The effect of prebiotics on intestinal digestion of carbohydrates in lead intoxicated rats

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THE EFFECT OF PREBIOTICS ON INTESTINAL DIGESTION OF CARBOHYDRATES IN LEAD INTOXICATED RATS

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Abstract

It has been shown the lead intoxication of growing rats result in increase the cavity and membrane carbohydrate hydrolysis and glucose absorption from small intestine which leads to hyperglycemia. The oral treatment of intoxicated rats with inulin or lactulose results in decrease of carbohydrate assimilation in small intestine and content glucose level in blood. The correcting effect of lactulose on normalization of carbohydrate assimilation is more expressed in compare with inulin. So, inulin and/or lactulose take part in improving of adaptation of the carbohydrate assimilation system in the small intestine during intoxication with lead ions in growing rats. This suggests the prospect of their use as physiologically acceptable additives to stabilize carbohydrate digestion and blood glucose levels in lead and, possibly, other heavy metal intoxication in the growing organism.

Keywords: growing rats, lead intoxication, small intestine, carbohydrates activity, glucose absorption, inulin, lactulose.

1 Introduction

The gastrointestinal tract contains various microorganisms that play an important role in maintaining human and animal health. Many bacteria of the gastrointestinal tract have beneficial for health functions including production of vitamins, absorption of ions (Ca, Mg, and Fe), protection against pathogens, histological development, enhancement of the immune system, and the fermentation of "non-digestible foods" [13, 21]. Development and growth of beneficial intestinal microorganisms largely depends on the undigested food components or prebiotics. Although prebiotics have been in the human diet for many years, the healing properties of inulin, fructooligosaccharides, galactooligosaccharides have been discovered relatively recently [27]. Prebiotics affect the intestine health as well as the whole body health by stimulating the growth of obligate symbiotic microflora [21, 40, 45, 54]. Prebiotics, contributing to the propagation of beneficial microflora, selectively ferment ingredients that cause specific changes in the gastrointestinal environment [40, 45, 57, 58]. For example, increasing the number of binding toxins and heavy metals to their cell wall strains, they can reduce the intestinal absorption of toxin and excrete them from the body with feces [67].
Among the toxic substances entering the gastrointestinal tract, lead compounds are of concern to specialists. In fact, being a widely distributed lead compounds cause effects on the blood, as well as the nervous, immune, bone, renal, cardiovascular, reproductive systems [4, 9, 38, 60]. Intake and uptake of lead in the general population take place mainly via the gastro-intestinal tract. For ingested lead, the rate of absorption by the body is almost 20–70\%\). Lead absorption and its negative effect in children is higher than in adult [16, 32]. Biological factors operating in the gastrointestinal tract are the main determinants of lead bioavailability [32, 37].

Despite the fact that lead compounds, as well as prebiotics, with water and food enter the cavity of the gastrointestinal tract the effect of prebiotics on digestion and absorption at lead intoxication in the small intestine in growing organism is not studied.

The aim of the current work is to study the effect of inulin and lactulose on the carbohydrate assimilation in the small intestine in growing rats with lead intoxication.

2 Materials and methods

Animals. White outbred growing rats were used in the experiment. To obtain offspring, females (body weight 200-220 g) were selected. They were kept in a well-ventilated bright room in plastic cages measuring 50x30x28 cm\(^3\), 4 individuals each. Then, one male (the same body weight) was put into the cage with females for 2 days. With the appearance of obvious signs of pregnancy, rats were put into private cages measuring 35x28x28 cm\(^3\) and the date of birth was recorded. Newborns were mixed and eight of them were left in each litter. The growing rats were with a lactating female until the end of experiment. Rats were kept under natural light and humidity, at room temperature and unlimited access to water and food.

The rat ration included dark wheat bread, millet, red carrots, oats, unrefined sunflower oil, brewer’s yeast, salt, cooked and chopped meat waste.

The experiment was carried out in strict compliance with international bioethics rules, in accordance with the Helsinki Declaration of the World Medical Association 2010 [63].

Animals were divided into one control (control) and three experimental groups. In the first experimental group (experiment 1), rats were treated orally with lead acetate solition (5 mg/kg/day) (Areolab, Russia) from the 7th to the 21st days of postnatal life. Then saline was given them orally in equal volume for a week. In the second (experiment 2) and third (experiment 3) experimental groups rats were also treated orally with lead acetate in the same dose and at the same time. Then inulin (200 mg/kg/day (Pharm Product, Russia)) and lactulose (100 mg/kg/day, Pharmtechnology, Russia)) were administrated to the second and third experimental group rats respectively for 7 days. Animals were killed at the age of 7, 14, 21 and 28 days by decapitation in the morning between 9.00-10.00.

