g loaf). The study subjects' post-prandial blood glucose levels were measured after they had consumed the breads following an overnight fast. There was a significant reduction in the blood glucose areas-under-the-curve for the inulin and OF group compared to the control group ($P < 0.05$).

Causey et al. (2000)

Twelve U.S. men participated in a randomized, double blind, cross-over study in which they consumed a control diet, including ice cream that contained either 20 g/day of inulin or no inulin (control) each for three weeks. Blood glucose (and insulin) levels measured after the administration of a glucose-containing beverage did not differ significantly between the two diets ($P > 0.05$).

Daubioul et al. (2005)

The effect of daily ingestion of OF on blood glucose in seven Belgian men with nonalcoholic steatohepatitis (NASH) and normal blood glucose levels was evaluated in a randomized, double-blind cross-over study. NASH is asymptomatic and identified through elevated liver enzyme activity. The study subjects were fed 16 g/day of OF or maltodextrin (placebo) for eight weeks. There was no significant difference in fasting blood glucose levels between the two diets ($P > 0.05$).

Daud et al. (2014)

In a parallel, single-blind and placebo controlled study, 22 healthy overweight or obese English men and women received 30 g/day OF or cellulose (control) for six weeks. After consuming OF or cellulose, along with a study meal, post-prandial blood glucose levels were measured for up to

420 minutes. There was no significant difference in the area under the curve for blood glucose (and insulin) between the OF and cellulose groups ($P = 0.744$).

van Dokkum et al. (1999)

Twelve healthy Dutch men participated in a randomized, double-blind, cross-over study in which they were provided a diet containing either 15 g/day of inulin or OF, or a diet that contained no inulin or OF (control) for three weeks. There was no significant difference in the subject's glucose tolerance after consuming 50 g glucose with or without inulin or OF ($P > 0.05$).

Fernandes et al. (2011)

In a cross-over design study conducted in Canada, 18 healthy, overnight fasted men and women with normal or high plasma insulin levels consumed 300 mL of drinks containing 75 g of glucose that also contained either 24 g or inulin or no inulin at all. No significant difference was observed in post-prandial glucose (and insulin) responses between the control and inulin groups ($P > 0.05$).

Giacco et al. (2004)

In a randomized, double-blind, cross-over study, 30 Italian men and women with normal fasting blood glucose levels consumed 10.6 g/day of short chain FOS or 15 g/day of maltodextrin (control) with tea or coffee for two months each. No significant difference was observed for fasting plasma glucose levels between the FOS and control diets ($P = 0.7$). In addition, there was no significant difference in post-prandial glucose areas under the curve between the two diets ($P = 0.7$).

Grysman et al. (2008)

In a double-blind, randomized, cross-over design study, after an overnight fast, 10 healthy Canadian men and women consumed a beverage of 80 g of carbohydrate that contained either: (1) high fructose corn syrup (fructose and glucose), (2) sucromalt (fructose and glucose oligosaccharides), or (3) a mixture of fructose, glucose and 24 g of inulin. Post-prandial blood glucose levels were measured for up to 360 minutes. The study subjects consumed a standard lunch within 20 minutes after blood samples had been taken at the 240 minute mark. There was no significant difference in the glucose (or insulin) areas under the curve between the inulin-containing beverage and the other two beverage groups ($P > 0.05$).

Kaminskas et al. (2013)

In a sequential design study, 25 Lithuanian men and women with metabolic syndrome consumed their diet with yogurt that contained either 5 g of inulin or no inulin for 28 days. The study subjects' fasting blood glucose levels were measured at the end of the 28 days, and no significant fasting blood glucose level differences were observed between the two groups ($P > 0.05$).

Luo et al. (1996)

Twelve healthy French men received either 20 g/day short chain FOS or sucrose (control) in a cookie as part of a low-fiber diet for four weeks in a double-blind cross-over study. There was no significant difference in fasting glucose levels between the control and short chain FOS groups ($P < 0.05$).

Nishimura et al. (2015)

Forty-seven healthy adults consumed a daily beverage (300 mL) containing either 10 grams (0.75 g inulin/300 mL) of chicory root extract or a placebo for four weeks in a randomized, double-blind, parallel study. There was no significant difference in fasting blood glucose levels between the treatment and placebo groups ($P > 0.05$).

Russo et al. (2010)

Twenty-two Italian men were provided a diet that included pasta that contained either 11% inulin or no inulin (control). This randomized, double blind, cross-over study provided the study subjects with each diet for five weeks. There was no significant difference ($P > 0.05$) in the fasting blood glucose (and insulin) levels between the two diets.

Tarini and Wolever (2010)

In a cross-over design study, 12 overnight fasted Canadian men and women consumed drinks containing 56 g high fructose corn syrup that contained either 24 g of inulin or no inulin at all. A standard lunch was served to the study subjects four hours after they had consumed the test drink. Post-prandial glucose levels were not significantly different between the two drink groups when measured after the subjects had consumed the lunch ($P > 0.05$).

Tovar et al. (2012)

In a randomized trial, 144 Mexican women with normal or slightly elevated blood cholesterol levels consumed for three months a partial meal replacement, that contained either: (1) 10 g/day inulin, or (2) no inulin (control); (3) 10/day of inulin only, or (4) no inulin (control). There was no significant difference in total or LDL cholesterol levels between the treatment and control groups ($P > 0.05$).

Laxation/Bowel Function

We identified forty-three studies that evaluated the effect of inulin and/or OF or synthetic short chain FOS consumption on bowel function (i.e., stool frequency, intestinal transit time, and ease of defecation). Scientific conclusions could not be drawn from twenty four of these studies (Alles et al., 1997; Bruhwyler et al., 2009; Clegg et al., 2010; Cummings et al., 2001; Dahl et al., 2005; Dahl et al., 2014; De Preter et al., 2008; Garcia-Peris et al., 2016; Gomez-Reyes et al.,

2010; Grasten et al., 2003; Hunter et al.; 1999; Isakov et al., 2013; Kleesen et al., 1997; Kleesen et al., 2007; Olesen and Gudmand-Hoyer et al., 2000; Mendlik et al., 2012; Menne et al., 2000; Micka et al., 2016; Ramnani et al., 2015; Rumessen and Gudmand-Hoyer, 1998; Shadid et al., 2007; Sobotka et al., 1997; Tulk et al., 2013; Wiazberg et al., 2012) for one or more of the following reasons: (1) a mixture of probiotics, other types of fructans or non-digestible carbohydrates, along with inulin or OF, was provided and therefore the physiological effect of inulin *per se* could not be evaluated, (2) an inappropriate control was provided (e.g., lactulose or wheat pentosan were used as controls), (3) statistical analysis was not conducted between the control and inulin group on the frequency of bowel movements, (4) the study did not measure bowel function in response to inulin or OF as part of a meal but rather inulin or OF in isolation, (5) unhealthy individuals were evaluated (i.e., individuals with irritable bowel syndrome and chronic constipation) and/or subjects received a laxative, (6) the study population was conducted in countries where the risk of contracting diarrhea is high, for example, where 40% of the subjects experienced diarrhea, and (7) only an abstract was available, which provides insufficient information for evaluating a study.

Alles et al. (1996)

In a randomized, placebo-controlled, cross-over study, 24 Dutch males consumed the following treatments daily for 7 days each: (1) a placebo, (2) 4.1 g of glucose, (3) 5 g of OF and 2.7 g of glucose, and (4) 15 g OF. There was a washout period of 14 days between treatments. There were no differences in defecation frequency or fecal weight between the treatment groups and the control groups ($P > 0.05$).

Bouhnik et al. (2007)

In a double-blind, randomized, placebo-controlled study, 39 French adults ingested, along with their diet, either 2.5 g of inulin or a placebo twice a day for four weeks. Stool weight and the average number of stools over measured over 14 days were not significantly different between the control and inulin group ($P > 0.05$).

Brighenti et al. (1999)

Twelve healthy normocholesterolemic young Italian men were provided with a rice-based, ready-to-eat cereal (control) and the same cereal containing 18% inulin for four weeks in a cross-over design study. There were no significant differences in the self-reported number of bowel movements per day or fecal weights between the treatment and control groups ($P > 0.05$).

Castiglia-Delavaud et al. (1998)

Nine healthy, young French men participated in a randomized, cross-over study in which they consumed a control diet and a diet that contained 50 g/day of inulin for 28 days each. There was a 15% increase in defecation frequency in the inulin diet groups compared to the control diet ($P < 0.05$; raw data not reported). Stool weight also was significantly higher in the inulin diet groups compared with the control groups ($P < 0.05$).

Causey et al. (2000)

Twelve U.S. men participated in a randomized, double blind, cross-over study in which they consumed a control diet, including ice cream that contained either 20 g/day of inulin or no inulin (control) each for three weeks. There was no significant difference in oro-fecal transit time (P = 0.33) or 5-day fecal weight (P = 0.2) between the control and inulin diets.

Costabile et al. (2010)

In a double-blind cross-over study, 32 German men and women consumed a diet that included 10 g/day maltodextrin (control) or a very long chain inulin derived from artichokes for three weeks each. There was no significant difference (P > 0.05) in stool frequency (1.34 vs. 1.45 per day) between the two diets.

Den Hond et al. (2000)

In a double-blind, placebo controlled, cross-over study, six Belgian men and women with a low stool frequency pattern consumed a standardized diet that contained either 15 g/day of inulin or no inulin (control). After one week on each diet, the fecal frequency (measured as the number of stools per week) for the study subjects was significantly higher for the inulin diet (6.5 stools per week) compared to the control diet (4.0 stools per week) (P = 0.02). There was no significant difference in fecal weight between the treatment and control diets (P > 0.05).

van Dokkum et al. (1999)

Twelve healthy Dutch men participated in a randomized, double-blind, cross-over study in which they were provided a diet with a diet containing either 15 g/day of inulin or OF, or a diet that contained no inulin or OF (control) for three weeks. There was no significant difference in oro-fecal transit time and fecal wet or dry weight between the two diets (P > 0.05).

Francois et al. (2014)

In a randomized, placebo-controlled, cross-over study, 20 healthy Belgian adults consumed OF (15 g/day in the first week, 30 g/day in the second week) and placebo for two weeks each. There was a two week run-in period before the first treatment period and two week washout period between treatments. There was no significant difference in defecation frequency or fecal weights between the OF diets and the control diet (P > 0.1).

Gibson et al. (1995)

In a cross-over design study, eight healthy English adults were provided with a controlled diet that contained either 15 g/day inulin or OF, or no inulin or OF (control) for 15 days each. There was no significant difference in the defecation rate (measured as the number of stools per 5 days) or mean transit times (measured in hours) between the inulin and the control group (P > 0.05). The defecation rate (stools per 5 days) was significantly greater when OF was consumed

compared to the control group ($P < 0.05$). However, there was no significant difference in mean transit time (hours) between the inulin and control groups. Finally, there was no significant differences in fecal weight between both the OF and inulin groups and the control group ($P > 0.05$).

Kolida et al. (2007)

Thirty English men and women participated in a double-blind, placebo-controlled, cross-over study in which the study subjects consumed a chocolate drink that contained either 8 g/day of maltodextrin (control), 5 g/day of inulin, or 8 g/day of inulin for a two week period. There were no significant difference in the self-reported rate of stool frequency between the placebo group (1.48 stools per day) and the 5 and 8 g/day of inulin groups (1.501 and 1.46 stools per day, respectively) ($P > 0.05$).

Marteau et al. (2011)

In a randomized, double-blind, placebo controlled trial, elderly French subjects (n = 25 in each group) supplemented their diets with 15 g/day of chicory inulin or were administered a placebo (control) for four weeks. Stool frequency was not significantly different between the treatment and control groups. Complaints of defecation difficulties were significantly lower for the inulin group compared to the control group ($P < 0.01$).

Nishimura et al. (2015)

Forty-seven healthy adults consumed a daily beverage (300 mL) that contained either 10 grams (0.75 g inulin/300 mL) of chicory root extract or no inulin (control) for four weeks in a randomized, double-blind, parallel study. There was no difference with respect to defecation straining between the treatment and control groups ($P > 0.05$).

Ramnani et al. (2010)

In a three-arm, parallel, placebo-controlled, double-blind study, 66 Dutch men and women consumed as part of their diet either pear-carrot-sea buckthorn or plum-pear-beetroot that contained 5 g/day of inulin or a placebo twice daily for three weeks each. There was no significant difference in stool frequency or stool consistency between the treatment and control groups ($P > 0.05$).

Ripoll et al. (2010)

Thirty-five French men and women participated in a randomized, double-blind study in which they consumed diets that included coffee that contained either 8 g/day of sucrose (control) or 5 g/day of inulin in the form of soluble chicory extract for four weeks. No significant change in stool frequency ($P = 0.37$) was observed between the control and inulin group.

Sairanen (2007)

In a randomized, double-blind, parallel study, after a 12 day baseline lead in period, 66 healthy adults were provided either fermented milk containing probiotics (control) or fermented milk containing the same probiotics and 4 g/day of inulin for three weeks. Oro-fecal transit time (measured in hours) was not significantly different between the treatment and control groups ($P > 0.05$). Self-reported defecation frequency, fecal weight, and difficulty in defecation also were not significantly different between the treatment and control groups ($P > 0.05$).

Scholtens et al. (2006)

Eleven healthy Dutch men and women participated in a cross-over study in which either 25 to 30 g/day of OF or maltodextrin (control) was consumed with meals for two weeks each. Stool frequency was significantly higher in the OF group compared to the control group (1.2 versus 1.6 stools per day) ($P = 0.014$). Total stool output tended to be higher in the OF group compared to the control group, but this difference was not statistically significant ($P = 0.097$).

Slavin and Feirtag (2011)

In a randomized, double-blind, cross-over study, 12 US men consumed a controlled diet that contained either 20 g/day of chicory inulin or no inulin (control) for three weeks each. There were no significant differences in fecal weights measured at 24 hours ($P = 0.20$), intestinal transit times ($P = 0.33$), or stool frequencies between the inulin and control diets ($P = 0.14$).

Swanson et al. (2002)

In a randomized, double-blind, placebo-controlled, parallel study, 68 healthy adults, after a four week baseline lead in period, consumed one of the following treatments twice daily for four weeks: 3 g sucrose and 80 mg cornstarch (control) or 3 g FOS and 80 mg cornstarch. The stool frequencies (measured as stools per day) were not significantly different between the control and FOS groups ($P > 0.05$).

Energy Intake

We identified fifteen studies that evaluated the effect of inulin and/or OF or synthetic short chain FOS consumption on energy intake. Scientific conclusions could not be drawn from seven of these studies (Archer et al., 2004; Cani et al., 2009; Liber and Szajewska, 2014; Perrigue et al., 2009; Peters et al., 2009; Savastano et al., 2014; Sheth et al., 2014) because: (1) a mixture of non-digestible carbohydrates, along with inulin, was provided to the study subjects and therefore the physiological effect of inulin *per se* could not be evaluated, (2) the study measured satiety/hunger but not energy/food intake, or (3) appropriate statistical analysis was not conducted on energy intake.

Cani et al. (2006)

In a cross-over study, 10 Dutch men and women received either 16 g/day of OF or 16 g/day of dextrin maltose (control) dietary supplements for two weeks each as part of their diet. After this period, subjects were provided with breakfast, lunch, and dinner *ad libitum*. Appetite ratings were determined using VAS. Consumption of the OF supplements significantly increased satiety after the breakfast meal ($P = 0.04$), without any significant difference in hunger, fullness and prospective food consumption. No significant difference in the VAS ratings was observed after lunch. After dinner, the VAS ratings for the OF group compared to the control group was significantly increased for satiety ($P = 0.04$), reduced hunger ($P = 0.04$) and prospective food consumption ($P = 0.05$). Energy intake was significantly lower for the OF group compared to the control group during breakfast ($P = 0.01$) and lunch ($P = 0.03$), as was total energy intake for all three meals ($P = 0.05$).

