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## Review Article

### Bread designed for impaired glucose metabolism, recipe composition and protein enrichers for it

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#### Abstract

Glucose metabolism is a significant factor in the health of the human organism. It's influenced by an individual genetic characteristics and lifestyle. When disturbances are created, conditions arise such as: impaired fasting glycaemia, impaired glucose tolerance, insulin resistance, metabolic syndrome, non-insulin-dependent diabetes mellitus, which can lead to other diseases progressing. In support of medical therapy for prevention and control, low-calorie dietary patterns are recommended to maintain the body's energy balance through increased protein content, dietary fiber, rich mineral composition, unsaturated fats, antioxidants and vitamins. To making diet-compatible bread, raw materials should not have a negative impact on the sick organism, taking into account their nutritional profile and possible allergens. The addition of proteins to bread, through protein concentrates with indicators of a beneficial impact on the expressed problem, such as: whey protein, brown rice protein, protein powder from edible insects, implies giving this value to the product as well. As basic and supplementary raw materials suitable according to the findings are: whole rye flour, whole wheat flour, carob flour and Himalayan salt. Bread with such recipe composition would have a low glycaemic index and useful biochemical profile, but appropriate studies are needed to prove the claim.

#### Keywords

glucose, metabolism, impaired, nutrition, protein, bread

#### Abbreviations

EU – European Union; FAO – Food Agriculture Organization of the United Nations; mRNA – messenger ribonucleic acid; TNF- $\alpha$  – tumor necrosis factor alpha; WHO – World Health Organization

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## **Introduction**

Nowadays, impaired glucose metabolism is the subject of intensive research in connection with the progressive increase in the number of patients with associated diseases. Genetic defects and/or specific lifestyle characteristics lead to disturbances in the processes of glucose metabolism. These include: obesity, insulin resistance, metabolic syndrome, impaired glucose tolerance, impaired fasting glycaemia or type 2 diabetes mellitus, and other complications may occur with their progression (Astamirova and Ahmanov 2016; Tankova 2013; Mihneva et al. 2021). Their regulation is carried out on the basis of benchmarks for proper lifestyle and nutrition (Davies et al. 2022; Bodhini et al. 2023; Thirunavukkarasu et al. 2024).

Diets for impaired carbohydrate metabolism are based on foods with a low glycemic index, increased protein content, beneficial fats, antioxidants and are distinguished by low calorie intake. Their reduced total energy value allows to increase protein consumption without overloading the body (Grundy et al. 2005; Pfeiffer et al. 2020; Dimova et al. 2023; Thirunavukkarasu et al. 2024). Studies on proteins such a plant brown rice protein, whey milk protein, the alternative new food – insect protein etc. indicate that they have a positive effect on metabolic processes in the human body. Their amino acid composition and biological activity facilitate the creation of beneficial conjugates with other substances and determine a number of positive effects on the human organism (Jakubowicz and Froy 2013; Matheswaran et al. 2020; Brotman et al. 2021; Prieto-Vázquez del Mercado et al. 2022).

In the current food models for people with problems in carbohydrate metabolism, bread is strongly isolated. However, the evolution of nutritional science allows its development towards a functional direction. With appropriate recipes and technologies, bread can be introduced as a beneficial part of the diets of individuals with problems in glucose metabolism. Existing such products already rely on a low glycaemic index and a high fibre concentration. However, the application of beneficial dietary proteins, which as mentioned have a markedly positive effect on glucose metabolism, has been limited in previous formulations. There is a high need for research on this topic, and the follow-up of their impact as raw materials for bread for special medical purposes

would lay the basis for further extended research in food technology, medicine and dietetics.