Obtaining biologically active preparations. After decapitation the blood was immediately collected in centrifuge tubes and the samples were defended in the cold.
for 30 minutes. Samples were centrifuged at 3000 rpm for 15 minutes. In the obtained serum, glucose was determined by glucose oxidase method using a kit (Human, Germany).

Then, the rat abdominal cavity was quickly opened. The pancreas was separated from neighboring tissues, weighed and placed in a test tube. Cold Ringer’s solution (pH 7.4) was added in the tube (0.9 ml per 0.1 g of pancreas tissue) and the pancreas was homogenized in an automatic glass homogenizer with a Teflon pestle at 300 rpm for a minute.

The removed from the abdominal cavity small intestine was carefully disecparated from the mesentery, washed with cold Ringer’s solution (pH 7.4), weighed and homogenized in the same way.

The obtained intestinal flush was collected in test tubes on ice, sedimented and its volume was adjusted to a ratio of 9:1 with Ringer’s solution in relation to the small intestine weight.

Then, the activity of α-amylase (α-1,4-glucan-glucanohydrolase) of pancreatic tissue and intestinal contents was determined in the obtained pancreatic homogenate and intestinal flushing [Ugolev, 1969].

The activity of sucrase (sucrose-a-glucohydrolase; EC 3.2.1.48), maltase (a-D-glucoside glucosehydrolase EC 3.2.1.20), and lactase (3-D-galactoside galactohydrolase; EC 3.2.1.23) were determined by glucose oxidase Dahlqvist method [6] in the small intestine homogenate.

Absorption of glucose from maltose and glucose solutions was studied in rats underwent with intra peritoneal nembutal (3.5 mg / 100 g body weight) anesthesia. The rat abdominal cavity was opened in the midline. Then the small intestine segment was removed, and the first polyethylene cannula was inserted near the Treitz ligament. Departing from the first canal by 10 cm, the second one also was inserted. Both canulas were fixed by ligature. The intestine segment was lowered into the abdominal cavity and the edges of the skin wound were sutured. The obtained intestine segment was washed with 10 ml of warm Ringer’s solution (pH 7.4) and perfused with 2% maltose or glucose solutions preheated to 37°C. The perfusate was collected in ice-cooled tubes every 5 minutes for 15 minutes and used for biochemical analysis. The perfusion rate was 0.3 ml/min, the fluid volume in the system was relatively constant and did not exceed 0.4 ml.

The determination of glucose transport systems activity was calculated by the difference in the entering and leaving isolated intestine segment substrate concentration and expressed in µmol/min/g of raw tissue. The absorption rate of free glucose was determined by the glucose oxidase method [6], while we investigated the rate of glucose transport resulting from maltose digestion using the anthrone method [47].

The protein in the homogenates of the pancreas, whole small intestine and perfused segment of the intestine was determined by the method of Lowry et al 1951) [31].

The t and P values were calculated and all values were expressed as mean±standard error. If the P-value was less than 0.05, the difference between values of control and experimental animal groups was considered statistically significant.
3 Results and its discussion

Body, pancreas and small intestine weight. The change of the body weight and digestive organ weight in control and experimental groups is given in Table 1. It can be seen that body weight in the control rats increased sharply as they grew and developed. However, in rats treated orally with lead acetate (experiment 1), body weight was significantly less than the control value throughout the experiment. If intoxicated rats were treated with inulin, their body weight also reduced compared with the control rats during all observation (experiment 2). However, if intoxicated with lead acetate rats were given lactulose (experiment 3), their body weight restored by 21st day of experiments.

The pancreas weight was increased from the 7th to the 21st day of life both in the control and all experimental groups. However, the increase in pancreatic weight in animals treated orally with lead acetate was significantly higher throughout the experiment. If lead intoxicated rats were given inulin an increase in pancreas weight was observed on the 14th and 21st days of observation. If intoxicated and treated with lactulose rats an increase in pancreas weight was observed only in 14-day-old rats.