Daud et al. (2014)

In a parallel, single-blind and placebo controlled study, 22 English men and women received 30 g/day of OF or cellulose (control) for six weeks. Cellulose was provided as a control because it is non-fermentable and therefore would not affect appetite as a result of fermentation. Based on VAS scores, the consumption of OF significantly reduced hunger, motivation to eat, and the desire to eat, but did not have a significant effect on fullness when compared to cellulose. There was no significant difference ($P = 0.578$), however, in energy intake of an *ad libitum* meal between the treatment and the control groups.

Harrold et al. (2013)

Fifty-eight English women consumed a study breakfast followed four hours later by an *ad libitum* lunch. In this double-blind, placebo controlled cross-over study, the women were administered an herb extract with or without an inulin-based soluble fiber (5 g/100 mL) 15 minutes before the meals. Appetite was assessed by VAS and energy intake was measured at lunch. While the effect of inulin on appetite and hunger was not reported, the inclusion of inulin significantly reduced intake (measured in grams) of the meals, as well as caloric intake (80 kcal) ($P = 0.001$).

Hess et al. (2011)

In a double-blind, randomized, cross-over design study, 20 U.S. men and women were assigned to consume two separate doses of 0, 5 or 8 g of short chain FOS. The first dose was mixed into a hot cocoa beverage and served with a breakfast meal of a bagel and cream cheese. Satiety was assessed using VAS through 240 minutes after the study subjects had consumed the breakfast. The subjects consumed the same three doses of short chain FOS in the form of solid chocolate flavored chews without additional food or drink two hours before they consumed their dinner meal. There were no significant differences on measures of satiety between the treatment and control groups ($P > 0.05$). There also were no significant differences between the treatment and control groups in calorie intake at the *ad libitum* lunch ($P > 0.05$). During the remainder of the

day, the women' mean calorie intake with 16 g of FOS was significantly lower than with the placebo ($P < 0.05$) while in men it was significantly higher ($P < 0.05$).

Karalus et al. (2012)

In a randomized, cross-over design study, 22 U.S. women were provided with a chocolate crisp bar that contained either 10 g of inulin or OF, or no inulin or OF (control). The study subjects consumed the crisp bar twelve hours (evening) before they were assessed for satiety using VAS. The following morning, the subjects consumed the crisp bar and a beverage. Three hours later, they were served three pieces of French bread pizza and water. The pizza and water were weighed before and after consumption. Food intake was recorded 24 hours after the start of each visit. Based on VAS and food intake data, there was no significant difference in any of the satiety measures, in energy consumed at the pizza lunch or during the 24 hours following the study between the inulin or OF and control groups ($P > 0.05$).

de Luis et al (2013)

Thirty-three obese Spanish men and women were randomized to consume a diet that included 10 cookies per day providing approximately 8 g of OF or 10 control cookies for one month. The study subjects rated their feelings of satiety/hunger before the start of the study and one month after the start of the study with a test meal of five cookies. After the one-month period, satiety was measured immediately before and up to 40 minutes after the subjects consumed 5 of the control or OF cookies. Satiety was significantly greater in the treatment group compared to the control group ($P<0.05$). Daily food consumption, however, was not significantly affected.

Parnell and Reimer (2009)

In a randomized, placebo-controlled weight loss trial, 48 Canadian men and women were randomly assigned to supplement their meals with 21 g/day of OF or with a placebo (maltodextrin) for 12 weeks. Subjective hunger and satiety were measured with the use of VAS . There was no significant difference between measures of hunger or satiety between the OF and control groups. There were significant reductions in energy intake, however, in the OF group ($P = 0.002$)

Pedersen et al. (2013)

Twelve English men and women participated in a five week dose-escalation study in which the daily intake of OF was increased every week from 0, to 15, to 25, to 35, to 45 to 55 g/day. Satiety was measured using VAS and energy intake was measured. Satiety VAS scores (e.g., hunger) in all of the OF groups were significantly lower ($P < .039$) when compared to the control group. However, energy intake levels measured in the OF groups during an *ad libitum* test meal was not significantly different compared to the control group ($P = 0.244$).

Verhoef et al. (2011)

In a randomized, double-blind cross-over study, 31 Dutch men and women received either 0, 10 or 16 g/day of OF for 13 days. Satiety was measured at the beginning and the end of each interval using VAS. There was no significant difference in reported satiety between the OF and control diets ($P > 0.05$). Energy intake of an *ad libitum* dinner was significantly lower after consuming 16 g/day of OF compared to 10 g/day of OF ($P < 0.05$), but not compared to the placebo.

Mineral Absorption

We identified nineteen studies that evaluated the effect of inulin and/or OF or synthetic short chain FOS consumption on mineral absorption. Scientific conclusions could not be drawn from four of these studies (Abrams et al., 2007; Adolphi et al., 2009; Dahl et al., 2005; Yap et al., 2005 because: (1) no control or an inappropriate control group was used, (2) it was unclear from the studies whether the control and treatment periods were comparable and whether appropriate statistical analyses were used in the studies, and/or (3) unhealthy individuals were included in the studies.

Abrams et al. (2005)

American adolescents were randomly assigned to receive 8 g/day of inulin and OF or a maltodextrin placebo (n = between 48 and 50 subjects per group) that was mixed in calcium fortified orange juice for as long as one year. Calcium absorption was measured using a stable isotopically labeled calcium. After adjusting for various factors, including calcium intake, the consumption of inulin and OF significantly increased calcium absorption after eight weeks ($P < 0.001$) and one year ($P < 0.04$) compared to the control group. Bone mineral content ($P = 0.03$) and density ($P = 0.01$) also were significantly greater in the inulin and OF group compared to the control group.

Coudray et al. (1997)

Nine French men were given a control diet or the same diet that included 40 g/day of inulin in a 28-day cross-over designed study. The intestinal absorption of calcium (as well as magnesium, iron and zinc) was measured. Inulin increased the percent of ingested calcium that was absorbed compared to the control group (21% versus 33%) ($P < 0.01$). There was no significant effect of inulin on the intestinal absorption of magnesium, iron, or zinc ($P > 0.05$).

Ducros et al. (2005)

In a randomized, cross-over, double-blind study, eleven post-menopausal women were given short chain FOS or sucrose (control) for 35 days each. During the treatment period, participants consumed 5 g/day of short chain FOS for the first four days and 10 g/day for the remainder of the diet period to allow for adaptation. Participants were provided a controlled diet for the last 10 to 12 days of each diet period and received stable-isotopically labeled zinc, copper, and

selenium on day 28. There was a significant increase in absorption of copper in the short chain FOS group compared to the control group ($P = 0.04$). There were no significant differences in zinc or selenium absorption, however, between the short chain FOS and control groups ($P > 0.05$).

Griffin et al. (2002) and (2003)

Fifty-nine U.S. girls participated in a randomized, cross-over study in which they were provided 8 g/day sucrose (control), OF, or inulin and OF in orange juice for three weeks each. Calcium absorption was measured using stable isotopically labeled calcium. There was no significant difference in the average calcium absorption between the control (31.8%) and OF (31.8%) groups ($P = 0.75$). A significant increase in calcium absorption, however, was observed in the inulin and OF group compared to the control group (38.2%) ($P = 0.01$).

Data from 29 girls in the Griffen et al. 2002 study were combined with 25 additional recruited girls to evaluate the effect of 8 g/day inulin and OF, compared to a placebo (sucrose) on calcium absorption, reported in the Griffen et al. 2003 study. The treatment and control diets were administered to the 25 new study subjects for three weeks each in calcium-fortified orange juice. The findings of the 2003 study showed that overall calcium absorption in the inulin and OF group was significantly higher (36.1%) compared to the control group (33.1%) ($P = 0.027$).

van den Heuvel et al. (1998)

In a randomized, cross-over design study, twelve Dutch men received a basal diet that provided 0 g/day (control) or 15 g/day of inulin or OF for 21 days. Intestinal absorption was measured using stable isotopically labeled calcium (and iron). Compared to the control diet, inulin and OF had no significant effect on calcium ($P = 0.933$) and iron ($P = 0.503$) absorption.

van den Heuvel et al. (1999)

Twelve Dutch male adolescents received 15 g/day of either OF or sucrose (control) for nine days in a randomized, double-blind, cross-over study. On the eighth day of each of the treatment periods, stable isotopically -labeled calcium was given orally to the study subjects to measure calcium absorption. Mean percent of ingested calcium that was absorbed during the control treatment was 47.8 ± 16.4% and 60.1 ± 17.2% with consumption of OF. The mean increase in ingested calcium absorption for the OF group of 10.8% was significantly higher compared to the control group ($P < 0.05$).

van den Huevel (2009)

The effect of short-term and long-term consumption of short chain FOS on mineral absorption was evaluated in adolescent girls (n = 14) in a randomized, cross-over, double-blinded study. Participants were provided with short chain FOS (10 g) and maltodextrin (control) for 37 days each, separated by a 12 day washout period. Short chain FOS was consumed daily for the first 8 days of each treatment period, followed by intermittent use for the remainder of the diet period.

Short chain FOS was taken on 28 random days alternated with placebo). Calcium and magnesium absorption was measured from isotope enrichment in urine on day 8 and 36 of each period. There were no significant differences in calcium absorption between the short-chain FOS group (short- or long-term consumption) on and the control group ($P > 0.05$). Compared to control group, short-chain FOS did not significantly affect magnesium absorption after eight days. Magnesium absorption, however, was significantly higher after 36 days of short-chain FOS consumption ($P = 0.04$).

Holloway et al. (2007)

In a double-blind, cross-over design study, 15 U.S. post-menopausal women consumed 10 g/day inulin and OF with two meals for six weeks or inulin and a placebo (maltodextrin) in a beverage for six weeks with two meals. The absorption of stable isotopically labeled calcium (^{46}Ca) and magnesium (^{26}Mg) was significantly higher in the inulin and OF group compared to the control group ($P < 0.05$).

Kim et al. (2004)

In a double-blind, parallel study, 26 healthy Korean post-menopausal women received eight g/day of fructan supplement (inulin and OF) or a placebo (maltodextrin/sucrose) with water for three months. Absorption of calcium, phosphorous, iron, and zinc was determined by measuring mineral intake and fecal excretion. Based on this method, the fructan supplement significantly increased the absorption of calcium and iron ($P < 0.05$), but not of phosphorous and zinc.

López-Huertas et al. (2006)

In a randomized, cross-over, double-blind study, 15 adults consumed five different milk beverages for four days each, separated by two week washout periods. The study subjects consumed the following milk beverages during the study: (1) standard milk (control), (2) milk enriched with calcium from milk solids and tricalcium phosphate, (3) milk enriched with calcium from concentrated milk, (4) milk with added short chain FOS (FOS milk; 5 g/liter), and (5) milk with added caseino-phosphopeptides. All of the beverages were labeled with ^{42}Ca as $CaCl_2$. The quantity of calcium in each drink consumed by the study subjects was similar by varying the volume administered to the subjects. Participants recorded dietary intake in food diaries for four days before the first absorption test and were instructed to consume the same foods and beverages throughout the study. Mean calcium absorption was measured in 24-hour pooled urine samples collected on the second day of each study period (24 to 48 hours after dosing). Calcium absorption was not significantly different between the FOS milk groups and the control groups ($P = 0.055$).

Martin et al. (2010)

Fourteen healthy U.S. adolescent girls participated in a randomized, cross-over design study in which they consumed a study diet that included calcium fortified cereal that provided 0 g/day

(control) or 9 g/day of inulin and OF for three weeks each. The absorption of stable isotopically labeled calcium was not significantly different between the two groups ($P > 0.05$), nor were there any differences in calcium retention between the two groups.

Mathey et al. (2008)

In this randomized, parallel, placebo-controlled, double-blind study, post-menopausal women (n = 39) were provided soy products (100 mg/day of isoflavones aglycon equivalents) for 30 days and then randomized to one of the following groups for 30 days: (1) soy (n = 12; control), (2) soy and short chain FOS (7 g/day; n = 13), or (3) soy and lactic bacteria (n = 14). Markers of osteoblastic activity and bone formation (serum bone-specific alkaline phosphatase) and bone resorption (urinary deoxypyridinoline) were measured and reported as percent changes from baseline. There was no significant difference between the short chain FOS on bone-specific alkaline phosphatase compared to the control group ($P > 0.05$). There was a 13% decrease in deoxypyridinoline with the short chain FOS group compared to the control group. Statistical values were not reported, and so it is not clear if this finding was statistically significant. Subgroup analysis comparing individuals in early versus late stages of menopause demonstrated a significant decrease in deoxypyridinoline in individuals in the early stage of menopause ($P < 0.02$).

de Souza et al. (2010)

In a randomized, double-blind, cross-over study, 60 pre-pubertal girls consumed calcium-enriched formulations, supplemented with or without inulin and OF (8 g/day) for 11 weeks each, with a three week washout in between the study periods. Blood was collected at 4, 8, and 11 weeks during each study period. There was no significant difference in serum bone alkaline phosphatase activity between the treatment and control groups at any time ($P > 0.05$).

Tahiri et al. (2001)

Eleven post-menopausal women received 10 g/day of short chain FOS or placebo (sucrose) for five weeks each in a randomized, cross-over, double-blind study. A washout period of at least three weeks separated the diet periods. Intestinal absorption of magnesium was significantly increased in the short chain FOS group compared with the control group ($P < 0.05$). During the first four days of the treatment period, 5 g/day of short chain FOS was provided for adaptation. Participants consumed their usual diet for the first 23 days of each diet period. A controlled diet was provided for the remainder of each diet period, and a stable isotope was provided on day 28. There was a significant increase in intestinal magnesium absorption in the short chain FOS group compared to the control group ($P < 0.05$).

Tahiri et al. (2003)

In a randomized, cross-over, double-blind study, twelve post-menopausal women received short chain FOS (10 g/day) or a placebo (sucrose) for five weeks each, separated by a three week

washout period. The treatment subjects received 5 g/day of short chain FOS during the first four days of the treatment period for adaptation. Participants consumed their usual diet for the first 23 days of each diet period and were then provided a controlled diet for the remainder of each diet period. Isotopically labeled calcium was administered to the treatment subjects on day 29. There was no significant difference in isotopically labeled calcium absorption or urinary calcium excretion between the short chain FOS and control groups ($P > 0.05$).

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Karaya Gum

Background

Karaya gum (sterculia gum) is the dried gummy exudate from the trunk of trees of various species of the genus *Sterculia*. Karaya gum is a partially acetylated polysaccharide that contains interior galatourono-rhamnan chains to which are attached rhamnose and galactose (Kubal and Gralen, 1948). Karaya gum is used as a stabilizer, thickener, and/or emulsifier in frozen dairy desserts and mixes, milk products, candy and other foods (21 CFR 184.1349). Karaya gum has a relatively high molecular weight compared to other non-digestible carbohydrates, and while it swells in water, it is not freely soluble (Eastwood et al., 1986).

Blood Cholesterol Levels

We identified two studies that evaluated the effect of karaya gum consumption on blood cholesterol levels. Scientific conclusions cannot be drawn from one of the studies because it was conducted for an insufficient amount of time (one week for the control group) for purposes of measuring fasting blood cholesterol levels (Eastwood et al., 1983).

Behall et al. (1984)

Twelve U.S. men with normal blood cholesterol levels were provided with a low-fiber basal diet (control) followed by a diet that included 19 to 27 g/day (0.75 g/100 calories) of added karaya gum for four weeks. Consumption of karaya gum significantly reduced total blood cholesterol levels (196 *versus* 177 mg/dL) and LDL cholesterol levels (131 *versus* 118 mg/dL) compared to the control basal diet ($P < 0.05$).

Blood Glucose Levels

We identified two studies that evaluated the effect of karaya gum consumption on blood glucose levels.

Behall et al. (1984/1990)

Twelve healthy U.S. men were provided a low-fiber basal diet (control) followed by a diet that included 19 to 27 g/day (0.75 g/100 calories) of added karaya gum for four weeks. Fasting glucose levels were not significantly different between the control and karaya gum diet groups after four weeks ($P > 0.05$). In addition, serum glucose levels in response to a glucose tolerance test were not significantly different between the two groups.