## **Impaired Glucose Metabolism - Symptoms and Basis of Nutritional Pattern**

Metabolism in the human organism is carried out through a series of interrelated, constituting cycles of synthesis and conversion into other vital benefits. Its regulation is carried out by various bodies. At the cellular level, glucose is processed by the pathway of glycolysis, which is converted into energy powering our smallest building blocks (Piszczyski and Ivanova 2010; Tankova 2013; Holeček 2023). Disturbances in these mechanisms can occur with independent (genetic) or dependent factors of the individual's lifestyle and environment. The resulting conditions include: metabolic syndrome, insulin resistance, impaired fasting glycaemia and glucose tolerance, or type 2 diabetes mellitus accompanied by hyperglycaemia. Their progression in case of untimely detection or as a consequence of non-treatment can lead to other risks and diseases: obesity, dyslipidemia, cardiovascular diseases, neurological, eye diseases, etc. To the disorders, the levels of plasma glucose in the blood and the levels of insulin secretion are monitored, indicating the sensitivity of tissue cells to the hormone of the same name, the presence of oxidative stress (World Health Organization 2006; Astamirova and Akhmanov 2016; Tankova 2013; Mihneva et al. 2021; Succurro et al. 2020; Cosentino et al. 2020). Insulin is a protein structure that binds to blood sugar, which transports and regulates the entry of glucose into the cell. With low sensitivity of tissue cells to the hormone, they do not accept glucose, which induces its accumulation in the blood. Individuals who most often develop this problem are over 40 years old and race and gender have no determining importance, but prevalence of diabetes in aged 18-99 years predicted to rise to 2045. This makes impaired glucose metabolism a global social problem (DECODE Study Group 2003; Wild et al. 2004; World Health Organization 2006; Lin et al. 2020).

In the practice of controlling glucose metabolism disorders, in addition to the selected medical therapy different dietary patterns are prescribed, individually selected according to the needs of the organism. The basis on which they are all laid is the consumption of foods with a low glycemic index, increased protein content, high concentration of

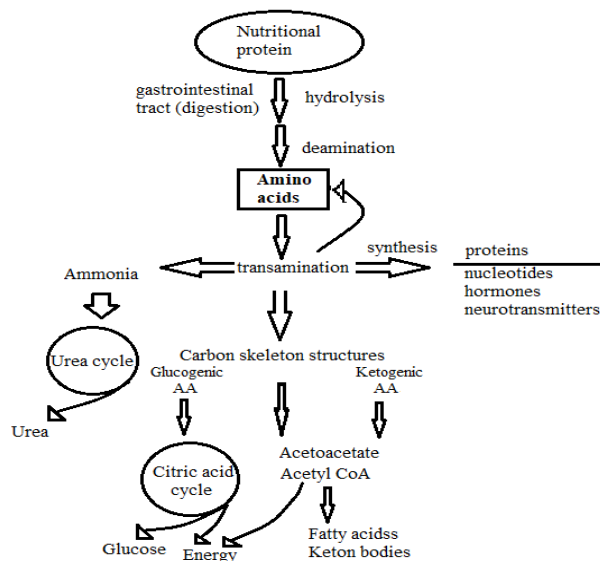
fiber, vitamins, useful minerals, unsaturated fatty acids, antioxidants. These diets aim to act nutraceutical on the pathogenesis of disorders, inducing immunostimulatory, antioxidant and replenishing regenerative processes in the body. (Soliman 2019; Prieto-Vázquez del Mercado et al. 2022). Especially the consumption of rapidly assimilable carbohydrates is avoided, which enter the bloodstream at a high rate and consequently can't be assimilated, remaining there with a tendency to accumulate. Low-calorie diets with increased protein intake are one possible option for a good dietary pattern because of the usefulness of protein and the reduced total glycemic load (Grundy et al. 2005; Pfeiffer et al. 2020; Lin et al. 2020; Davies et al. 2022).

### Protein Metabolism in the Human Organism

Protein-dependent processes in the human organism are strongly influenced by nutrition, hormonal activity and inflammatory processes. Protein substances do not have the ability to form large reserves in the body, therefore it is necessary to provide them through the daily intake of complete ones. During digestion, they undergo degradation, releasing their constituent amino acids, including their available essential ones. This promotes the stimulation, regeneration and synthesis of many vital structures of a protein nature (mRNA, hormones, enzymes, etc.). The hydrolysis processes of protein residues in the gastrointestinal tract produce peptides with antioxidant potential (Liu and Barrett 2002; Piszczyski and Ivanova 2010; Food Agriculture Organization of the United Nations 2011).

Due to the connectedness of life cycles in the human body, under certain conditions the nature of proteins allows them to be transformed into carbohydrates, but this is a limited function. This takes place after the deamination of amino acids, from where ketoacids are finally produced. Through pyruvate they are incorporated into the processes of gluconeogenesis, with the end product being glucose. In individuals with disturbances in carbohydrate metabolism, this sequence is involved in the balance of hepatic and other related functions. An important point in protein metabolism is the accumulation of fatty acids and their metabolites in the body (obesity), as well as their release in a state of starvation (from adipose tissue). They express a

protein-sparing effect, but there is a predisposition to defective insulin signaling receptors, leading to reduced activation of glucose transport, hence insulin resistance (Kalhan 2009; Piszczyski and Ivanova 2010; Tankova 2013).