Table 1. Effect of inulin and lactulose on the body, pancreas, and small intestine weight in growing rats at lead intoxication (M ± m; n = 6 – 7)

<table>
<thead>
<tr>
<th>Animal groups</th>
<th>Age (days)</th>
<th>Body (g)</th>
<th>Pancreas (mg)</th>
<th>Small intestine (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>7</td>
<td>14</td>
<td>21</td>
<td>28</td>
</tr>
<tr>
<td>Control</td>
<td>13,0±0,2</td>
<td>27,1±0,6</td>
<td>33,0±0,3</td>
<td>42,5±2,2</td>
</tr>
<tr>
<td>Experiment 1 P</td>
<td>-</td>
<td>19,4±0,9</td>
<td>&lt;0,001</td>
<td>31,4±1,4</td>
</tr>
<tr>
<td>Experiment 2 P</td>
<td>-</td>
<td>21,4±1,3</td>
<td>&lt;0,02</td>
<td>35,1±2,1</td>
</tr>
<tr>
<td>Experiment 3 P</td>
<td>-</td>
<td>24,3±1,4</td>
<td>&gt;0,10</td>
<td>37,4±2,4</td>
</tr>
<tr>
<td>Control</td>
<td>32,0±0,1</td>
<td>47,2±4,3</td>
<td>102,4±8,1</td>
<td>132,2±9,4</td>
</tr>
<tr>
<td>Experiment 1 P</td>
<td>-</td>
<td>59,1±0,4</td>
<td>&lt;0,02</td>
<td>161,4±8,1</td>
</tr>
<tr>
<td>Experiment 2 P</td>
<td>-</td>
<td>58,4±0,6</td>
<td>&lt;0,05</td>
<td>157,3±12,1</td>
</tr>
<tr>
<td>Experiment 3 P</td>
<td>-</td>
<td>56,6±1,3</td>
<td>&gt;0,05</td>
<td>149,1±11,4</td>
</tr>
<tr>
<td>Control</td>
<td>901,2±58,6</td>
<td>1018,3±23,1</td>
<td>1291,3±91,3</td>
<td></td>
</tr>
<tr>
<td>Experiment 1 P</td>
<td>-</td>
<td>910,4±62,4</td>
<td>&gt;0,25</td>
<td>1002,1±76,3</td>
</tr>
<tr>
<td>Experiment 2 P</td>
<td>-</td>
<td>751,3±44,1</td>
<td>&lt;0,001</td>
<td>1034,4±68,4</td>
</tr>
<tr>
<td>Experiment 3 P</td>
<td>-</td>
<td>801,2±42,3</td>
<td>&gt;0,25</td>
<td>1319,3±89,4</td>
</tr>
</tbody>
</table>

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The small intestine weight in control rats was increased sharply as they grew. In rats orally treated with lead acetate, the small intestine weight significantly decreased compared to control only on 14th day observation. In the experimental groups where intoxicated growing rats were given either inulin or lactulose the small intestine weight did not differ from the control values throughout the observation.

**Protein content.** The data on the protein content in the pancreas and small intestine tissue are given in Table 2. The pancreas protein content in growing rats was slowly increased in all studied groups. However, the increase in pancreas protein content in rats received solution of lead acetate was significantly higher in comparison with control group rats until the end of the observing period.

Table 2. Effect of inulin and lactulose on the protein content (mg/g wet tissue) in the pancreas and small intestine in growing rats at lead intoxication

\[(M \pm m; n = 6 - 7)\]

<table>
<thead>
<tr>
<th>Animal groups</th>
<th>Age (days)</th>
<th>Pancreas</th>
<th>Small intestine</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>7</td>
<td>14</td>
<td>21</td>
</tr>
<tr>
<td>Control</td>
<td>65,7±1,3</td>
<td>81,2±1,2</td>
<td>85,0±1,5</td>
</tr>
<tr>
<td>Experiment 1 P</td>
<td>88,2±2,4</td>
<td>&lt;0,05</td>
<td>91,2±2,3</td>
</tr>
<tr>
<td>Experiment 2 P</td>
<td>89,6±2,7</td>
<td>&lt;0,05</td>
<td>89,6±3,7</td>
</tr>
<tr>
<td>Experiment 3 P</td>
<td>87,6±2,7</td>
<td>&lt;0,05</td>
<td>86,5±3,4</td>
</tr>
</tbody>
</table>

Administration of both prebiotics to the intoxicated with lead acetate rats resulted in decrease protein content in the pancreas. On the 14th day of postnatal life the pancreas protein content was higher than in control in all experimental groups. After administration to intoxicated rats inulin and/or lactulose in 21 and 28 day old day rats protein content were documented on control level.