Eastwood et al. (1983)

After a seven day control diet, five Scottish men consumed 10.5 g/day of karaya gum for 21 days. There was no significant difference in glycemic responses to the ingestion of glucose with or without karaya gum.

Laxation/Bowel Function

We identified two studies that evaluated the effect of karaya gum consumption on laxation. Scientific conclusions could not be drawn about the effect of karaya gum on bowel function from one of the studies because the duration of the study varied between the control and karaya gum intervention groups (Eastwood et al., 1983).

Behall et al. (1987)

Eleven U.S. men consumed a basal diet with and without (control) 7.5 g/day of karaya gum/1,000 calories for four weeks each. Consuming karaya gum resulted in a higher wet and dry fecal weight *(P* < 0.05) compared to the control group. However, there was no significant difference in average oro-fecal transit times (26.7 versus 27.2 hours) (*P* > 0.05) between the control and karaya gum diets, as well as the frequency of defecation (7.4 versus 7.9 stools/8 days).

Mineral Absorption

We identified two studies that evaluated the effect of karaya gum consumption on mineral absorption.

Behall et al. (1987)

Eleven U.S. men consumed a basal diet with and without (control) 7.5 g/day of karaya gum/1,000 calories for four weeks each. There was no significant difference on the apparent mineral balance of calcium, magnesium, manganese, iron, copper, or zinc between the Karaya gum and control groups (*P* > 0.05).

Behall et al. (1990)

Twelve healthy U.S. men were provided with a low-fiber basal diet (control) followed by a diet with 19 to 27 g/day of added karaya gum (0.75 g/100 calories) for four weeks. Compared to the basal diet, karaya gum did not significantly affect mineral retention of calcium, magnesium, manganese, iron, copper, or zinc (*P* > 0.05).

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Oat Hull (Insoluble Oat) Fiber

Background

Oat hull fiber is isolated from oat hulls, which are separated from other oat grain components such as the groat (kernels) that are used to make whole grains and grain-based food products (FDA GRAS Notification No. 261 and 342). Oat hull fiber is generally composed of at least 85% non-digestible carbohydrate, with most of it being insoluble (cellulose and hemicellulose). Oat hull fiber is added to foods for its adhesive and texture properties, and as an extender in some meat products.

Blood Glucose Levels

We identified three human studies that evaluated the effect of insoluble oat fiber consumption on blood glucose levels. Conclusions could not be drawn from one of these studies (Sunvold et al., 1995) because a mixture of non-digestible carbohydrate was provided to the study subjects and the role of insoluble oat fiber *per se* on blood glucose levels therefore could not be determined.

Weickert et al. (2005)

In a randomized cross-over study, the acute and delayed effects of the consumption of insoluble oat fiber on post-prandial blood glucose were evaluated. The acute effects were evaluated by providing 14 German women three matched portions of bread enriched with (13.5 g/portion) or without oat hull fiber, which the study subjects consumed over a 24 hour period. The oat hull fiber contained 75% cellulose and 25% hemicellulose. Post-prandial glucose levels were measured over a 300 minute period after an overnight fast and the findings were mixed. The post-prandial blood glucose (and insulin) areas under the curve were not significantly different between the treatment and the control group after 24 hours of consumption. For purposes of evaluating the delayed effects of consuming insoluble oat fiber, only the control bread was consumed on the 2nd day. The post-prandial glucose area under the curve was reduced by 32% after the prior intake of insoluble oat fiber compared to the control ($P = 0.011$).

Weickert et al. (2006)

A randomized, controlled, single-blind, cross-over study was conducted on 17 overweight or obese German subjects to test the effect of oat hull fiber on plasma glucose levels. The oat hull fiber contained 75% cellulose and 25% hemicellulose. After the study subjects consumed either white bread enriched with 31 g of oat hull fiber or a white bread that did not contain any oat hull fiber (control) over a 72 hour period, their plasma glucose levels were measured. There was no significant difference in plasma glucose levels between the two groups ($P = 0.676$).

Blood Cholesterol Levels

We identified two human studies that evaluated the effect of oat hull fiber consumption on blood cholesterol levels.

Stephen et al. (1997)

Ten healthy Canadian men consumed a low fiber study diet either with 25 g/day of oat hull fiber or without any oat hull fiber (control) for three weeks. The oat hull fiber contained approximately 30% cellulose. There was no significant difference in total or LDL cholesterol levels between the two diets ($P > 0.001$).

Weickert et al. (2006)

A randomized, controlled, single-blind, cross-over study was conducted on 17 overweight or obese German subjects to test the effect of oat hull fiber on plasma glucose levels. The oat hull fiber contained 75% cellulose and 25% hemicellulose. After the study subjects consumed white bread enriched with 31 g of oat hull fiber or white bread that did not contain any oat hull fiber (control) over a 72 hour period, their plasma total and LDL cholesterol levels were measured. There was no significant difference between plasma total cholesterol or LDL cholesterol levels between the two groups.

Laxation/Bowel Function

We identified three human studies that evaluated the effect of oat hull fiber consumption on laxation/bowel function. Conclusions could not be drawn from one of these studies (Weickert et al., 2005) because data on transit time and stool consistencies was not provided.

Grain Millers Laxation Study (2008)

Twenty men and women participated in a cross-over study in which they consumed several diets for three weeks each. The metabolic diets included a low-fiber bread or cereal (control) or the metabolic diet plus either oat hull cereal (6 g of oat hull fiber) or oat hull bread (6 g oat hull fiber). The study did not provide the fiber content of the oat hull fiber. After the study subjects consumed the diets for three weeks, their average daily fecal weights for the oat hull bread and cereal dietary groups resulted in a significantly greater fecal weight compared to the control group ($P = 0.48$, cereal; $P = 0.0027$, bread). Cumulative oro-anus transit time rate was significantly higher for the oat hull fiber cereal and bread dietary groups compared to the control.

Stephen et al. (1997)

In a cross-over design study, ten healthy Canadian men consumed a low fiber study diet that contained 25 g/day of oat hull fiber and a diet that did not contain any oat hull fiber (control) for three weeks. The oat hull fiber contained approximately 30% cellulose. With consumption of the oat hull fiber, there was a significant increase in fecal weight for subjects in the oat hull fiber group compared to the control group ($P < 0.0001$). There was no significant difference, however, in the mean oro-anus transit time between the control (44.3 ± 4.1 hours) and oat hull (42 ± 3.9 hours) groups ($P > 0.001$).

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Insoluble Pea Fiber, Pea Hull Fiber and Soluble Pea Fiber

Background

Peas (the seed coat and cotyledon) are commonly consumed in the American diet. The seed coat (hull) contains largely water-insoluble nondigestible carbohydrates (primarily cellulose). Cotyledon fiber consists of carbohydrates having various degrees of solubility, including hemicellulose and pectin, along with cellulose. Mechanically isolated "pea hull fiber" generally contains approximately 65% cellulose and approximately 25% hemicellulose plus pectin (Gudeon et al., 1996). Soluble pea fiber is obtained from the fibrous residue of peas and predominately contains soluble fibers. Soluble pea fiber is used as an ingredient in various foods as fillers and bulking agents and for purposes of retaining moisture and maintaining fat emulsions.

We identified a limited number of studies that evaluated the physiological effects of pea fiber. However, scientific conclusions could not be drawn from some of these studies because it is unclear which portion of the pea was used to isolate the study fiber, that is, the seed coat/hull, the cotyledon, or both) (Hamberg et al., 1989; Sandstrom et al., 1994). In some of these studies, pea fiber also was provided to the study subjects with other nondigestible carbohydrates (Knopp et al., 1999; Whelan et al., 2006) and therefore it was not possible to evaluate whether the pea fiber *per se* had on a beneficial physiological effect.

Blood Cholesterol Levels

We identified two studies that evaluated the effect of insoluble pea fiber consumption on blood cholesterol levels. Scientific conclusions could not be drawn from one of the studies because an appropriate control was not used (Marinangeli et al., 2011).

Dubois et al. (1993)

In a double-blind, randomized, cross-over study, six healthy males consumed a test meal low in fiber (2.8.g) that contained either 10 g of pea fiber or no pea fiber at all (control). No information was provided on which portion of the pea was used to isolate the fiber, but the pea fiber was identified as being insoluble (9.06 g insoluble and 0.94 g soluble). Post-prandial cholesterol levels were measured up to seven hours after the study subjects consumed test meals. The blood cholesterol area under the curve was significantly lower for the group that consumed the insoluble pea fiber compared to the control group ($P < 0.05$).

Blood Glucose Levels

We identified five studies that evaluated the effect of pea fiber on blood glucose levels. Scientific conclusions could not be drawn from two of these studies (Gonzalez-Anton et al., 2015; Marinangeli et al., 2011) either because a mixture of non-digestible carbohydrates was provided to the study subjects, and the effect of pea fiber *per se*, therefore, could not be evaluated or an appropriate control was not used.

Dubois et al. (1993)

In a double-blind, randomized, cross-over study, six healthy males consumed a test meal low in dietary fiber (2.8.g) that contained either 10 g of pea fiber or no pea fiber at all (control). No information was provided on which portion of the pea was used to isolate the fiber, but the pea fiber was identified as being insoluble (9.06 g insoluble and 0.94 g soluble). The blood glucose area under the curve was not significantly different for the group that consumed the insoluble pea fiber compared to the control group ($P < 0.05$).

Raben et al. (1994)

Ten males were fed a low fiber meal (control) and a high-fiber meal containing 3.5 g of pea fiber in a cross-over design study. The pea fiber was composed of 7.9% cellulose, 56.6% soluble noncellulose polysaccharides, 33.6% insoluble noncellulose polysaccharides and 2% lignin. It is unclear if this fiber can be properly categorized as soluble pea fiber. After an overnight fast, the study subjects consumed the meals for measuring post- prandial glucose responses. There was no significant difference in post-prandial glucose (and insulin) levels between the two dietary groups ($P > 0.05$).

Smith et al. (2012)

In a cross-over design study, 20 males consumed tomato soup that contained either 10 g of pea hull fiber, 20 g of pea hull fiber, or no pea fiber at all (control). The pea hull fiber contained 85% insoluble and 15% soluble fiber. Post-prandial blood glucose was measured after the study subjects had consumed pizza for up to approximately 2 hours. There was no significant difference for either pea hull fiber dose group on post-prandial glucose levels when compared to the control group ($P > 0.05$).

Laxation/Bowel Function

We identified three studies that evaluated the effect of pea fiber on bowel function. Scientific conclusions could not be drawn from these three studies (Dahl et al., 2003; Flogan and Dahl, 2010; Guedon et al., 1996) because: (1) a mixture of digestible carbohydrates was provided to the study subjects and the effect of pea hull fiber *per se* therefore could not be evaluated, (2) a control group was not used, or (3) the endpoints did not directly evaluate improved bowel function, that is, the degree of bowel contractions was recorded as a measure of clinical tolerance.

Energy Intake

We identified two studies that evaluated the effect of pea fiber on satiety (Raben et al., 1994; Smith et al., 2012). Scientific conclusions could not be drawn from these two studies because energy intake was not measured.

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Polydextrose

Background

Polydextrose is a synthetic and partially metabolizable water-soluble polymer which primarily consists of D-glucose. Polydextrose is added to foods for multiple technical effects including as a bulking agent, a formulation aid, a humectant, and a texturizer in various food products (21 CFR 172.841). Polydextrose is a soluble non-digestible carbohydrate that is partially fermented in the colon (Roytio and Ouwehand, 2014).

Blood Cholesterol Levels

We identified three studies that evaluated the effect of polydextrose consumption on blood cholesterol levels. Scientific conclusions could not be drawn from these three studies (Pronczuk et al., 2006; Saku et al., 1991; Schwab et al., 2006) for one or more of the following reasons: (1) no control was used, (2) statistical comparisons were not conducted between the control and polydextrose group, and (3) the intervention provided non-digestible carbohydrates, in addition to polydextrose, and the effect of polydextrose *per se* therefore could not be evaluated.

Blood Glucose Levels

We identified seven studies that evaluated the effect of polydextrose intake on blood glucose levels. Scientific conclusions could not be drawn from two of these studies (Cicek et al., 2009; Wilson et al., 2010) because they were conducted on individuals with type 2 diabetes.

Three studies evaluated the glycemic index of polydextrose in which the glycemic response of polydextrose alone was compared to an isolated sugar (Abdallah et al., 1997; Jie et al., 2000; Kurotobi et al., 2010). As expected for any non-digestible carbohydrate, the glycemic index would be less compared to a sugar and therefore does not reflect how carbohydrates affect blood glucose levels as part of a food or beverage. Studies evaluating the glycemic index of polydextrose therefore were not included in this review.

Astbury et al. (2014)

Ten English men consumed a whey protein snack bar that contained 6.2 g of polydextrose or an isocaloric snack bar (control) daily as a midmorning snack for two weeks each in a double-blind, randomized, cross-over study. The polydextrose replaced carbohydrate such that the carbohydrate content level was lower in the polydextrose snack bar. Post-prandial blood glucose levels were measured on the first and the 14^{th} days of the study for up to 90 minutes after the study subjects had consumed the snack bars. Replacing carbohydrate with polydextrose in the snack bar resulted in a significantly lower blood glucose area under the curve ($P < 0.01$).

Konings et al. (2014)

Eighteen Dutch men and women participated in a single-blind, randomized, cross-over study in which they consumed a diet containing 56.7 g/day of polydextrose (equivalent to 30% of available carbohydrate) and two control diets. One control diet contained 30% of available carbohydrate (e.g. starch and sugars) instead of polydextrose. The other control diet was adjusted to be isocaloric to the polydextrose diet, considering that polydextrose has a lower caloric contribution compared to available carbohydrates. When replacing carbohydrate with polydextrose, the post-prandial peak glucose (and insulin) response after breakfast was significantly lower ($P = 0.03$).

Lummela et al. (2009)

In a randomized, cross-over study, 26 healthy Finnish men and women consumed a milk drink (200 mL) that contained either 1.5 g/100 g of polydextrose or no polydextrose at all (control), after an overnight fast. The 1.5 g/100 g polydextrose replaced carbohydrate such that the carbohydrate content was higher in the control milk drink (1.8 vs. 3.1 3/100 mL). Twenty minutes after the study subjects consumed the milk drinks, their blood glucose levels were measured at various time points up to 180 minutes. Replacing carbohydrate with polydextrose resulted in no significant difference in the area under the curve for glucose between the 2 milk products ($P = 0.31$).

Schwab et al. (2006)

In a placebo-controlled, randomized, parallel, double-blinded study, 22 Finnish men and women consumed a breakfast drink enriched with either 0 g or 8 g polydextrose daily for 12 weeks. Fasting blood glucose was significantly lower after the study subjects consumed polydextrose for 12 weeks. Post-prandial glycemia was examined in eight subjects in each group. There was no significant difference in the area under the curve between the control and polydextrose groups ($P > 0.05$).

Shimomura et al. (2005)

In this cross-over design study, five Japanese men ingested chocolate containing 41 g or sucrose or15 g of polydextrose and 19 g or lactitol to test the effect on post-prandial blood glucose levels. There was no rise in blood glucose after consuming the polydextrose/lactitol chocolate, resulting in significantly greater blood glucose area under the curve after consuming the sucrose-containing chocolate ($P > 0.05$).

Laxation/Bowel Function

We identified eleven human studies that evaluated the effect of polydextrose consumption on bowel function (intestinal transit time or frequency of defecation, but not treatment of constipation). Scientific conclusions could not be drawn from eight of these studies (Achour et

al., 1994; Beards et al., 2010; Endo et al., 1991; Hashimoto and Chizuru, 2007; Hengst et al., 2009; Jie et al., 2000; Saku et al., 1991; Tomlin and Read, 1988) because: (1) an appropriate control was not used, (2) statistical analysis was not conducted or it was unclear if it was conducted between the control and polydextrose groups, (3) a mixture of carbohydrate, including polydextrose, was provided to the study subjects and the effect of polydextrose *per se* on bowel function therefore could not be evaluated, and/or (4) the study did not measure intestinal transit time or frequency of defecation.