**Figure 1.** Conditional scheme of protein metabolism in the human organism (Compiled by Emery 2015 and Lal et al. 2022)

Increased protein consumption is associated with a number of positive health outcomes, specifically in individuals with low physical activity and advanced age, maintaining body protein mass within normal norms, but individual determine factors for proper metabolic adaptation are tracked. In conditions necessitating low-calorie diets, this approach compensates for energy imbalances through their thermogenic contribution and highly satiating effect (World Health Organization 2000).

The completeness of the nutritive protein is determinant of the benefits on the human body. It is in turn determined by the composition of its constituent amino acids, as well as the degree of absorption by the organism. The safe quantitative intake established in the Report of a joint FAO/WHO/UNU expert consultation published by World Health Organization (2007) is in units of grams per kilogram of body weight (g.kg<sup>-1</sup>). In their recent reports they have adopted the value of 0.79 g.kg<sup>-1</sup> per day, but age, physical activity and individual body physiology are important

(Scrimshaw 1996; World Health Organization 2007; Moughan 2021).

### **Influence of Nutritional Proteins on Impaired Glucose Metabolism**

Nutritional proteins from different origins have been the subject of studies for possible beneficial effects. A representative of those of animal origin, with an established improving effect on glucose homeostasis in an organism with impaired carbohydrate metabolism is whey protein. It is a milk protein in amounts of only 20% of the total protein content of milk, but is considered to be rapidly digestible by the human organism, with an excellent amino acid profile. The essential amino acids in its content are predominantly leucine, isoleucine, valine, lysine and threonine. Whey protein has the highest presence of leucine compared to other protein sources. This essential amino acid has been identified as a feedback activator in enzymatic reactions of nitrogen balance and as a substrate in phosphorylation processes. It enhances also the postprandial response of the gastric inhibitory peptide coupled to the  $\beta$ -cell insulin production receptor (Yang et al. 2010; Jakubowicz and Froy 2013).

During digestion, whey protein releases amino acids and generates bioactive peptides - endogenous inhibitors, stimulators of incretin secretion (increased insulin secretion, after feeding), increased energy release. The collective action of the products of these processes lead to satiety and decreased food intake. While results have been reported on the effect of whey protein on insulin response, there are no specific reasons for its beneficial effect on glucose homeostasis. Therefore, it continues to be a subject of research (Salehi et al. 2012; Jakubowicz et. Froy 2013; Comerford and Pasin 2016). For using in research, it is important to emphasize the type of whey protein. Whey protein concentrate, isolate and hydrolysate are commercially available. The hydrolyzate is derived from hydrolysis by proteolytic enzymes and is thought to be more rapidly digestible relative to the other representatives, but considering the nature of these proteins, their nutritional value is generally similar. On the other hand, isolates have the highest protein content of about 90%, while concentrates have up to 80%, the remaining content is filled by residual sugars, lipids and mineral components. In

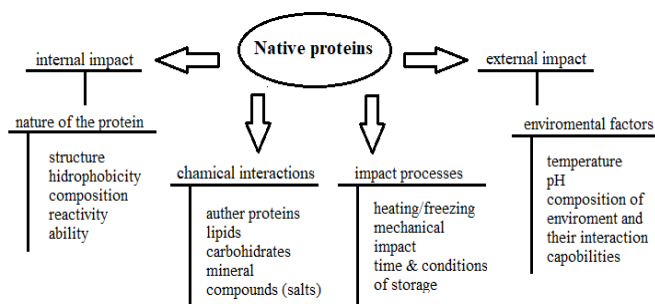
the absence of evidence of significant differences of strength between different forms of whey protein, usage can be judged by other indicators. The concentrates and isolates are superior in taste, but the former are more affordable in price, which is of financial relevance when using larger quantities (Claessence 2009; Hulmi et al. 2010; Mignone 2015).