Noticeable quantitative differences in the small intestine protein content were not noted in control and three experimental groups throughout the observation.

**α-Amylase activity.** Pancreatic α-amylase is the main enzyme involved in the breakdown of food polysaccharides to oligomers in the small intestine cavity. The results of α-amylase activity change in the pancreatic tissue and small intestine chyme in the control and experimental growing rats are shown in Table 3.
Table 3. Effect of inulin and lactulose on the $\alpha$-amylase activity in the pancreas tissue and small intestine chyme in growing rats at lead intoxication ($M \pm m; n = 6 - 7$)

<table>
<thead>
<tr>
<th>Animal groups</th>
<th>Age (days)</th>
<th>Pancreatic tissue g/min/g protein</th>
<th>Pancreatic tissue g/min/g protein</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>7</td>
<td>14</td>
<td>21</td>
</tr>
<tr>
<td>Control</td>
<td>0.8±0.1</td>
<td>24.6±1.2</td>
<td>82.5±5.6</td>
</tr>
<tr>
<td>Experiment 1</td>
<td>-</td>
<td>32.2±2.2</td>
<td>&lt;0.02</td>
</tr>
<tr>
<td>Experiment 2</td>
<td>-</td>
<td>31.4±2.1</td>
<td>&lt;0.02</td>
</tr>
<tr>
<td>Experiment 3</td>
<td>-</td>
<td>30.1±2.1</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Chyme (mg/min/ml)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>2.5±0.1</td>
<td>21.4±1.3</td>
<td>80.5±6.3</td>
</tr>
<tr>
<td>Experiment 1</td>
<td>-</td>
<td>15.1±0.2</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Experiment 2</td>
<td>-</td>
<td>15.4±1.4</td>
<td>&lt;0.02</td>
</tr>
<tr>
<td>Experiment 3</td>
<td>-</td>
<td>22.1±2.1</td>
<td>&gt;0.5</td>
</tr>
</tbody>
</table>

The activity of $\alpha$-amylase in pancreatic tissue of control group was low in suckers (7-day-old rats) and increased during transition from milk to definitive nutrition (28-day-old rats). In rats orally treated with lead acetate the development of the pancreatic $\alpha$-amylase activity was the same as in controls, but the level of enzymatic activity was significantly increased. An increase in $\alpha$-amylase activity compared to the control data was noted on the 14th and 21st days of life. There were no statistically significant differences in $\alpha$-amylase activity of pancreatic tissue of the control and treated with lead acetate groups in 28-day-old rats.

After treatment of intoxicated rats with inulin, an increase of the pancreatic $\alpha$-amylase activity was noted on the 14th and 21st days of the observation. Oral administration of lactulose to intoxicated with lead acetate sucker rats resulted in an increase in enzyme activity compared with the control rats only on the 14th day of the experiment.

In the small intestine chyme of control group the $\alpha$-amylase activity was increased in developing rats. However, in lead acetate intoxicated rats, the age-dependent increase in the activity of $\alpha$-amylase in intestinal contents was significantly decreased. A decrease of the enzyme activity in the small intestine cavity as compared with the control data was observed in 14-day and 21-day-old rats. Administration of inulin or lactulose to treated with lead acetate rats resulted in normalizing of the enzyme activity in intestine cavity.

**Intestinal disaccharidases.** Membrane-bound disaccharidases - maltase, sucrcharase, and lactase - are enzymes that complete the hydrolysis of odigosaccharides...
in the small intestine to monomers. The results of the intestinal carbohydrate activity in control and intoxicated rats treated with prebiotics are shown in Table 4.

Table 4. Effect of inulin and lactulose on the intestine disaccharidases activity (µmol/min/g protein) in growing rats at lead intoxication (M ± m; n = 6 – 7)