Costabile et al. (2012)

In a double-blind, randomized, placebo-controlled, cross-over study, the diets of 31 healthy English men and women was supplemented with 8 g/day polydextrose or a maltodextrin (control) for three weeks each. Subjects were instructed not to alter their usual diet or fluid intake during the study. There was no significant difference in the number of stools per day between the two interventions (1.5 versus 1.3) ($P > 0.05$).

Timm et al. (2013)

A randomized, double-blind, placebo-controlled, cross-over study compared the laxative effects of 20 g/day of polydextrose compared to a low-fiber diet that did not contain any polydextrose (control). Each phase lasted ten days and fecal samples were collected during the last five days. This study demonstrated that consumption of polydextrose resulted in a significant increase in the mean number of stools collected over the five day period (5.5/day) compared to the control (4.4/day) ($P < 0.0005$).

Vester Boler et al. (2011)

Twenty-one U.S. healthy adult men were provided, in a cross-over design study, a snack bar that contained either 21 g/day of polydextrose or no polydextrose at all (control) for 21 days each. There was no significant difference in ease of stool passage scores or in the number of defecations during the last five days of the feeding period between the two interventions ($P > 0.05$).

Energy Intake

We identified thirteen studies that evaluated the effect of polydextrose consumption on energy intake. Scientific conclusions could not be drawn from eight of these studies (Astbury et al., 2014; Costabile et al., 2012; Konings et al., 2014; Lummela et al., 2009; Olli et al., 2015; Rolls et al., 1998; Schwab et al., 2006; Willis et al., 2009) because: (1) an inappropriate control was used such that the satiating effect of polydextrose *per se* could not be evaluated, (2) there were large differences in the volume of food provided to the study subjects between the study groups and volume has been shown to affect satiety, and/or (3) energy/food intake was not measured.

Astbury et al. (2013)

In a single-blinded, randomized, cross-over study, 21 English men and women consumed isocaloric liquid meals containing 0 g (control), 6.3 g, 12.5 g, or 25 g of polydextrose. The study subjects ate a standard breakfast before they consumed the liquid meals. Appetite ratings were collected immediately and 30, 60, and 90 minutes after consumption of the liquid meals. After 90 minutes, the study subjects were provided a test lunch and instructed to consume as much as they wished until they felt comfortably full. Using VAS, there was no significant difference in "fullness," "hunger," and "desire- to-eat" ratings between the four liquid meals. However, there was a significant dose-response reduction in energy intake from the test lunch containing polydextrose compared to the control ($P < 0.05$). Energy intake for the entire day was significantly lower for those who consumed the liquid meal containing 12.5 g/day or 25 g/day of polydextrose, but not 6.3 g/day, compared to the control group ($P < 0.05$).

Hull et al. (2012)

Thirty-four English men and women participated in a randomized, single-blinded, placebo controlled, cross-over study. Study subjects consumed yogurt-based drinks containing 0 g (control), 6.25 g, or 12.5 g of polydextrose and that were similar in calories and volume 90 minutes before an *ad libitum* lunch, followed by an *ad libitum* dinner. Analysis of data collected from VAS showed that the "desire to eat" scores were significantly lower during lunch ($P < 0.001$) and dinner ($P = 0.002$) when 6.25 g of polydextrose was consumed compared to the control. "Fullness" scores were significantly lower with 6.25 g ($P < 0.04$) and 12.5 g ($P < 0.007$) polydextrose consumption compared to the control. There was also a significant reduction in energy intake during lunch after consumption of 12.5 g polydextrose ($P = 0.022$), but not with 6.25 g/day polydextrose, when compared to the control. There was no significant difference in energy intake during dinner for either dose of polydextrose ($P > 0.05$). Furthermore, there was no significant difference in the total daily energy intake for either polydextrose dose groups compared to the control group ($P > 0.05$).

King et al. (2005)

Sixteen U.S. men and women were provided a control yogurt providing 25 g/day of sucrose or yogurt providing 25 g/day of polydextrose for up to ten days to evaluate the effect of polydextrose on hunger and energy intake. The yogurts were not isocaloric because the addition of sucrose to the control yogurt increased its calorie content. One and a half hours after they had consumed the yogurt, the study subjects consumed a test lunch *ad libitum* and were instructed to eat to a comfortable level of fullness. Using an electronic appetite rating system, there was no significant difference in "fullness" scores between the two groups on days one and ten of the study. When the energy differential of the yogurts was accounted for, the energy intake of the lunch with prior polydextrose consumption was significantly lower compared to the control ($P = 0.002$).

Monsivais et al. (2011)

In a double-blind, cross-over study, 36 U.S. men and women each consumed a solid snack and a liquid beverage containing 11.8 g polydextrose and a low-fiber control. The caloric content of the solid snack and liquid beverage combined was the same. Afterwards, lunch was served to measure energy intake. Participants used a VAS to rate hunger, fullness and desire-to-eat at 20 minute intervals up to 220 minutes after ingestion. There was no significant difference in hunger, desire-to-eat or fullness between the control and polydextrose intervention ($P > 0.05$). Furthermore, there was no significant difference in energy intake from lunch between the isocaloric control and polydextrose group ($P < 0.05$).

Ranawana et al. (2013)

A randomized, blinded, cross-over study, 26 English males consumed a fruit smoothie containing 0 g (control) or 12 g of polydextrose. Both the treatment and control fruit smoothies weighed 400 g and provided the same number of calories. Lunch was provided to the study subjects 60 minutes after they had consumed the smoothies. VAS ratings were measured before and 15, 30, and 45 minutes after drinking the smoothies, and before and after the lunch. There was no significant difference in the ratings for "hunger," "fullness," "desire-to-eat" and "prospective eating" between the two groups. However, there was significantly lower food intake observed at lunch following the consumption of polydextrose compared to the control ($P = 0.0007$). The reduction in intake resulted from a reduced intake of calories from protein, carbohydrate, and fat. Therefore, there was a significant reduction (10%) in energy intake (100 calories) between the polydextrose and control groups ($P < 0.05$).

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Potato Fibers

Background

There are different forms of nondigestible carbohydrates extracted from potatoes including insoluble potato fiber, solubilized potato polysaccharide, and resistant starch (type 2). Insoluble potato fiber contains mostly cellulose and hemicellulose and is used to improve the texture, stability, and oil/water binding capacity of certain foods.

Blood Cholesterol Levels

We identified two studies that evaluated the effect of potato fiber on blood cholesterol levels. Scientific conclusions could not be drawn from one of the studies because it was conducted for an insufficient duration of time (one week for the control group) for measuring fasting blood cholesterol levels (Eastwood et al., 1983).

Cherbut et al. (1997)

In randomized, double-blind, cross-over study, 18 healthy men and women consumed supplements that contained either 15 g/day of potato fiber or no potato fiber at all (control) for one month each. The potato fiber was isolated from potato pulp and contained approximately 59% insoluble fiber and 10% soluble fiber. The composition of individual fibers was not provided. Post-prandial and fasting cholesterol levels were measured. While potato fiber significantly lowered post-prandial (area under the 6 hour curve) blood cholesterol levels (P = 0.038), there was no significant difference in fasting total cholesterol levels (5.8 *versus* 5.1 mmol/L) between the potato fiber and control supplement groups (P = 0.138).

Blood Glucose Levels

We identified two studies that evaluated the effect of potato fiber on blood glucose levels.

Cherbut et al. (1997)

In randomized, double-blind, cross-over study, 18 healthy men and women consumed supplements that contained either 15 g/day of potato fiber or no potato fiber at all (control), in addition to a basal diet, for one month each. The potato fiber was isolated from potato pulp and contained approximately 59% insoluble fiber and 10% soluble fiber. The composition of the individual fibers was not provided. There was no significant difference in fasting blood glucose levels (4.0 *versus* 3.9 mmol/L) between the potato fiber and control supplement groups (P = 0.523).

Heijnen and Deurenberg (1995)

Ten healthy males consumed three test meals consisting of 50 g raw potato starch (550 g resistant starch (RS2)/kg or 50 g pregelatinized potato starch (0 RS2/kg (control). Each meal was

consumed in the morning after an overnight fast. The findings on postprandial glucose levels were mixed. At 1 hour after consumption of the meals, plasma glucose concentration was significantly higher after the control meal compared to the raw starch meal ($P < 0.001$). However, at 3 hours, plasma glucose concentration was significantly higher after the raw starch meal compared to the control meal ($P < 0.001$).

Laxation/Bowel Function

We identified four studies that evaluated the effect of potato fiber on laxation/bowel function. Scientific conclusions could not be drawn from two of these studies because an appropriate control was not used (Eastwood et al., 1983; Olesen et al., 1998).

Cherbut et al. (1997)

In a randomized, double-blind, cross-over study, 18 healthy men and women consumed supplements that contained either 15 g/day of potato fiber or no potato fiber at all (sucrose) for one month each. The potato fiber was isolated from potato pulp and contained approximately 59% insoluble fiber and 10% soluble fiber. The composition of the individual fibers was not provided. Oro-cecal transit time was significantly higher in the potato fiber groups compared to the control groups ($P < 0.05$).

Cummings et al. (1996)

In a cross-over design study, 12 healthy men and women consumed biscuits containing fully digested wheat starch (control) or resistant starch (RS2) (116 g/kg) derived from potatoes for 15 days each. There was no significant difference in stool frequency (3.7 *versus* 4.6 stools per 5 days) or mean oro-fecal transit time (730 *versus* 756 hours) between the control and RS2 diets.

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Pullulan

Background

Pullulan is a naturally-occurring exopolysaccharide produced by *Aureobasidium pullulans*, a ubiquitous fungus. Pullulan is a glucan consisting predominantly of repeating maltotriose units, which consist of three 1,4-linked glucose molecules, linked by α-1,6-glycosidic bonds (Catley, 1971). Occasionally, maltotetraose units consisting of four 1,4-linked glucose molecules are distributed randomly in the polymer (Catley, 1986). Pullulan is a soluble fiber with film-forming properties that is used as a matrix to hold flavors (breath fresheners), as a coating for foods to extend shelf-life, and as a substitute for gelatin in capsules used for dietary supplements (FDA, 2002).

Blood Cholesterol Levels

We identified one study that evaluated the effect of pullulan consumption on blood cholesterol levels (Stewart et al., 2010). Scientific conclusions could not be drawn from this study because it was not conducted long enough to evaluate the effect of pullulan on fasting blood cholesterol levels.

Blood Glucose Levels

We identified five studies that evaluated the effect of pullulan consumption on blood glucose levels. Scientific conclusions could not be drawn from one of these studies (Klosterbuer et al., 2012) because a mixture of non-digestible carbohydrate, including pullulan, was used in the study and the physiological effect of pullulan *per se* therefore could not be evaluated.

Wolf et al. (2003)

Twenty-eight non-diabetic healthy U.S. adults consumed 50 g of pullulan or maltodextrin (control) in a randomized, double-blinded, cross-over study in which subjects participated in two separate three hour meal tolerance tests. The incremental peak blood glucose concentration was reduced by 54% when subjects consumed pullulan compared to the control group (4.24 ±0.35 vs. 1.97 ± 0.10 mmol/L) ($P < 0.001$). At 180 minutes, the blood glucose concentration was higher when subjects consumed pullulan, supporting the hypothesis that pullulan is digested slowly ($P < 0.05$). The positive incremental area under the curve was significantly reduced by 50% when subjects consumed pullulan compared with the control ($P < 0.001$).

Kendall et al. (2008)

Twelve healthy Canadian volunteers participated in a randomized, cross-over study in which they consumed 25 g of glucose in a beverage (control) and seven test beverages that contained 25 g of total carbohydrates. One of the test beverages contained pullulan as the carbohydrate. The

measured blood glucose (as well as insulin) area under the curve (mmol × min/L) was significantly lower for the study subjects who consumed the pullulan test beverage (8.7 ± 4.1) compared to the control group (103.7 ± 13.7) ($P < 0.05$).

Peters et al. (2011)

Thirty-five healthy subjects from the Netherlands participated in a randomized, double-blind, cross-over study in which they were provided with a test beverage containing 15 g of long-chain pullulan (LCP), medium-chain pullulan (MCP), or maltodextrin (control). Blood samples were collected from only a subset of the study subjects (n=12). The blood glucose area under the curve for the period of 0 to 150 minutes was significantly higher for LCP and MCP groups compared to the control group ($P < 0.05$).

Stewart et al. (2010)

In a single-blind, cross-over design study, 20 healthy U.S. subjects consumed 12 g/day of one of five non-digestible carbohydrates, including pullulan, or maltodextrin (control) for 14 days each. There was no significant difference in fasting blood glucose levels between the pullulan and the control diets ($P > 0.05$).

Laxation/Bowel Function

We identified one study that evaluated the effect of pullulan consumption on laxation.

Stewart et al. (2010)

In a single-blind, cross-over study, 20 healthy US subjects consumed 12 g/day of one of five non-digestible carbohydrates including pullulan, or maltodextrin (control) for 14 days. There was no significant difference in the number of recorded stools per day between the pullulan and control diets ($P > 0.05$).

Energy Intake

We identified one study that evaluated the effect of pullulan consumption on energy intake (Klosterbuer et al. 2013). Scientific conclusions could not be drawn from this study because a mixture of non-digestible carbohydrate along with pullulan was provided to the study subjects and the physiological effect of pullulan *per se* therefore could not be evaluated.

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Rice Bran Fiber

Background

Defatted rice bran is mechanically cleaned to separate rice bran from rice fragments and to remove any residual impurities following the aqueous extraction of protein and starch. Rice bran fiber contains at least 40% nondigestible carbohydrate with at least 90% of which is insoluble. Rice bran fiber is used as an ingredient in foods (FDA, 2011).

Blood Cholesterol Levels

We identified one study that evaluated the effect of rice bran fiber on blood cholesterol levels. Scientific conclusions could not be drawn from this study (Qureshi et al., 2002) because the study did not use an appropriate control.

Blood Glucose Levels

We identified one study that evaluated the effect of rice bran fiber on blood glucose levels. Scientific conclusions could not be drawn from this study (Qureshi et al., 2002) because the study was conducted in individuals with type 1 and 2 diabetes.

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High Amylose Corn/Maize Starch (Resistant Starch 2)

Background

Resistant starch 2 (RS2) is uncooked native starch that is inaccessible to enzymes due to the starch conformation (e.g., raw green banana, raw potatoes, and uncooked high amylose maize/corn and potato starch, which is comprised primarily of α-1,4 glycosidic links) (IOM, 2002). The following studies have evaluated the various physiological effects of RS2 derived from high amylose corn starch.

Blood Cholesterol Levels

We identified seven human studies that evaluated the effect of RS2 consumption on blood cholesterol levels. Scientific conclusions could not be drawn from one of the studies because, although blood cholesterol levels were measured, the data were not presented in the study (Jenkins et al., 1998).

Behall et al. (1989)

Twelve men consumed a diet containing 35% of calories as 70% amylose or amylopectin starch for five weeks each in a cross-over design study. The amount of RS2 in the 70% amylose diets was not provided. Mean fasting blood total cholesterol levels were significantly lower with the RS2 high amylose corn starch diet compared to the amylopectin diet ($P = 0.015$)

Behall and Howe (1995)

In a cross-over design study, 10 healthy and 14 hyperinsulinemic men consumed foods that contained either 70% amylopectin (control) or 70% amylose from corn starch for 14 weeks each. The amount of RS2 in the 70% amylose diets was not provided. After 4, 8, and 13 weeks on the two diets, fasting blood cholesterol levels were measured. At week 4, total cholesterol was significantly higher ($P < 0.01$) in the amylose group than in the amylopectin group. This difference, however, was not observed at weeks 8 and 13.