One of the plant proteins with high bioactive properties is that of brown rice. The amino acids found in it, according to a study by Kalman (2014), are 78%, with 36% essential and 18% with branched chain. He also found that heat treatment over brown rice did not disturb its amino acid profile, from which it can be argued that its protein concentrates are suitable for incorporation into formulation to enrich products subject to heat treatment. Kalman (2014) even compared the amino acid composition of a brown rice protein concentrate with that of soy and whey protein. His results showed a high completeness of essential amino acids, comparable to soy and yet lower than whey. Similar data were also derived by Amagliani et al. (2017) with the difference that their study considered amino acids in rice bran and pure rice products separately, but it is indicative enough that the results showed that the amino acid profile was in higher concentrations in rice bran products. They explained the effect by the albumin fraction being higher in bran, and it having the highest proportion of lysine among rice proteins. According to Brotman et al. (2021), the raw material has high antioxidant activity, antidiabetic and anticancer potential, and bioactive structures in it have regulatory functions on amylase activity. They also detected the presence of unclassified protein substances in the pericarp of the grain. In the review we didn't find specific data about the effect of brown rice protein on glucose metabolism, but that it's suggested biological richness and lack of allergens make it an excellent supplier of metabolites for the human organism. Further research in this direction would provide data for discussion and greater clarity (Kalman 2014; Amagliani et al. 2017; Brotman et al. 2021).

A potential high quality protein supplement in the human nutrition and introduced by the European Union (EU) legislation as a "novel food" is an insect protein. Researchers such as Verheyn et al. (2021) inform that the product has antidiabetic and weight-reducing effects. Through hydrolysis processes,

they discovered bioactive peptides impacting the inactivation of hormones from the gastrointestinal tract. Inhibitors of  $\alpha$ -lipase and  $\alpha$ -glucosidase have also been found to reduce lipid absorption and reduce postprandial hyperglycemia (Verheyn et al. 2021; Matheswaran et al. 2020). However, the characteristics of insect proteins are directly correlated with the insect kind and its way of life. This implies the initiation of more research on glucose metabolism disorders involving the products, accepted by Commission Implementing Regulation (EU) 2017/2470 under different variations. There are other studies of nutritional proteins considered to be wholesome, but as with the above, the information is on their individual impacts on glucose metabolism disorders, not as components of a complex product, which is the purpose of this article.

Protein individual specificities in their spatial structure determine their physicochemical properties, including their solubility and potential for restructuring under certain catalytic conditions: pH, enzymatic action, temperature, etc. The protein molecules' reactivity in result from amino acid building radicals allows them to interact with other molecules (lipid, carbohydrate, salts, enzymes, etc.), producing new bioactive complex structures (lipoproteins, glycoproteins, etc.). (Fig. 2) In the human body, derivatives enter into protective and catalytic functions, and in food they participate in determining its digestibility.



**Figure 2.** Factors determining the functional properties of proteins (Compiled by De Wit 1998 and Piszczyski 2010)

Their overall nature also qualifies them as a technological factor determining the texture of many food products such as cheese, bread, etc.

## Bread Suitable for Persons with Impaired Glucose Metabolism

**Appropriate raw materials and enrichers.** The basic raw materials used to obtain bread intended for persons with impaired glucose metabolism include flours with an appropriate glycaemic response. Whole meal rye and wheat flours have such characteristics. Rye and its derived flours (type 1000 or 1750) contain fractions of gluten protein, but they don't form a gluten matrix during dough kneading. Therefore, rye flour doesn't produce bread with the organoleptic characteristics of white wheat bread. It has high moisture, low volume and low elasticity of the crumb. However, the beneficial characteristics of rye flour are significant and unite those of its constituents: phenolic acids, arabinoxylans,  $\beta$ -glucans, fructans, lignans, mineral elements, cellulose, the rich presence of the essential lysine, etc. It is believed that by interacting with the gastrointestinal tract, during digestion, the following help the absorption of the carbohydrates taken, at lower insulin levels. Researchers such as Jonson et al. (2018) refer to this effect as the "rye factor". Hartvigsen et al. (2013) have found that arabinoxylans reduce postprandial glucose peaks and  $\beta$ -glucans induce a lower glycaemic response, which confirms their beneficial effects on glucose metabolism in human organism. The bioactive fullness makes rye flour a proper foundation for dietary bread intended for individuals with impaired glucose metabolism (Jonson et al. 2018; Hartvigsen et al. 2013).

Another flour widely recommended for use is whole wheat flour, known as type 1850. This is owing to the fact that it comes from grinding the whole grain without separating out the side fractions. Apart from the endosperm, the most nutritious part of the wheat, the flour retains the broken seed coat, which contains minerals (Cu, Se, Fe, Zn, Mg), vitamins and dietary fibres. The germinal content, in turn, supplements the fullness with vitamins of group B, vitamin E, unsaturated fatty acids, phosphates, essential amino acids (lysine is 47% more than the total amount in the whole grain). The bioactive components of whole wheat flour stimulate positive processes in digestion and metabolism, and give whole wheat bread lower glycaemic index values (Yu et al. 2013; Gomez et al. 2020).