<table>
<thead>
<tr>
<th>Animal groups</th>
<th>Age (days)</th>
<th>7</th>
<th>14</th>
<th>21</th>
<th>28</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maltase</td>
<td></td>
<td>1,2±0,1</td>
<td>47,2±4,3</td>
<td>82,4±7,1</td>
<td>102,4±8,1</td>
</tr>
<tr>
<td>Control</td>
<td></td>
<td>59,1±0,4</td>
<td>89,1±4,2</td>
<td>113,6±4,2</td>
<td>&gt;0,25</td>
</tr>
<tr>
<td>Experiment 1</td>
<td>P</td>
<td>&lt;0,05</td>
<td>&gt;0,5</td>
<td>&gt;0,25</td>
<td>&gt;0,25</td>
</tr>
<tr>
<td>Experiment 2</td>
<td>P</td>
<td>54,0±0,6</td>
<td>87,2±7,4</td>
<td>117,3±7,4</td>
<td>&gt;0,25</td>
</tr>
<tr>
<td>Experiment 3</td>
<td>P</td>
<td>&gt;0,25</td>
<td>&gt;0,5</td>
<td>&gt;0,25</td>
<td>&gt;0,25</td>
</tr>
<tr>
<td>Saccharase</td>
<td></td>
<td>1,3±0,1</td>
<td>17,1±0,6</td>
<td>33,3±0,3</td>
<td>53,0±0,8</td>
</tr>
<tr>
<td>Control</td>
<td></td>
<td>24,4±0,9</td>
<td>41,1±0,8</td>
<td>52,1±2,1</td>
<td>&gt;0,5</td>
</tr>
<tr>
<td>Experiment 1</td>
<td>P</td>
<td>&lt;0,001</td>
<td>&lt;0,001</td>
<td>&gt;0,5</td>
<td>&gt;0,5</td>
</tr>
<tr>
<td>Experiment 2</td>
<td>P</td>
<td>20,4±1,3</td>
<td>44,3±1,1</td>
<td>54,3±2,2</td>
<td>&gt;0,5</td>
</tr>
<tr>
<td>Experiment 3</td>
<td>P</td>
<td>&gt;0,05</td>
<td>&gt;0,001</td>
<td>&gt;0,5</td>
<td>&gt;0,5</td>
</tr>
<tr>
<td>Lactase</td>
<td></td>
<td>59,1±3,4</td>
<td>61,2±1,6</td>
<td>28,3±2,1</td>
<td>15,3±0,7</td>
</tr>
<tr>
<td>Control</td>
<td></td>
<td>72,3±3,2</td>
<td>38,4±2,4</td>
<td>21,1±2,1</td>
<td>&lt;0,05</td>
</tr>
<tr>
<td>Experiment 1</td>
<td>P</td>
<td>&lt;0,02</td>
<td>&lt;0,02</td>
<td>&gt;0,05</td>
<td>&gt;0,05</td>
</tr>
<tr>
<td>Experiment 2</td>
<td>P</td>
<td>74,3±2,1</td>
<td>33,1±1,2</td>
<td>21,3±2,2</td>
<td>&lt;0,05</td>
</tr>
<tr>
<td>Experiment 3</td>
<td>P</td>
<td>&lt;0,002</td>
<td>&gt;0,10</td>
<td>&gt;0,5</td>
<td>&gt;0,5</td>
</tr>
</tbody>
</table>

The activity of maltase was increased markedly in control growing rats. In rats orally treated with lead acetate, the age-dependent increase in maltase activity was significantly higher in 14-day-old rats compared with control. Administration of inulin and/or lactulose to treated with lead acetate rats smoothed the inducing effect of lead acetate on the activity of membrane-bound maltase. Succharase activity in the control group was almost absent until two weeks of age and sharply increased by the time of weaning, remained at a higher level in older age. In intoxicated with lead acetate rats, the succharase activity was increased markedly compared with the control at 14 and 21 days of age. In orally treated with lead acetate 28-day-old rats, statistically significant increase in succharase activity was not observed. Succharase activity remained higher in intoxicated and treated with inulin rats in the second and third week of the experiment. Oral administration of lactulose to intoxicated rats resulted in equalization of intestinal succharase activity to the control level throughout the observation period.
Lactase activity, in contrast to maltase and sucrase, was not increased in the control group of animals, but, on the contrary, decreased. However, when growing rats were treated with lead acetate the lactase activity decrease was noticeably delayed. The administration of both prebiotics to intoxicated rats caused the smoothing of lactase activity in intoxicated rats. The intestinal lactase activity was almost equal to the control value in treated with prebiotics intoxicated rats.