Bodinham et al. (2012)

In a cross-over design study, 12 men and women consumed either 40 g/day RS2 from high amylose cornstarch or a placebo containing a high digestible starch (control) for four weeks each. The study evaluated the effect of replacing high digestible starch with RS2 in meals. Consuming 40 g/day of RS2 did not have a significant effect on blood total cholesterol when compared to the placebo ($P > 0.05$).

Heijnen et al. (1996)

In a randomized, single-blind, sequential study, 57 men and women consumed supplements containing glucose (control) or 30 g/day of RS2 for three weeks each. The RS2 was uncooked

high amylose corn starch. At the end of each phase of the study, fasting blood samples were collected from the study subjects. There was no significant difference in total or LDL cholesterol levels between the control group and the group that consumed the RS2 supplement ($P > 0.05$).

Kwak et al. (20120

In a parallel design study, 85 Korean men and women with pre-diabetes or type 2 diabetes were randomly assigned to either a group ingesting rice containing 6.51 g RS2 or a control rice for four weeks. There was no significant difference in blood total or LDL cholesterol between the RS2 and control groups ($P > 0.05$).

Noakes et al. (1996)

In a random, cross-over design study, 23 hypertriglyceridemic Australian men and women consumed diets that contained 25% of carbohydrate as low (control) or high amylose corn starch for four weeks each. The high amylose corn starch contained 17 g to 25 g of RS2. After four weeks of consuming the two diets, there was no significant difference in plasma total or LDL cholesterol between the low amylose and high amylose diets ($P > 0.05$).

Blood Glucose Levels

We identified twenty-five studies that evaluated the effect of RS2 consumption on blood glucose levels. Both fasting blood glucose and post-prandial blood glucose levels were considered. Scientific conclusions could not be drawn from four of these studies for one or more of the following reasons: (1) an inappropriate control was used, (2) it was unclear which type of RS was provided to the study subjects, (3) glucose response was measured solely in response to RS2 consumption rather than consumed as part of a food and/or beverage, and (4) the subjects had type 2 diabetes (Haub et al., 2010; Kwak et al., 2012; MacNeil et al., 2013; Quilez et al., 2007).

Anderson et al. (2010)

In a cross-over design study, 17 men consumed five soups containing either maltodextrin (6 g RS2), whole grain high amylose starch (27 g RS2), high amylose corn starch (23 g RS2), regular cornstarch (19 g RS2), or no added starch (3 g RS) at one week intervals. The four soups with added starches contained 41g to 48 g of carbohydrate and were compared. The soup with no added starch was not considered because it contained only 4 g carbohydrate and would be expected to have a lower post-prandial blood glucose response. The soup with added maltodextrin served as the control. The subjects consumed the soups after fasting and then ate a pizza meal. Post-prandial glucose response was measured beginning at 30 or 120 minutes after consumption. Post-prandial blood glucose area under the curves beginning at 30 minutes were significantly lower for the three RS2 soup groups compared to the control group ($P < 0.05$). When post-prandial blood glucose was measured 120 minutes after the study subjects consumed the pizza meal, the high-amylose and regular cornstarch soup groups had significantly lower areas under the curve compared to the control group ($P < 0.05$).

Behall et al. (1988)

Twenty five U.S. men and women consumed meals containing cornstarch with 70% of the starch in the form of amylopectin (control) or amylose to evaluate the postprandial glucose response to the two forms of starch. The RS2 content of the 70% (high) amylose cornstarch meal was not provided. The study evaluated the effect of substituting amylopectin with high amylose corn starch. The glycemic (and insulin) response at 30 minutes after consuming the high amylose meal was significantly lower compared to the control meal ($P < 0.004$) and was sustained at 180 minutes after ingestion ($P < 0.001$).

Behall et al. (1989)

Twelve men consumed a diet containing 35% of calories as 70% amylose or amylopectin starch for five weeks each in a cross-over design study. The amount of RS2 in the 70% amylose diets was not provided. The study evaluated the effect of substituting amylopectin with high amylose corn starch. Plasma glucose responses were not significantly different between the two starch diets after four weeks. After the fifth week, glycemic (and insulin) response data showed that mean glucose levels for the amylose groups were significantly lower at one-half and one hour but at three hours was significantly higher than were the mean glucose levels for the amylopectin groups. Mean fasting blood glucose levels were not significantly different between the two starch diets.

Behall and Howe (1995)

In a cross-over design study, 10 healthy and 14 hyperinsulinemic men consumed foods that contained either 70% amylopectin (control) or 70% amylose from corn starch for 14 weeks each. The amount of RS2 in the 70% amylose diets was not provided. The study evaluated the effect of substituting amylopectin with high amylose corn starch. After 4, 8 and 13 weeks on the two diets, post-prandial blood glucose levels were measured. At weeks 4, 8, and 13, while insulin levels were lower in the amylose groups, there was no significant difference in post-prandial blood glucose area under the curve ($P > 0.05$) between the two starches for healthy and hyperinsulinemic men.

Behall and Hallfrisch (2002)

Twenty five men and women participated in different glucose tolerance tests that measured the glucose response of breads containing 70% amylose corn starch, 30% corn starch, and blends of the two starches. This study evaluated the effect of substituting varying amounts of amylopectin with high amylose corn starch. A standard menu was provided to the study subjects for three days. The RS2 content (% of total starch) of the breads was 30% amylose (2.6%), 40% amylose (4.7%), 50% amylose (10.2%), 60% amylose (21.5%), and 70% (27.6%). Peak glucose concentration after consumption of the breads that contained 50-70% amylose starch was significantly lower than peak glucose concentration after consumption of the 30 and 40% amylose breads ($P < 0.05$).

Behall and Scholfield (2005)

Twenty-four U.S. men and women consumed corn chips or corn muffins made with low amylose (30%) or high amylose (70%) corn starch. The study evaluated the effect of substituting amylopectin with high amylose corn starch. The low amylose corn chips and corn muffins did not contain RS2 and served as a control. The RS2 content was 8.7 or 11.9 g for the high amylose corn chips and 16 or 24.7 g for the high amylose corn muffins. The study subjects' post-prandial blood glucose levels were measured immediately after they consumed the corn chips or muffins for up to three hours. The post-prandial glucose (and insulin) area under the curve was significantly lower for the high amylose products group compared to the low amylose products group ($P < 0.05$).

Behall et al. (2006a)

In a cross-over study, 20 U.S. men and women consumed muffins made with standard corn starch (0.71 g of RS2/100 g), a 50/50 blend of standard and high amylose cornstarch (2.57 g of RS2/100 g), or high amylose corn starch (5.06 g of RS2/100g). The study evaluated the effect of substituting amylopectin with high amylose corn starch. Each of the three starches was combined with 0.26, 0.68, or 2.3 g β-glucan/100 g of the muffins. While insulin response was significantly lower with higher RS2 intake, there was no significant difference in the plasma glucose area under the curve between the three levels of RS2 when low, medium or high levels of β-glucan were present ($P > 0.05$).

Behall et al. (2006b)

In a cross-over design study, 20 U.S. normal-weight or overweight men and women consumed nine different muffins containing: (1) 75 g of available carbohydrate, (2) either 0.1 g, 3.1 g, or 5.8 g of β-glucan, and (3) either 0.1 g, 6.1 g, or 11.6 g of RS2 from high amylose cornstarch that replaced standard starch. There was no significant difference in the plasma glucose area under the curve between the three levels of RS2 when low, medium or high levels of β-glucan were present ($P > 0.05$).

Bodinham et al. (2010)

Twenty young men consumed either 48 g of RS2 from 80 g high amylose corn starch or 32 g of a rapidly digestible starch (control) that was added as a supplement to test breakfasts and lunch meals. There was no significant difference in post-prandial blood glucose (and insulin) levels between the RS2 supplement group and the control group ($P > 0.05$).

Bodinham et al. (2012)

In a cross-over design study, 12 men and women consumed either 40 g/day RS2 from high amylose cornstarch or a placebo containing a high digestible starch for four weeks each. The study evaluated the effect of replacing high digestible starch with RS2 in meals. Consuming 40

g/day of RS2 resulted in significantly lower fasting blood glucose levels compared to the placebo (4.8 versus 5.0 mmol/L) ($P < 0.049$).

Brighenti et al. (2006)

Ten healthy Italian men and women consumed study breakfasts consisting of sponge cakes made with either high amylose corn starch and cellulose or amylopectin and cellulose (control). The study involved substituting amylopectin with high amylose corn starch. The RS2 content of the high amylose sponge cake was not provided. Five hours after they consumed the breakfasts, the study subjects consumed a standard lunch that contained 96 g of digestible carbohydrate. The subjects' post-prandial glucose responses of the breakfast and lunch meal were measured. The glucose (and insulin) response was significantly lower when high amylose corn starch was consumed as part of the breakfast meal compared to the control group, especially at 30 minutes after ingestion ($P < 0.03$). The post-prandial blood glucose response continued to be lower for the lunch meal after consuming the high amylose breakfast (i.e., the second meal effect) compared to the control group ($P < 0.05$).

Heijnen et al. (1995)

In a cross-over study, 12 men and women consumed either a drink, pudding, or a roll as breakfast and the same amount of food as a mid-morning snack. The foods were prepared with high or normal (control) amylose starch. The study substituted low amylose starch with high amylose corn starch. A blood sample was taken from the study subjects 30 and 90 minutes after they consumed the food. The RS2 meal resulted in a significantly lower post-prandial glucose (and insulin) concentrations from the drink and pudding that contained RS2 compared to the control diet ($P < 0.05$), but this was not the case for the rolls.

Hoebler et al. (1999)

Eight healthy men and women consumed three different test meals (white wheat bread, high amylose wheat bread, and spaghetti) of equivalent nutrient composition after an overnight fast. This study substituted digestible starch with high amylose corn starch. The RS content was 16.5 g in the high amylose bread, whereas RS content in the white wheat bread and spaghetti was 1.3 and 2.5 g, respectively. Post-prandial blood glucose (and insulin) concentrations were significantly lower after consuming the high amylose bread compared to white wheat bread and spaghetti at certain time points after ingestion ($P < 0.05$).

Luhovvy et al. (2014)

Thirty healthy Canadian men participated in cross-over design study in which they consumed study cookies once a week for three weeks. The cookies contained either 100% wheat flour (control), low-dose high amylose maize flour (11.1 g of RS2), or high-dose high amylose maize flour (22.2 g of RS2). The high amylose maize flour replaced wheat flour in the study cookies. The study subjects' post-prandial blood glucose was measured for two hours after they had

consumed each cookie, as well as an additional 80 minutes later to evaluate the effect of a second meal (pizza). Post-prandial glucose area under the curve was significantly lower with RS2 intake and in a dose response manner after consumption of the cookie ($P < 0.05$). The area under the curve was significantly higher for both RS2 groups compared to the control group after consumption of the pizza ($P < 0.05$). The cumulative effect of RS2 on post-prandial blood glucose levels after both meals was significantly lower only in the 22.2 g or RS cookie group ($P < 0.05$).

Maki et al. (2012)

In a double blind, placebo controlled, cross-over study, 33 men and women consumed 0, 15, or 30 g RS2/day as a supplement for four weeks each. Highly digestible corn starch served as the control for the study. There was no significant difference in fasting blood glucose (and insulin) levels between the three diets ($P = 0.29$).

Nilsson et al. (2008)

Cereal-based test meals were provided to 15 men and women. The test meals contained white wheat flour that contained either approximately 7 g of RS2 from high amylose corn starch or no RS2 from high amylose corn starch at all (control). Post-prandial blood glucose was measured after the study subjects had consumed the two test meals. There was no significant difference in the blood glucose (and insulin) areas under the curve between the two test meal groups ($P > 0.05$).

Noakes et al. (1996)

In a randomized, cross-over study, 23 hypertriglyceridemic Australian men and women consumed diets that contained 25% of carbohydrate as low (control) or high amylose corn starch for four weeks each. The study substituted amylopectin with high amylose corn starch. The high amylose corn starch contained approximately 20 g of RS2. After four weeks of consuming the two diets, there was no significant difference in fasting plasma glucose levels between the low amylose (control) and high amylose diets ($P > 0.05$). After consuming a muffin that contained low or high amylose corn starch, the post-prandial glucose response was significantly lower when the high amylose corn starch muffin was consumed ($P <0.03$).

Penn-Marshall et al. (2010)

In a double blind, cross-over study, 15 men and women at risk of type 2 diabetes consumed bread containing 12 g of added RS2 or control bread for six weeks each. RS2 was isolated from high amylose corn starch. There was no significant difference in fasting blood glucose levels between the RS2 and control diets ($P = 0.057$).

Ranganathan et al. (1994)

After an overnight fast, six men consumed 50 g of a glucose solution with and without 30 g high amylose RS2. There was no significant difference in the glycemic (or insulin) response between the two solutions ($P > 0.05$).

Robertson et al. (2003)

For 24 hours, ten healthy men and women consumed two identical low fiber diets except that one diet was supplemented with 60 g of RS2 from high amylose corn starch. On the following morning, a fiber-free meal tolerance test was carried out for five hours to measure the effect of the prior meals on post-prandial glucose. The glycemic (and insulin) response was significantly lower when consuming high amylose corn starch compared to low amylose cornstarch (control) ($P = 0.037$).

Robertson et al. (2005)

Ten healthy men and women were provided a placebo supplement or a supplement containing 30g of RS2 for four weeks each. No significant difference in fasting plasma glucose was observed between the control and the RS2 diets (5.04 vs. 5.06 mmol/L). There also was no significant difference in the post-prandial glucose (and insulin) area under the curve after consuming a meal along with either the placebo or the RS2 supplement.

Laxation/Bowel function

We identified seven studies that evaluated the effect of RS2 consumption on bowel function.

Heijnen et al. (1996)

In a randomized, single-blind, sequential design study, 57 men and women consumed supplements containing glucose (control) or 30 g/day of RS2 for three weeks each. The RS2 was uncooked high amylose corn starch. During supplementation with RS2, there was a significantly higher number of bowel movements per day (1.4) compared to the control (1.3) ($P < 0.05$).

Heijnen et al. (1998)

In a single-blind, randomized, cross-over study, 24 healthy men consumed a daily supplement containing 32 g/day of RS2 or glucose (control) for one week each. The RS2 was high amylose cornstarch. There was no significant difference between the number of stools per week between the control (5.6) and RS2 (5.5) supplementation groups ($P > 0.05$).

Hylla et al. (1998)

During two, four week periods, 12 healthy men and women consumed a controlled basal diet enriched with either amylose corn starch (55 g of RS2/day) or available corn starch (cornstarch).

There was no significant difference in mean transit time (68 hours for the RS2 group vs. 58 hours for the control group).

Muir et al. (2004)

In a randomized, cross-over study, 20 men and women consumed a wheat bran diet (12 g of fiber/day) (control) and the control diet plus high amylose corn starch (22 g of RS2/day). During five consecutive days (days 15 through 19) of each dietary period, bowel function was measured. While fecal output (g/day) was increased with the inclusion of RS2, there was no significant difference in mean oro-anal transit time (37 vs. 38 hours) or stools per day (1.3 vs. 1.4).

Noakes et al. (1996)

In a random, cross-over study, 23 hypertriglyceridemic Australian men and women consumed diets that contained 25% of carbohydrate as low or high amylose corn starch for four weeks each. The high amylose corn starch contained 17 to 25 g of RS2. After four weeks of consuming the two diets, there was a significant increase in the number of stools per day (1.43 vs. 1.23) ($P < 0.02$) after consuming the high amylose diet compared to the low amylose diet (control).

Phillips et al. (1995)

In a three week randomized, cross-over study, 11 men and women consumed diets containing a control diet or a diet containing 39 g of RS2/day. Ease of defecation was reported to be higher with RS2 consumption compared to the control (P=0.04).