A raw material with a high benefit in glucose metabolism, referred to a number of studies, which can be incorporated additionally to the composition of basic flours is carob flour. A raw material with a high benefit in glucose metabolism, referred to a number of studies, which can be incorporated additionally to the composition of basic flours is carob flour.

The rich biochemical composition of this flour, which includes the so-called cyclitols, makes it a

natural regulator of the carbohydrate metabolism of the human organism. Cyclitols and inositols are participating in signal and regulator functions of the cell membrane. In organism with impaired glucose metabolism, these structures reverse insulin resistance and regulate cellular processes, inhibit  $\alpha$ -glucosidase in the blood and reduce concentration of plasma glucose. From this group of substances, d-pinitol (1D3-0-methyl-hydro-inositol) has been found in carob (Ghani 2020).

**Table 1.** Nutritional value of commercial selected whole meal rye flour, whole meal wheat flour, carob flour, whey protein concentrate, rice protein concentrate and defatted cricket powder

Nutrients	Whole grain rye flour	Whole grain wheat flour	Carob powder	Whey protein concentrate	Rice protein concentrate	Defatted cricket powder
Energy, kJ/ kcal.100g <sup>-1</sup>	1355/ 324	1443/ 345	1334/ 318	1705.8/ 404	1465.4/ 350	1515/ 362
Proteins, g.100g <sup>-1</sup>	9.6	11.9	4.7	76.0	71.6	75.0
Total carbohydrates, g.100g <sup>-1</sup>	59.4	68.3	54.1	3.0	3.0	4.6
incl. sugar	1.9	2.1	48.2	3.0	0.0	0.0
Fats, g.100g <sup>-1</sup>	1.9	1.7	1.4	7.75	3.0	11.6
incl. unsaturated fats	0.2	0.7	0.2	-	<1.5	7.0
..... dietary fiber	13.9	11	-	3.5	0.0	8.8
Na, g.100g <sup>-1</sup>	<0.01	<0.01	-	-	0.48	0.4

\*The nutrition facts are taken from labels of relevant products

Bates et al. (2000) believe as well as antihyperglycaemic effects, the has an enhancing effect on glucose absorption in muscle tissue, helping the body to use it as energy. Carob also has anticancer, anticholesterol and diuretic potential (Bates et al. 2000; Goulas et al. 2016; Basharat 2023).

For higher potency and better health benefits, supporting the product goals is Himalayan salt. Its mineral composition consisting by Mg, S, Si, K, Mn, Fe etc. and their balance in it's beneficial for human body. It is a raw material used extensively in culinary environments and doesn't adversely affect the taste and scent of the finished products in which it is used. That makes it a suitable alternative to table salt in recipes and here. Concerning the protein component for enrichment of bread, participating in the nutritional pattern for persons with glucose

metabolism disorders, according the review, whey protein concentrate can be considered. It is necessary to take into account its purity, because concentrates may contain residues of milk sugar (lactose) and lipids. As per the researchers Indrani et al. (2007), samples with up to 10% whey protein showed an enhanced plastic and elastic properties and reduced water absorption, but exceeding these are suggesting dilution of gluten and disruption of its structural formation (Indrani et al. 2007).

From the conducted review, we didn't find any published studies on whole rye and whole wheat flour bread enriched with whey protein concentrate, which permits free variation of dosage to specify both technological and health parameters.

Another potential enrichment - protein concentrate could be the vegetal from brown rice. In the works of Joy et al. (2013) and Kalman (2014) concluded

that it can be considered equal to other protein concentrates, such as soy or whey, without loss of essential nutritional value (Joy et al. 2013; Kalman 2014). In bread, it is most generally used as a raw material for a gluten-free one. Reported by Zhao et al. (2022) whose work monitored its impact in technological terms on gluten-free dough was found to improve dough elasticity, with imported amounts of rice protein up to 5% of the main rice flour (Zhao et al. 2022).

In the bibliographic research on breads designed for persons with disorders of glucose metabolism, we didn't find results, so we can consider the undertaking of a study of this character as an innovation.

Interesting to consider as high protein supplement is the powder of edible insects. Representative samples of studies on their incorporation into bread for persons with problems in glucose metabolism were not found. Authors as Osimani et al. (2018) and González et al. (2019), however, monitored the technological impact of insect protein powder and found some products from different species of insects gave good bread characteristics, with contents incorporated by recipe is up to 15% of the total flour amount. It is also pointed out, that the colour and flavour of the samples are uncharacteristic of traditional bread (Osimani et al. 2018; González et al. 2019).