**Glucose absorption and blood glucose.** Glucose and other monosaccharides absorption is the last stage of carbohydrates assimilation in the small intestine. The results of glucose absorption rate from maltose and glucose in the control and experimental groups, are presented in Table 5. It can be seen that in control rats the rate of glucose absorption from maltose solution was increased. Intoxication of growing rats with lead acetate caused an increase of the glucose rate absorption from maltose solution up to 21 days of age. Administration of inulin to intoxicated rats led to a decrease of bounded in the maltose molecule glucose transport as compared with the control only on the 14th day of the experiments. Administration of lactulose to intoxicated growing rats smoothed to a control value the rate of glucose transport from maltose throughout the observation period.

The rate of glucose transport from glucose solution decreased in all groups of growing rats (Table 5). But, in suckers treated with lead acetate, the rate of absorption of "pure" glucose prevailed over the control values during whole experiment. In rats treated with lead acetate and inulin, the transfer of "free" glucose from the small intestine to the blood circulation was higher than in the control rats only at the 14th day of the experiment. In rats treated with lead acetate and lactulose, the rate of glucose absorption from the monomer solution throughout the experiment did not differ from the control values.

**Blood glucose.** It can be seen from Table 5 that in the control group of growing animals blood glucose level was slowly increased. However, in rats treated with lead acetate, a steady increase in blood glucose level was registered throughout the experiment period. Administration of inulin to intoxicated rats led to normalization of blood glucose in 21- and 28-day-old rats. Administration of lactulose completely eliminated the effect of lead acetate intoxication on blood glucose level during whole observation period.

### 4 Discussion

The obtained data indicate that used prebiotics - inulin and lactulose are able to normalize hydrolysis and absorption of carbohydrates in the small intestine, as well as blood glucose levels, in chronic lead intoxication in the growing rats. This is manifested in the fact that administration of inulin and/or lactulose to intoxicated with lead acetate growing rats leads to decrease the rate of hydrolysis and absorption of carbohydrates, which is increased markedly at lead intoxication. Such shifts in carbohydrate assimilation have a normalizing effect on lead-induced hyperglycemia. It should be noted, the optimizing effect of lactulose on carbohydrate hydrolysis and blood glucose level appears earlier and more expressed in compare with inulin in lead
intoxicated growing rats.

Table 5. Effect of inulin and lactulose on the glucose absorption from maltose and glucose solution in the small intestine and blood glucose content in growing rats at lead intoxication ($M \pm m; n = 6 - 7$)

<table>
<thead>
<tr>
<th>Animal groups</th>
<th>Age (days)</th>
<th>7</th>
<th>14</th>
<th>21</th>
<th>28</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Absorption glucose from maltose solution ($\mu$mol/min/g protein)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>1,2±0,1</td>
<td>40,1±1,2</td>
<td>72,3±1,1</td>
<td>102,4±8,1</td>
<td></td>
</tr>
<tr>
<td>Experiment 1</td>
<td>-</td>
<td>44,3±1,3</td>
<td>&lt;0,05</td>
<td>79,2±3,1</td>
<td>&lt;0,05</td>
</tr>
<tr>
<td>Experiment 2</td>
<td>-</td>
<td>46,5±1,6</td>
<td>&lt;0,02</td>
<td>77,2±5,4</td>
<td>&gt;0,5</td>
</tr>
<tr>
<td>Experiment 3</td>
<td>-</td>
<td>42,1±1,1</td>
<td>&gt;0,25</td>
<td>69,2±2,1</td>
<td>&gt;0,5</td>
</tr>
</tbody>
</table>

| Control       | Absorption glucose from glucose solution ($\mu$mol/min/g protein) |   | 67,2±4,2 | 60,3±3,4 | 58,4±2,1 | 49,4±2,2 |
| Experiment 1  | -         | 69,1±2,1 | <0,05 | 66,9±2,9 | <0,05 | 57,4±3,1 | <0,05 |
| Experiment 2  | -         | 68,4±1,3 | <0,05 | 63,3±5,4 | >0,5 | 54,1±2,4 | >0,25 |
| Experiment 3  | -         | 62,4±1,1 | >0,5 | 69,2±2,1 | <0,01 | 98,3±1,2 | <0,001 |

| Control       | Content of blood glucose (Mmol/l) |   | 3,9±0,2 | 4,1±0,1 | 4,3±0,3 | 4,5±0,2 |
| Experiment 1  | -         | 5,9±0,2 | <0,001 | 6,2±0,2 | <0,001 | 6,4±0,3 | <0,002 |
| Experiment 2  | -         | 5,1±0,3 | <0,02 | 5,2±0,3 | <0,05 | 4,7±0,3 | >0,05 |
| Experiment 3  | -         | 4,3±0,2 | >0,5 | 4,5±0,5 | >0,5 | 4,3±0,2 | >0,5 |

Before future discussing it must be emphasized that in immaturity mammal new-borns, including rats, needs in carbohydrate are provided mainly by milk lactose. At weaning which take place in the end of third postnatal week the breast milk is replaced by hard food containing carbohydrates such as maltose, sucrose and other poly- and disaccharides. The diet change corresponds to the shift in the carbohydrase’s activity in the small intestine [11, 19, 39, 55].