Silvester et al. (1997)

Eight men consumed a high meat diet with and without high amylose corn starch (40 g of RS2) provided in cookies for 19 days each. There was no significant difference in oro-fecal transit time (74 vs. 67 hours) between the two diets ($P > 0.05$).

Energy Intake

We identified six studies that evaluated the effect of RS2 consumption on energy intake. Scientific conclusions could not be drawn from two of these studies because an inappropriate control was used or energy intake was not measured (Nilsson et al., 2008; Quilez et al., 2007).

Anderson et al. (2010)

In a cross-over design study, 17 men consumed five soups containing either maltodextrin (6 g RS2), whole grain high amylose starch (27 g RS2), high amylose corn starch (23 g RS2), regular corn starch (19 g of RS), or no added starch (3 g RS2) for one week each. The four soups with added starches contained 41g to 48 g of carbohydrate and were compared. The soup with no

added starch was not considered because it contained only 4 g carbohydrate and provided markedly lower calories. The soup with added maltodextrin served as the control. *Ad libitum* food intake was measured at 30 or 120 minutes after the study subjects had consumed the soups as well as satiety before and after consumption using VAS. Appetite scores and food/energy intake levels were not significantly different between the four test diets. This lack of significant differences, however, could be attributed to the differences in the content of the digestible starches rather than the RS2 levels.

Bodinham et al. (2010)

In a randomized, cross-over study, 20 English men consumed a study breakfast and lunch supplemented, or not supplemented (control), with high amylose corn starch (48 g RS2). Four hours after they consumed the lunch, the participants consumed *ad libitum* a pre-weighed meal until they were comfortably full. Supplementation with RS2 over the two meals resulted in a significantly lower energy intake (1253 kcal) compared to the control (1340 kcal) ($P < 0.033$).

De Roos et al. (1995)

Twenty-four men consumed a daily supplement with either glucose or high amylose corn starch (30 g/day of RS2) in a cross-over study conducted over four weeks. The supplements were consumed for a week each. At the end of each week, the subjects rated their appetite using VAS and food intake was measured one day per week using a 24-hour recall. There was no significant effect of RS2 intake on satiety or energy intake ($P > 0.05$).

Luhovvy et al. (2014)

Thirty healthy Canadian men participated in cross-over design study in which they consumed study cookies once a week for three weeks. The cookies contained either 100% wheat flour (control), low-dose high amylose maize flour (11.1 g of RS2), or high-dose high amylose maize flour (22.2 g of RS2). The high-amylose maize flour replaced wheat flour. *Ad libitum* appetite and food intake was measured 120 minutes after a pizza meal. While both RS2 treatments significantly reduced appetite, there was no significant difference in energy intake.

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Retrograded Corn Starch (Resistant Starch 3)

Background

Retrograded corn starch is produced by cooking and then cooling high amylose corn starch/maize and/or the extrusion of corn starch (e.g., corn flakes). The non-digestible carbohydrate present in these products is called resistant starch type 3 (RS3) and is added to foods as ingredients (e.g., flour) (IOM, 2002). The following studies evaluated the various physiological effects of RS3 isolated from high amylose corn starch when added to foods.

Blood Cholesterol Levels

We identified four human studies that evaluated the effect of RS3 consumption on blood cholesterol levels. Scientific conclusions could not be drawn from three of these studies because: (1) while data were collected on blood cholesterol levels, the data were not presented in the studies or statistical analysis was not conducted between the control and RS3 treatment groups, or (2) the study was not conducted long enough to evaluate the effect of RS3 on fasting blood cholesterol levels (Jenkins et al., 1998; Park et al., 2004; Stewart al., 2010).

Heijnen et al. (1996)

In a randomized, single-blind, sequential design study, 57 men and women consumed supplements containing glucose (control) or 30 g/day of RS3 for three weeks each. The RS3 was retrograded, high amylose corn starch. Nutrient intake from the two diet groups was similar. At the end of each study phase, fasting blood samples were collected from the study subjects. There was no significant difference between total or LDL cholesterol levels between the control and RS3 supplement groups ($P > 0.05$).

Blood Glucose Levels

We identified seven human studies that evaluated the effect of RS3 consumption on blood glucose levels. Scientific conclusions could not be drawn from four of these studies because: (1) an appropriate control group was not used to test the effect of the RS3 on blood glucose levels, (2) it was unclear whether processed or unprocessed high amylose starch was being used in the studies, and/or (3) statistical analysis was not conducted between the control and RS3 groups (Granfeldt et al., 1995; Kendall et al., 2008; Lobley et al., 2013; Park et al., 2004).

Achour et al. (1997)

Eight healthy men and women participated in two 27-hour test periods during which the study subjects consumed breakfast and dinner that included either 50 g pre-gelatinized, digestible corn starch (control) or 50 g of retrograded high amylose cornstarch. The amount of RS3 consumed was not presented in the study. Post-prandial blood glucose (but not insulin) levels in the study subjects were significantly lower after the consumption of the RS3 meals compared to the control group ($P < 0.05$)

Klosterbuer et al. (2012)

In a randomized, double-blind, cross-over study, 20 men and women consumed a low-fiber breakfast (control) or a breakfast containing 25 g of RS3 after fasting. The insoluble RS3 was produced from heat moisture-treated high amylose maize starch. Post-prandial glucose was measured up to 180 minutes after the study subjects had consumed each breakfast. Consumption of the RS3 breakfast resulted in a significantly reduced glucose area under the curve compared to the control breakfast ($P < 0.05$).

Stewart et al. (2010)

Twenty U.S. subjects participated in a single-blind, cross-over study in which apple sauce containing either 12 g/day of retrograded high amylose cornstarch (RS3) or maltodextrin (control) was consumed for 14 days each. There was no significant difference in fasting blood glucose levels between the RS3 and control groups ($P > 0.05$).

Laxation/Bowel function

We identified seven human studies that evaluated the effect of RS3 consumption on bowel function.

Cummings et al. (1996)

In a cross-over study, twelve healthy men and women consumed a diet that included a biscuit containing fully digested starch (control), retrograded wheat starch that contained 85 g of RS3 or retrograded maize starch that also contained 85 g of RS3 for 15 day each. There was no significant difference in mean oro-fecal transit time or stool frequency between the two diets when compared to the control diet ($P > 0.05$).

Heijnen et al. (1996)

In a randomized, single-blind, sequential design study, 57 men and women consumed supplements containing glucose (control) or 30 g/day of RS3 for three weeks each. The RS3 was retrograded high amylose corn starch. During supplementation with RS3, there was a significantly higher number of bowel movements per day (1.4) compared to the control (1.3) ($P < 0.05$).

Heijnen et al. (1998)

In a single-blind, randomized, cross-over study, 24 healthy men consumed a daily supplement containing 32 g/day of RS3 or glucose (control) for one week each. The RS3 was extruded and retrograded high-amylose cornstarch. There was no significant difference between the number of stools per week between the control group (5.6) and RS3 (5.5) supplementation group ($P > 0.05$).

Klosterbuer et al. (2013)

Twenty healthy men and women consumed maltodextrin (control) or 20 to 25 g/day RS3 for seven days each in a cross-over design study. RS3 was retrograded high-amylose maize starch. The number of stools per day was significantly higher for the RS3 consumption group (1.71) compared to the control group (1.15) ($P < 0.05$).

Maki et al. (2009)

In a randomized, double-blind, cross-over study, following a 14-day low fiber feeding period (control), 14 healthy men and women consumed 25g of RS3 or wheat bran fiber as a positive control for 14 days each. RS3 was resistant corn starch. There was no significant difference in average frequency of defecation between the two intervention groups (0.9 vs. 0.9 stools/day) ($P = 0.875$).

Stewart et al. (2010)

Twenty U.S. subjects participated in a single-blind, cross-over study in which they consumed applesauce that contained 12 g/day of RS3 in the form of retrograded high amylose cornstarch or maltodextrin (control) for 14 days each. There was no significant difference in the number of daily stools, or the number of stools over the course of four days, between the RS3 and the control group ($P > 0.05$).

Tomlin and Read (1990)

The effect of RS3 from a corn-based cereal on colonic function was measured in eight men. The study subjects consumed either 10.33 g/day of RS3 in the form of corn flakes or 0.86 g/day of RS3 in the form of rice krispies (control) for one week each. There was no significant difference in oro-fecal transit times, stool frequency, or ease of defecation between the two dietary groups ($P > 0.05$).

Energy Intake

We identified four human studies that evaluated the effect of RS3 consumption on energy intake. Scientific conclusions could not be drawn from one of the studies because it did not measure energy intake (Willis et al., 2009).

Klosterbuer et al. (2012)

In a randomized, double-blind, cross-over study, 20 men and women consumed a low-fiber breakfast (control) or a breakfast containing 25 g of RS3 after they had fasted. The insoluble RS3 was produced from heat moisture-treated high amylose maize starch. VAS assessed measures of satiety ("hungry," "could eat more/less," "satisfied" and "feeling of fullness." VAS measurements were collected up to 180 minutes after the study subjects had consumed the two breakfasts. There was no significant difference in the measures of satiety between the control

and RS3 breakfast groups ($P > 0.05$). There also was no significant difference between calories consumed by the two groups during the breakfast and the following lunch ($P > 0.05$).

Monsivais et al. (2011)

In a double-blind, cross-over study, 36 U.S. men and women each consumed a combination of a beverage and a solid snack containing 11.2 g of RS3 and a beverage or a low-fiber solid snack (control). The caloric content of the solid snack and liquid beverage combined was the same. Afterwards, lunch was served to measure energy intake. Study participants used VAS to rate satiety (i.e., hunger, fullness, and their desire-to-eat) at 20 minute intervals up to 220 minutes after the lunch. There was no significant difference in hunger, desire-to-eat, or fullness between the control and RS3 intervention groups ($P > 0.05$). Energy intake was not significantly different with consumption of the RS3 meal compared to the control ($P < 0.05$).

De Roos et al. 1995

Twenty four men consumed a daily supplement that contained either glucose (control) or 30 g/day of RS3 from high retrograded amylose corn starch during a four week, cross-over study. The study subjects consumed the supplements for a week each. At the end of each week, the subjects rated their appetite using VAS and food intake was measured one day each week using a 24-hour recall. There was no significant effect ($P > 0.05$) of RS2 intake on satiety or energy intake.

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Resistant Wheat and Maize Starch (Resistant Starch 4)

Background

Resistant starch type 4 (RS4) are starches that are chemically modified from a source such as wheat or maize so that the starch is resistant to enzymatic digestion and therefore is considered to be a non-digestible carbohydrate (IOM, 2002). Crosslinking and esterification of the starch molecules are examples of chemical modifications that are made to starch to form RS4. RS4 is added to foods for various technical effects including formulation convenience (particularly in flour-based foods), enhancing crispness because of RS4's low water-holding capacity, and providing smooth textures.

Blood Cholesterol Levels

We identified one human study that evaluated the effect of RS4 consumption on blood cholesterol levels.

Nichenametia et al. (2014)

Eighty-six participants, with or without metabolic syndrome, participated in a cross-over study in which they consumed diets containing flour (control) or flour that was 30% substituted with cross-linked RS4 wheat starch for 12 weeks each. The study participants' blood cholesterol levels were measured at the end of 12 weeks. The mean total cholesterol level for the RS4 group was 7.5% ($P = 0.002$) lower than for the control group. However, no significant differences ($P > 0.05$) in LDL cholesterol levels compared to the control group were observed both for subjects with metabolic metabolic syndromes and for those without. The significant reduction in total cholesterol levels was reflected by a cumulative reduction in LDL, HDL and non-HDL cholesterol.

Blood Glucose Levels

We identified five human studies that evaluated the effect of RS4 consumption on blood glucose levels. Scientific conclusions could not be drawn from three of these studies because an inappropriate control was used (Haub et al., 2010; Heacock et al., 2004; Wolf et al., 2001). One study was not evaluated because the chemically treated starch was classified in the study as being a slowly digestible starch rather than a resistant starch (He et al., 2008).

Al-Tamimi et al. (2010)

In a cross-over study, 13 men and women consumed a puffed wheat bar that did not contain any RS4 (control) and a bar that contained approximately 15 g of RS4 from cross-linked wheat. Both bars contained 50 g of available carbohydrates. Consumption of the RS4 bar resulted in lower post-prandial glucose levels compared to consumption of the control bar. The glucose area under the curve was significantly reduced for the RS4 bar group (28 mmol/2hr) compared to the control bar group (84 mmol/2 hr) ($P < 0.05$).

Nichenametia et al. (2014)

Eighty six participants, with or without metabolic syndrome, participated in a cross-over study in which they consumed diets containing flour (control) or flour that was 30% substituted with cross-linked RS4 wheat starch for 12 weeks each. The study subjects' fasting and post-prandial blood glucose levels were measured after 12 weeks. There was no significant difference ($P > 0.05$) in either fasting glucose or post-prandial glucose levels between the RS4 and the control groups.

Energy Intake

We identified one human study that evaluated the effect of RS4 consumption on energy intake.

Karalus et al. (2012)

In a randomized, cross-over study, 22 U.S. women consumed either a chocolate crisp bar that contained 10 g of cross-linked wheat RS4 or a bar that did not contain any RS4 (control). Twelve hours after the subjects had consumed the study bars, they assessed their satiety using VAS. The following morning, the subjects consumed the crisp bar along with a beverage. Three hours later, they were served three pieces of French bread pizza and water, which were weighed before and after consumption. Food intake was recorded 24 hours after the start of each visit. There was no significant difference ($P > 0.05$), based on the VAS data and food intake data, in any of the satiety measurements, or in energy consumed at the pizza lunch or during the 24 hours following the study, between the RS4 group and the control bar group.

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Soluble Corn Fiber[2]

Background

Soluble corn fiber (SCF) is a resistant maltodextrin produced from the hydrolysis of corn starch and consists of glucose oligosaccharides with the glycosidic linkages resistant to digestion. SCF has physical properties similar to corn syrup because it can be easily be used as an ingredient in existing formulations of a variety of foods without changing the texture or taste of the foods.

Blood Cholesterol Levels

We have identified three human studies that evaluated the effect of SCF consumption on blood cholesterol levels. Scientific conclusions could not be drawn from one of the studies because the study was not conducted long enough to evaluate the effect of SCF on fasting blood cholesterol levels (Stewart et al., 2010).

Hashizume et al. (2012)

Thirty-eight Japanese men and women participated in a randomized, placebo-controlled, parallel study in which a tea beverage containing 0 g (control) or a 9 g of a corn resistant maltodextrin was consumed by the subjects along with their meals for 12 weeks. There was no signification difference in total (5.45 versus 5.57 mmol/L) and LDL (3.49 versus 3.66) cholesterol between the corn resistant maltodextrin and placebo group ($P < 0.05$).

Kishimoto et al. (2007)

Thirteen healthy Japanese men and women participated in a cross-over study in which they consumed a meal containing approximately 50 g of fat, with a beverage containing 0 (placebo), 5 or 10 g corn resistant maltodextrin. Post-prandial blood cholesterol levels were measured for up to six hours. The beverage containing 5 g of corn resistant maltodextrin resulted in significantly lower cholesterol levels compared to the placebo at 3, 4 and 6 hours. The beverage containing 10 g corn resistant maltodextrin demonstrated significantly lower cholesterol levels after three hours. The area under the curve was 75.9% (5 g) and 79.8% (10 g) and was not significantly different.

Blood Glucose Levels

We identified six human studies that evaluated the effect of SCF consumption on blood glucose levels.

Hashizume et al. (2012)

Thirty-eight Japanese men and women participated in a randomized, placebo-controlled, parallel

[2] Submitted as a citizen petition.

study in which tea containing 0 (placebo) or 9 g corn resistant maltodextrin was consumed along with their meals for 12 weeks. There was no significant difference in fasting blood glucose levels between the placebo and corn resistant maltodextrin group (5.18 vs. 5.36 mmol/L) ($P < 0.05$).