In process of researching the topic of this article, it has been found that only three species of edible insects are allowed in the EU and acknowledged as suitable food ingredients for special medical purposes. Of their manufactured products, the one with the highest protein richness is that of Cricket One Co. Ltd, Vietnam - partially defatted powder of *Acheta domesticus* (house cricket). The producer has indicated in his license: Commission Implementing Regulation (EU) 2023/5 conditions under which the novel food may be used, in multigrain bread and rolls; crackers and breadsticks at maximum levels (marketed as such or reconstituted according to the instructions) of 2 g.100g<sup>-1</sup>.

The conventional bread is recommendable isolated from the diet of individuals with disorders in the metabolic processes of glucose. The highly refined raw materials incorporated in its recipe give a high postprandial blood glucose response, i.e. it has a

high glycaemic index. Bread with a low glycaemic index should be composed of raw materials with a rich nutritional content of protein, dietary fiber, beneficial fats, minerals, etc. (Table 1). The ingredients listed in this section are a suitable basis for the formulation of enriched protein bread for persons with impaired glucose metabolism.

**Gastroenterological point of view over the considered raw materials.** Regarding the considered raw materials for bread with added proteins, intended for persons with impaired glucose metabolism, an opinion as a specialist in gastroenterology was given by Dr. Bozhidar Hristov, assistant professor at the II Department of Internal Medicine, Section "Gastroenterology", Medical University - Plovdiv, Bulgaria. His opinion is presented as follows:

**For whey protein concentrate** - the effects established so far are: it helps to slow stomach emptying, provoking prolonged satiety of the organism and reduces the postprandial glycaemic response, it positively influences pancreatic activity, it has an insulinotropic effect, stimulating incretin secretion. Since the raw material is a component fraction of milk, it is important for the body's reaction against it that it has no intolerance (Ma et al. 2009; Pal et al. 2014).

**For insect protein powder** - studies up to this point have not identified any significant side reactions. In addition to its high nutritional quality, its beneficial effects on the intestinal microbiota can be pointed out, especially its tendency to reduce the levels of certain proinflammatory cytokines, in specific tumour necrosis factor-alpha (TNF-α) (Cunha et al. 2023). There is certainly a risk of allergic reactions, and should be documented in the informed consent to participate in the in vivo research on human subjects, but this doesn't compromise its inclusion in the study.

**For brown rice protein concentrate** - here the comment is similar. It should only be pointed out that the manufacturer's prospectus may have described that it is prepared in a production facility that also processes eggs, wheat flour and milk. It would be prudent to consider the risk of allergies associated with these potential contaminants, and that it is not suitable for patients with gluten enteropathy. For patients with non-celiac gluten

intolerance, the quantity of impurities should not be sufficient to cause clinical sequelae (Wu et al. 2023).

Mention should be made that certain doses for the benefit of improving glucose metabolic processes are not fixed in terms of protein intake, but it's important to take these with especially caution in individuals with chronic kidney disease.

**For carob flour** - the selection of this product is excellent. It is good to point out that carob by itself reduces glucose absorption, which would have a strong positive effect (Papaefstathiou et al. 2018).

**Whole meal rye flour and whole meal wheat flour** - there is nothing to say about their use, they are wide-spread and their effects on health are well-known. They are rich in polyphenols, vitamins, minerals and dietary fiber which are a good source of accessible carbohydrates for intestinal microbiota (Singh et al. 2017).

**For Himalayan salt** - on consumption of the completed product it will be in a miniscule quantity to give a significant impact in the gastrointestinal tract, but it may be mention that its mineral composition is beneficial to the human body.

## Conclusions

From a review of data on impaired glucose metabolism and bread with added protein for individuals with its associated conditions, it was found that suitable raw materials could be: whole meal rye flour, whole meal wheat flour, carob flour, Himalayan salt, whey protein concentrate/brown rice protein concentrate/skimmed house pike nut powder. They have the required parameters but their beneficial effectiveness needs to be followed up in a study. We could find no available data on bread with similar formulation and intended use. Concerning the benefits and harms for the gastrointestinal tract, in conclusion, the specialist confirmed that the ingredients under consideration are suitable and safe in terms of gastrointestinal functions. The only considerations related to the renal load when using increased amounts of protein, as well as the presence of allergens and gluten when using commercial protein concentrates. Accordingly, this should be reflected where necessary.

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