Kendall et al. (2008)

In a random cross-over study, twelve Canadian men and women were fed a test beverage containing SCF (25 g total carbohydrate) or 25 g glucose (control), along with 2 test meals. Immediately following consumption, blood glucose levels were measured every 30 minutes for a total of 120 minutes. For the first hour, post-prandial blood glucose (and insulin) levels were significantly lower after consumption of the SCF beverage compared to the control ($P < 0.05$), as well as the area under the curve.

Kishimoto et al. (2007)

Thirteen healthy Japanese men and women participated in a crossover study in which they consumed a meal containing approximately 50 g of fat, along with a beverage containing 0 (placebo), 5 or 10 g of corn resistant maltodextrin. Post-prandial blood glucose levels were measured up to six hours. The peak value of blood glucose levels occurred 30 minutes after meal loading in each group and no significant difference was observed at either level of corn resistant maltodextrin.

Klosterbuer et al. (2012)

In a randomized, double-blind, cross-over study, 20 U.S. men and women consumed a low-fiber control breakfast or a breakfast containing 25 g of SCF after an overnight fast. The post-prandial glucose (and insulin) response following the SCF breakfast did not differ significantly from the control ($P > 0.05$).

Konings et al. (2014)

In a single-blinded, randomized cross-over study, 18 overweight Dutch men and women were provided two control meals (isocaloric and full diet) or meals that in which digestible carbohydrates were replaced with SCF to provide approximately 55 g/day. The macronutrient content of the full diet control, but not the isocaloric diet, was similar to the SCF diet. Therefore, the full diet was used for comparative purposes. Post-prandial blood glucose levels were measured immediately before and after the ingestion of the breakfast, lunch, and dinner meals throughout the day (approximately 13.5 hours), as well as continued blood glucose monitoring throughout the night (24 hours). When evaluating the post-prandial blood glucose response to each meal, the ingestion of SCF significantly reduced the response after the breakfast and lunch meal. There were no significant differences, however, in the post-prandial blood glucose response between the control and SCF meals throughout the day, as well as over the 24-hour period ($P > 0.05$).

Stewart et al. (2010)

Twenty U.S. subjects participated in a single-blind, cross-over study in which 12 g/day of SCF or a placebo (maltodextrin) was consumed via applesauce for 14 days each. The study subjects consumed their habitual diets throughout the study and it was determined that the dietary nutrient intake was similar between the two diets. There was no significant difference in fasting blood glucose (and insulin) levels between the SCF and placebo groups ($P > 0.05$).

Laxation/Bowel Function

We identified six human studies that evaluated the effect of SCF consumption on laxation. Scientific conclusions could not be drawn from one study because the data on stool frequency was not provided (Housez et al., 2012).

Fastinger et al. (2008)

U.S. men and women participated in a randomized, double-blind parallel study in which 15 g of maltodextrin (control) (n=12), 7.5 g maltodextrin/7.5 g SCF (n=13), or 15 g SCF (n=13) was consumed daily in a beverage for three weeks. A dose-response relationship with stools/day was found to not be significant ($P = 0.09$). There was a significant linear decrease in ease of stool passage with increased intake of SCF ($P < 0.01$).

Klosterbuer et al. (2013)

Twenty healthy U.S. men participated in a randomized, double-blind, cross-over study in which they consumed maltodextrin (control) or SCF (20-25 g/day) for seven days each. There was no significant difference in the number of self- reported daily stools between the two groups (1.15 vs. 1.15) ($P > 0.05$).

Stewart et al. (2010)

Twenty U.S. subjects participated in a single-blind, cross-over study in which 12 g/day of SCF or maltodextrin (control) was consumed via applesauce for 14 days each. There was no significant difference in the number of stools per day or per four days between the SCF and the control groups. Furthermore, there was no significant difference in total stool output (g/4 days).

Timm et al. (2013)

A randomized, double-blind, placebo-controlled, cross-over study compared the laxative effects of SCF (20 g/day) compared to a control (low-fiber diet without SCF). Each phase was 10 days with fecal samples collected during the last five days. Furthermore, the consumption of SCF resulted in a significant increase in the mean number of stools collected over the five day period (5.3/day) compared to the control group (4.4/day) ($P < 0.0005$).

Vester Boler et al. (2011)

Twenty-one healthy U.S. subjects participated in a cross-over design study in which 21 g/day SCF or no supplemental fiber (control) was provided in a snack bar for 21 days. There was no significant difference in ease of stool passage (2.6 versus 2.58) (1 = very easy, 2 = easy, 3 = neither easy nor difficult, 4 = difficult, 5 = very difficult). There was no significant difference in the number of defecations during the 21 day period (23.9 vs. 25.1) ($P > 0.05$).

Energy Intake

We identified four human studies that evaluated the effect of SCF consumption on energy intake. Scientific conclusions could not be drawn from one of the studies (Konings et al., 2014) because statistical comparisons were not conducted between the control and SCF groups.

Karalus et al. (2012)

In a random, cross-over study, 22 U.S. women consumed either a chocolate crisp bar that contained either 10 g of SCF or no SCF (control) the night before the study. Twelve hours after the subjects had consumed the study bars, they assessed their satiety using VAS. The following morning, the subjects consumed the crisp bar along with a beverage. Three hours later, they were served three pieces of French bread pizza and water, which were weighed before and after consumption. Based on VAS and food intake data, there was no significant difference in any of the satiety measures, in energy consumed at the pizza lunch or during the 24 hours following the study between the SCF and control bar groups.

Timm et al. (unpublished)

U.S. men and women (n=36) were provided a low-fiber control or SCF added to breakfast cereal or muffin in a cross-over design for ten days each. Prior to testing satiety and energy intake effects of SCF, the subjects fasted for 12 hours. Satiety was measured using VAS and food and beverage intake was recorded by the subjects on days one, two, and ten of each treatment. No significant differences were observed for any of the measure of satiety between the control and SCF diet groups ($P > 0.05$). Furthermore, there was no significant difference in energy and macronutrient intake when the three days were pooled.

Monsivais et al. (2011)

In a double-blind cross-over study, 36 U.S. men and women each consumed a solid snack and a liquid beverage containing 11.8 g SCF and a low-fiber control. The caloric content of the solid snack and liquid beverage combined was the same. Afterwards, lunch was served to measure energy intake. Participants used VAS to rate hunger, fullness, and desire-to-eat at 20 minute intervals up to 220 minutes after ingestion. There was no significant difference in hunger, desire-to-eat, or fullness between the control and SCF intervention groups ($P > 0.05$). Energy intake, however, was significantly lower with consumption of the SCF meal compared to the control ($P < 0.05$).

Calcium Absorption/Retention

We identified three human studies that evaluated the effect of SCF consumption on calcium absorption or retention.

Jakeman et al. (2016)

In a randomized, cross-over study, 12 post-menopausal women were provided 0, 10, and 20 g/day soluble corn fiber for 50 days. The urinary appearance isotopically labeled calcium in pre-labeled bone was measured for assessing the retention of calcium in bone. Biomarkers of bone metabolism (bone-specific alkaline phosphatase, osteocalcin, and n-terminal telopeptide) were measured. A significant positive dose-response relationship was observed with 10 g/day (4.8%; $P = 0.013$) and 20 g/day (7%; $P = 0.007$) SCF and bone calcium retention. The increase in calcium retention was estimated to represent an increase in bone calcium balance by 50 mg/day. While osteocalcin and n-terminal telopeptide (markers of bone turnover) were not significantly different, a significant increase in bone-specific alkaline phosphatase (a marker of bone formation) was observed between the control and 20 g/day SCF groups.

Whisner et al. (2014)

In two three-week metabolic balance cross-over studies, 24 U.S. adolescent boys and girls consumed 0 g/day of SCF (control) or 12 g/day SCF added to fruits snacks. Fractional absorption of calcium was measured using stable-isotopically labeled calcium. Calcium absorption was 12% higher in the SCF treatment group compared to the control group ($P = 0.02$).

Whisner et al. (2016)

Twenty-eight U.S. adolescent girls were provided with maltodextrin (control), 10 g/day and 20 g/day of SCF in a muffin for four weeks each in a double-blind, cross-over design study. Calcium absorption was measured using stable isotopically labeled calcium. The percent increase in fractional absorption of calcium increased significantly for both 10 g ($P = 0.042$) and 20 g SCF groups ($P = 0.026$) compared to the control group.

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Soy Fiber

Soy Fiber (Soy Polysaccharide), Soluble Soybean Polysaccharide and Soy Hull Fiber

Background

Non-digestible carbohydrates are located in the cotyledon and hull (seed coat) of soybeans. The fiber content of the cotyledon and hull are different.

The soy fiber content of the cotyledon mostly contains non-cellulosic fibers, with the predominant fiber being hemicellulose. "Soy fiber" isolated from okara (remains after pureed soybean cotyledon is filtered in the production of soy milk and tofu) is a mixture of soluble and insoluble fiber. Soluble soy fiber (soluble soybean polysaccharide) is a dietary fiber extracted and refined from okara. This isolation generally involves mechanical and aqueous extraction processes. Soy flour, which contains nondigestible carbohydrates, is produced from the cotyledon. "Soy hull fiber" is typically isolated from the hulls through mechanical means (rolling/flaking) and while depending on the procedure, the dried hulls generally contain 50% hemicellulose, 20% cellulose and 30% pectin.

Blood Cholesterol Levels

We identified eleven studies that evaluated the effect of soy fibers on blood cholesterol levels. Scientific conclusions could not be drawn from five of these studies (Hoie et al., 2005; Knopp et al., 1999; Schweizer et al., 1983; Shorey et al., 1985, Tsai et al., 1983) for one or more of the following reasons: (1) it was unclear from which part of the soybean the fiber was isolated, (2) a mixture on non-digestible carbohydrates, including soy fiber, was provided to the study subjects and the effect of soy fiber *per se* therefore could not be evaluated, (3) an appropriate control was not used, (4) the study was not conducted long enough to evaluate the effect of soy fibers on fasting blood cholesterol levels, and/or (5) statistical comparisons were not conducted between the control and soy fiber groups.

<u>Soy Fiber</u>

Dubois et al. (1993)

In a double-blind, randomized, cross-over design study, six healthy men consumed a test meal low in fiber (2.8 g/day) with and without (control) 10 g/day soy fiber extracted from cell wall components of defatted cotyledons. The soy fiber was identified as being insoluble (8.4 g insoluble and 1.6 g soluble). Post-prandial cholesterol levels were measured up to seven hours after consumption of the test meals. The blood cholesterol area under the curve was significantly lower in the soy fiber group compared to the control group ($P < 0.05$).

Hu et al. (2013)

Thirty-nine overweight Chinese men and women were randomly assigned to consume biscuits without (control) and with 24 g of soy (okara) fiber for 12 weeks. No information was provided on the fiber content of this soy fiber. There was a significant decrease in LDL cholesterol in the soy fiber treatment group compared to the control group ($P = 0.014$).

Lo et al. (1986)

Twenty Type II-A and Type IV hyperlipidemic men and women participated in a fixed sequence cross-over study in which they consumed a diet supplemented with a starch placebo or 25 g/day soy fiber for nine weeks each. The "soy fiber" was described as being isolated from soy cotyledon and contained 75% dietary fiber of which only 5% was soluble dietary fiber. The placebo and soy fiber intervention was provided for six weeks each and with the placebo being provided before and after the soy fiber intervention. The soy fiber intervention resulted in a significant decrease in total and LDL cholesterol levels in the Type II-A (n=11) ($P < 0.05$) subjects, but not in the Type IV (n=9) subjects.

Lo and Cole (1990)

Twenty hypercholesterolemic subjects participated in a cross-over design study in which they consumed, for six weeks each, diets with and without 20 g/day of "soy fiber." The soy fiber was isolated from soy cotyledon. There was no significant difference in the nutrient intakes during the two feeding periods. After six weeks of consuming the diets, total cholesterol was significantly lower with soy fiber consumption compared to the control ($P = 0.04$). There was no significant difference, however, in LDL cholesterol levels ($P = 0.62$).

<u>Soy Hull Fiber</u>

Mahalko et al. (1984)

Ten U.S. men and women with type 2 diabetes consumed, in addition to their usual diet, white bread and other foods without (control) or with 26 or 52 g/day of soy hull fiber for up to four weeks. The soy fiber was identified as being 42 to 49% cellulose and 29 to 34% hemicellulose. There was no significant effect of soy hull fiber (26 or 52 g/day) on total for LDL cholesterol levels compared to the control group ($P > 0.05$).

Munoz et al. (1979)

Ten healthy U.S. men consumed a control diet, followed by a diet containing 26 g of soy hull fiber for 30 days each. The soybean hull fiber was 53% cellulose and 33% hemicellulose. There was a significant reduction in plasma total cholesterol levels when soy hull fiber was consumed (1.47 mg/dL) compared to the control (1.63 mg/dL) ($P < 0.05$). There was no significant difference for LDL cholesterol levels ($P > 0.05$).

Blood Glucose Levels

We identified nine studies that evaluated the effect of soy fiber on blood glucose levels. Scientific conclusions could not be drawn from three of these studies (Librenti et al., 1992; Mahalko et al., 1984; Tsai et al., 1987) because they were conducted in individuals with type 2 diabetes.

Soy Soluble Polysaccharide

Au et al. (2013)

Twelve healthy Canadian men participated in a randomized cross-over postprandial study in which they consumed a beverage or pudding without (control) or with 2.5 g soluble soy fiber (soy soluble polysaccharide). The soluble soy fiber is extracted from okara (soy pulp, insoluble carbohydrate residue that is left over after the production of soymilk or tofu). No information was provided on the fiber content, however it was stated that the soluble soy fiber had low viscosity. The plasma glucose area under the curve was significantly lower following intake of the beverage or pudding containing soy soluble polysaccharide compared to the control ($P < 0.01$).

Soy Fiber

Dubois et al. (1993)

In a double-blind, randomized, cross-over design study, six healthy males consumed a test meal low in fiber (2.8.g/day) with and without (control) 10 g/day soybean fiber extracted from cell wall components from defatted cotyledons. The soy fiber was identified as being insoluble (8.4 g insoluble and 1.6 g soluble). Post-prandial glucose levels were measured up to seven hours after consumption of the test meals. The blood glucose area under the curve was not significantly different between the soy fiber and control groups ($P > 0.05$).

Hu et al. (2013)

Thirty-nine overweight Chinese men and women were randomly assigned to consume biscuits without (control) and with 24 g soy (okara) fiber for 12 weeks. No information was provided on the fiber composition. There was no significant difference in fasting blood glucose levels between the control and soy fiber diets ($P = 0.362$)

Lo et al. (1986)

Twenty Type II-A and Type IV hyperlipidemic men and women participated in a fixed sequence cross-over study in which they consumed a diet supplemented with a starch placebo or 25 g/day soy fiber for nine weeks each. The soy fiber was described as being isolated from soy cotyledon and contained 75% dietary fiber of which only 5% was soluble dietary fiber. The placebo and

soy fiber intervention was provided for six weeks each and with the placebo being provided before and after the soy fiber intervention. The soy fiber intervention did not significantly affect fasting plasma glucose levels or post-prandial glucose areas under the curve. Of those eight subjects who had impaired glucose tolerance, soy fiber supplementation significantly reduced their fasting blood glucose levels ($P < 0.03$) and post-prandial glucose area under the curve ($P < 0.03$).

Schweizer et al. (1983)

The study consisted of a control period and two experimental periods for three weeks each with six study subjects. In the experimental periods, the subjects' diet was supplemented with 21 g/day of soy fiber in soy pulp (21% insoluble and 18% soluble fiber) or fiber obtained from extraction of defatted soy flour (50%insoluble and 29% insoluble fiber). Neither source of soy fiber had an effect on peak post-prandial glucose levels when compared to the control ($P > 0.05$). The isolated soy fiber group had significantly higher post-prandial glucose levels at 120 and 180 minutes ($P < 0.05$). The blood glucose area under the curve was not reported.

Tsai et al. (1983)

In a randomized, cross-over design study, 14 U.S. males consumed for 17 days each a low-fiber control diet or the control diet with 25 g soy polysaccharide. In the morning of the ninth day of each feeding period, a glucose tolerance test was conducted in which 100 g glucose with or without 15 g of the soy fiber was consumed. There was no significant difference in peak blood glucose levels at 30 minutes between the two groups ($P > 0.05$). The only significant difference observed was an increase in blood glucose levels at 180 minutes with consumption of the soy fiber.

Laxation/Bowel Function

We identified six studies that evaluated the effect of soy fiber on bowel function. Scientific conclusions could not be drawn from two studies because an inappropriate control was used or soy fiber, along with other nondigestible carbohydrate, was provided to the study subjects so that the effect of soy fiber *per se* therefore could not be evaluated (Sunvold et al., 1995; Zarling et al., 1994).

<u>Soy Hull Fiber</u>

Munoz et al. (1979)

Ten healthy U.S. men consumed a control diet, followed by a diet containing 26 g/day of soy hull fiber for 30 days each. The average number of stools per week increased significantly with the inclusion of soy hull fiber in the diet (3.7 vs. 5.8) ($P < 0.05$).

Soy Fiber

Schweizer et al. (1983)

The study consisted of a control period and two experimental periods for three weeks each with six study subjects. During the experimental periods, the subjects' diet was supplemented with 21 g/day of fiber in never-dried soy pulp (21% insoluble and 18% soluble fiber) or fiber obtained from the extraction of defatted soy flour (50% insoluble and 29% insoluble fiber). While fecal weight was increased after consumption of the two soy fiber diets ($P < 0.05$), there was no significant difference in stool frequency (stools per day) or oro-fecal transit time (hours) between the three groups ($P > 0.05$).

Slavin et al. (1985)

Sixteen healthy U.S. men consumed, as their sole nutrient source, Ensure plus 0 (control), 9.3, 8.2, or 16.4 g/day of soy fiber. Although the processing method and fiber composition of the soy fiber used in the study is not known, it was noted that the soy fiber represented neutral detergent fiber (i.e., cellulose, hemicellulose, lignin, and pectin) and was high in hemicellulose, which suggests it was isolated from the cotyledon. The diets were consumed in random order for ten days each. Oro-fecal transit time was significantly longer on the fiber free diet ($P < 0.05$) compared to the diets containing the various doses of soy fiber.

Tsai et al. (1983)

In a randomized, cross-over design study, 14 U.S. males consumed for 17 days each a low-fiber control diet or the control diet with 25 g soy polysaccharide. Fecal weight was significantly increased with soy fiber consumption ($P < 0.05$). Oro-fecal transit time, however, was not significantly different ($P > 0.05$).

Mineral Absorption

We identified one study that evaluated the effect of soy fiber on mineral absorption. Scientific conclusions could not be drawn from the study because an appropriate control was not used (Sunvold et al., 1995).

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Sugar Beet Fiber

Background

Sugars beets are commercially grown for sugar production. Sugar beet fiber (SBF) is produced from the sugar beet pulp obtained after extracting the sugar from the sugar beets. SBF contains a mixture of dietary fibers (hemicellulose, cellulose, pectin and lignin) (FDA GRAS No. 420). SBF is used in various non-standardized meat and poultry products as a binder and texturizing agent, in bakery products as a binder, in cereals and muesli as a texturizing agent, in sauces as a thickening agent, and in cheese as an anti-caking and/or dispersing agent.

Blood Cholesterol Levels

We identified three studies that evaluated the effect of SBF consumption on blood cholesterol levels. Scientific conclusions could not be drawn from two of these studies because statistical comparisons to the control group were not conducted or because the study was not conducted long enough to evaluate the effect of sugar beet fiber on fasting blood cholesterol levels (Cossack et al., 1991; Lampe et al., 1991).

Karlander et al. (1991)

In a cross-over design study, 13 patients with type 2 diabetes consumed a diet with and without 16 g of sugar beet fiber for six weeks each. Eight of the subjects were also being treated with sulphonylurea. While sugar beet fiber consumption significantly reduced serum total cholesterol levels in patients taking sulphonylurea ($P < 0.05$), there was no significant effect of sugar beet fiber on lowering serum total cholesterol when consumed without sulphonylurea ($P > 0.05$).

Blood Glucose Levels

We identified eight human studies that evaluated the effect of SBF consumption on blood glucose levels. Scientific conclusions could not be drawn from two of these studies because they involved subjects with type 2 diabetes (Hagander et al., 1986; Karlander et al., 1991).

Frape (1995)

Sixteen English men and women were given a supplement containing six g of SBF or cellulose (control) for three weeks. After a 12 hour fast, the study subjects consumed a beverage containing glucose with and without SBF and their post-prandial plasma glucose levels were measured intermittently for up to 256 minutes. There was no significant difference in the area under the curve for blood glucose between the SBF and control groups ($P = 0.066$).

Hagander et al. (1988)

In a randomized, cross-over study and after an overnight fast, test meals with 10.9 g/day SBF and a corresponding control was given to eight Swedish men and women. The area under the

curve for postprandial glucose levels was not significantly different ($P > 0.05$) between the two meals.

Hamberg et al. (1989)

In a randomized, cross-over study, eight Danish men and women fasted overnight, and then ingested a meal consisting of 0 g (control) or 22 g of SBF. In response to these meals, the post-prandial blood glucose levels over 120 minutes (area under the incremental curve) was not significantly different ($P > 0.05$).

Thorsdottir et al. (1998)

In random order, 15 Icelandic men consumed formulas with or without (control) 7 g of SBF. Blood samples were collected from the study subjects up to 155 minutes after ingestions of the formulas. The formula with SBF resulted in a significantly lower rise in post-prandial blood glucose ($P < 0.05$) compared to the control formula.

Tredger et al. (1981)

In a cross-over design study, six men and women were provided a control meal or a meal containing an additional 20 g of sugar beet pulp. The sugar beet pulp contained 22% cellulose, 22% hemicellulose, and 48% pectic substances. Blood glucose levels were measured for up to three hours after the ingestion of each meal. No significant difference was observed in postprandial glucose (or insulin) levels between the two meals.

Ulmius et al. (2009)

After an overnight fast, 13 Swedish men and women consumed a test meal that contained 0 g (control) or 19 g SBF and that contained similar levels of carbohydrate. There was no statistically significant difference ($P > 0.05$) in the postprandial glucose response between the SBF and control meals.

Laxation/Bowel Function

We identified one study that evaluated the effect of SBF consumption on bowel function.

Lampe et al. (1993)

In a randomized, cross-over study, 17 U.S. men consumed a self-selected diet (control) that was also supplemented with 20 g/day SBF. Dietary nutrient intake was similar between the control and SBF diets. After three weeks on the diets, there was no significant difference in the mean oro-fecal transit time (measured in hours) or the frequency of defecation (stools/day) between the two diets ($P > 0.05$).

Energy Intake

We identified one study that evaluated the effect of SBF consumption on energy intake.

Burley et al. (1993)

On two separate occasions, 18 English men and women consumed a control breakfast or the breakfast supplemented with 29 g SBF. Other than the SBF content, the calorie and nutritional content was similar between the two breakfasts. Following consumption of the breakfast, subjects recorded their perceived level of hunger on an hourly basis using a VAS. Later the same day, the subjects consumed a lunch *ad libitum*. Food intake was measured and ratings of motivation to eat were recorded before and after eating the lunch. There was no significant difference between the VAS hunger ratings. A significantly lower (14%) intake of calories during lunch, however, was observed following consumption of the SBF breakfast ($P < 0.01$).

Calcium Absorption

We identified one study that evaluated the effect of SBF consumption on calcium absorption.

Courday et al. (1997)

Nine French men were given a control diet or the same diet that included SBF (40 g/day) in a 28-day cross-over designed study. The intestinal absorption rates of calcium (and magnesium, iron, and zinc) were measured. When compared to the control diet, there was no significant effect of SBF intake on the intestinal absorption of calcium, as well as the other minerals tested ($P > 0.05$).

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Sugar Cane Fiber

Sugar Cane fiber is produced by extraction of the stalks of sugar cane. While the composition may vary with different processing methods, sugar cane fiber is comprised of approximately 40% cellulose, 25% hemicellulose and 25% lignin (Mendes et al., 2013).

Laxation

We identified one study that was published in two different journals that evaluated the effect of sugar cane fiber on laxation.

Walters et al. (1975) and Baird et al. (1977)

In a cross-over study, twenty English women consumed a diet that included low fiber biscuits or biscuits that provided 5.1 g/day of fiber derived from sugar cane for 12 weeks each. The fiber content of the sugar cane fiber was not provided. Fecal weight was significantly higher in the sugar cane fiber consumption group ($P < 0.005$). While stool frequency (stools/day) was also significantly greater with sugar cane fiber consumption ($P < 0.001$), the findings were mixed for oro-fecal transit time. While one method (carmine dye) showed a significant reduction in transit time ($P < 0.01$), another method (radio-opaque) did not.

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Wheat Fiber

Background

Wheat fiber is isolated from wheat and is not the same as wheat bran, which we consider to be intact and intrinsic. Wheat fiber is added to foods and is claimed to provide volume stability, texture enhancement, and water/oil binding properties. Therefore, it is used as a texturizer and to stabilize fine emulsified systems in food processing.

Blood Cholesterol Levels

We identified two studies that evaluated the effect of wheat fiber consumption on blood cholesterol levels. Scientific conclusions could not be drawn from one of these studies because it did not measure fasting blood cholesterol levels over an insufficient amount of time (Vuksan et al., 1999).

Cara et al. (1992)

Six healthy men ingested on separate days either a low fiber meal that contained 10 g of wheat fiber or a meal that did not contain any wheat fiber (control). The treatment wheat fiber was 80% non-digestible carbohydrate, 80% of which was insoluble and 20% of which was soluble. The study subjects fasted overnight, and then consumed the treatment meal. Post-prandial chylomicron and serum cholesterol levels were measured for over the course of seven hours. (A chylomicron is a microscopic particle of fat that is approximately one micron in diameter.) The post-prandial chylomicron cholesterol levels were significantly lower when wheat fiber was consumed ($P < 0.05$). However, there was no significant difference between the wheat fiber consumption group on post-prandial serum cholesterol levels compared to the control group ($P > 0.05$).

Blood Glucose Levels

We identified one study that evaluated the effect of wheat fiber consumption on attenuation of blood glucose levels.

Cara et al. (1992)

Six healthy men ingested on separate days a low-fiber test meal, enriched or not (control) with 10 g of wheat fiber. The wheat fiber was 80% non-digestible carbohydrate, 80% of which was insoluble and 20% of which was soluble. After an overnight fast, the study subjects consumed the test meal and post-prandial glucose levels were measured for six hours. There was no significant effect of wheat fiber on post-prandial glucose (or insulin) levels compared to the control diet ($P > 0.05$).

Laxation

We identified one study that evaluated the effect of wheat fiber consumption on improved laxation.

Vuksan et al. (1999)

In a cross-over design study, 24 healthy men and women consumed a low fiber supplement (control) or a wheat fiber supplement (21 g/day) for two weeks each. The fiber portion of the wheat fiber was approximately 80% insoluble fiber and 20% soluble fiber. There was no significant difference in mean oro-fecal transit time between the two diets (30.7 versus 28.7 hours) ($P > 0.05$).

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Xanthan Gum

Background

Xanthan gum is produced by the fermentation of glucose or sucrose by *Xanthomonas campestris*. The polysaccharide is secreted into a growth medium by the bacterium and then is typically harvested by precipitation with isopropyl alcohol. The precipitate can be dried and milled to a readily soluble powder form. Xanthan gum can produce a large increase in the viscosity of a liquid. Xanthan gum is added to foods as an emulsifier, flavor enhancer, formulation aid, humectant, stabilizer and thickener, synergist, and texturizer (21 CFR 172.695).

Blood Cholesterol Levels

We identified two human studies that evaluated the effect of xanthan gum consumption on blood cholesterol levels. Conclusions could not be drawn from one of these studies (Eastwood et al., 1987) because it was conducted for an inadequate duration of time (7 days) for evaluating the effect on fasting blood cholesterol levels.

Osilesi et al. (1985)

Four healthy subjects and nine subjects with type 2 diabetes participated in a study that consisted of two consecutive six week periods during which they consumed either muffins that contained 12 g/day of xanthan gum or xanthan gum-free muffins (control). There was no significant difference in total cholesterol levels for the healthy subjects between the two study groups ($P > 0.05$). For the study subjects with type 2 diabetes, while total cholesterol was significantly reduced ($P < 0.05$) in the xanthan gum consumption group compared to the control group, there was no significant effect ($P > 0.05$) on LDL cholesterol levels between the two groups.

Blood Glucose Levels

We identified two human studies that evaluated the effect of xanthan gum consumption on blood glucose levels. Conclusions could not be drawn from one of these studies (Eastwood et al., 1987) because a statistical analysis was not conducted between the control and intervention groups.

Osilesi et al. (1985)

Four healthy subjects participated in a study that consisted of two consecutive six week periods in which the participants consumed either muffins that contained 12 g/day of xanthan gum or xanthan gum-free muffins. There was no significant difference in fasting blood glucose (or insulin) levels between the two groups ($P > 0.05$).

Laxation/Bowel Function

We identified three human studies that evaluated the effect of xanthan gum consumption on bowel function. Conclusions could not be drawn from one of these studies (Eastwood et al., 1987) because a statistical analysis was not conducted between the control and intervention groups.

Daly et al. (1993)

Eighteen English men consumed a control diet for ten days followed by a diet that included 15 g of xanthan gum (5 g ingested three times daily with meals) for ten days. Ingestion of xanthan gum did not result in a significant change ($P > 0.05$) in oro-fecal transit time (46.7 hours vs. 40.7 hours). There was, however, a significant increase in stool frequency for the xanthan gum group (11.31 stools per day) compared to the control group (1.14 stools per day) ($P < 0.035$).

Tomlin and Read (1988)

Six men and women consumed a control diet for one week, followed by a diet that included 14 or 15 g/day of xanthan gum for one week. There was no significant difference in stool frequency or oro-fecal transit time in the treatment group compared to the control group ($P > 0.05$).

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Xylooligosaccharides (XOS)

Background

Xylooligosaccharides (XOS) are water soluble, non-digestible oligosaccharides derived from xylans. XOS is a chain of 2-4 xylose molecules with β-1,4 linkages (Wang and Lu, 2013).

Blood Glucose Levels

We identified two human studies that evaluated the effect of XOS consumption on blood glucose levels. Scientific conclusions could not be drawn from these two studies (Campbell et al., 1997; Sheu et al., 2008) either because a mixture of non-digestible carbohydrates, including XOS, was used and the physiological effect of XOS *per se* therefore could not be evaluated or because the study was conducted in individuals with type 2 diabetes.

Blood Cholesterol Levels

We identified three human studies that evaluated the effect of XOS consumption on blood cholesterol levels. Scientific conclusions could not be drawn from one of these studies (Campbell et al., 1997) because a mixture of non-digestible carbohydrates, including XOS, was used and the physiological effect of XOS *per se* therefore could not be evaluated.

Chung et al. (2007)

The diets of 22 elderly Taiwanese men and women were supplemented with either 4 g/day XOS or a placebo control (0 g/day XOS) for 3 weeks. Daily dietary nutrient intake was similar between the two groups. There was no significant difference ($P > 0.05$)in total and LDL cholesterol levels between the two groups.

Sheu et al. (2008)

In a double-blind, placebo-controlled study, the diets of 26 Taiwanese men and women with type 2 diabetes were supplemented with either 4 g/day of XOS or a placebo for eight weeks. Daily caloric and nutrient intakes did not change throughout the study in either group. Total and LDL cholesterol levels were significantly lower after consumption of XOS compared to the placebo ($P < 0.05$).

Laxation

We identified one human study that evaluated the effect of XOS consumption on laxation. Scientific conclusions could not be drawn from the study (Tateyama et al., 2005) because it was conducted in individuals with severe constipation.

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