In fact, obtained data show in the control group, the activity of lactase was high in suckler rats (7-14-days-old rats), was decreased sharply by the time of weaning (21-days-old rat), and was remained at a high level (28-days old) after animal transition to self-nutrition (28-days-old rats). At the same time, the enzyme activity that digest carbohydrates of adult food was low in suckers and dramatically increased by the
time when rats switched to adult food. Such age-dependent changes in the activity of digestive carbohydrases were also noted by other authors [11, 19, 39, 55].

Shifts in intestinal carbohydrate digestion and absorption caused by chronic oral administration of lead acetate, first of all, confirm the findings of other authors that oral lead ions, overcome the gastrointestinal barrier and affect almost every organ [37, 48].

It has been shown that the weight loss found in lead intoxication is not related to changes in the amount of food consumed by rats [34]. Most likely, this is due to metabolic disorders in the activity of zinc-containing enzymes [haliullina SV] and a decrease in the level of erythropoietin [44] and sex hormones [24]. The increase in pancreatic weight in intoxicated rats may depend on the increase in the number of secretory granules of pancreatic acini upon activation of the axis of the hypothalamus-pituitary-corticoid system [10, 30]. In addition, the pancreas weight increase may be provided by metal-induced increased synthesis and secretion of binding lead ions metallothionein [8]. Intestinal epithelial cells, unlike pancreatic acini cells, have the ability of quickly self-renew due to the continuous migration of differentiating enterocytes from the crypt to the villi apical compartment, where they become competent for apoptosis and secrete into the intestinal lumen [5]. Such a quick substitution, of one epithelial cell population, with another, possibly provides relative stability of the small intestine weight during the oral administration of lead acetate to growing rats.

Obtained data show lead intoxication resulted in an increase in the activity of "definitive" (pancreatic α-amylase, intestinal maltase and sucrase, and the rate of glucose transport from maltose solution) hydrolytic and transport systems. The same premature maturation of the "definitive" digestive and transport system in developing small intestine was recoded after influence of stress factors or endogenous corticosteroids [25, 26, 28, 41, 42, 43, 68]. It can be assumed that chronic intoxication with lead compounds, being a stress factor, caused shifts in the rate of the "definitive" carbohydrate digestion enzymes development due to its effect on the hypothalamic-pituitary-corticoid system [2, 14].

The increase in the carbohydrate assimilation efficiency in the small intestine and blood glucose level in rats can be caused by both shifts in the insulin signaling system and the prediabetic state as a result of chronic stress caused by the introduction of lead acetate [13, 29, 35, 53]. This confirms the data of other authors showed that any kind of glycemia leads to an increase in the activity of intestinal sucrase, maltase, lactase [36].

It should be noted the premature induction of pancreatic and enteric "definitive" carbohydrases in intoxicated rats take place simultaneously with a delay in the natural decrease in the activity of "juvenile" lactase in the small intestine. The delay in the natural intestinal lactase activity repression in intoxicated rats was probably due to a decrease in the concentration of thyroid hormones caused by lead acetate [65]. Delay in natural decline of lactase activity in the small intestine as related to changes in their thyroid status was also observed in prematurely weaned rats [49]. In fact it is proved that a lack of thyroid hormones leads to an increase in lactase activity in rats [20].
It has been shown dietary fibers take place in the intestine and body detoxification [23]. They promote a shift in the gut toward different types of beneficial bacteria, such as acidophilus [22] and lactobacilli [18]. Perhaps used prebiotics reduce the effect of lead ions, through increasing the activity of bacteria that bind and remove heavy metal ions from the body [7, 18]. The effect of prebiotics on digestion in the small intestine may be associated with the correction of conditions for microbial homeostasis and concomitant metabolism in the colon [1, 61, 62].

Increase the activity of the digestive proteases and peptidases of the host, promote the release of microbial exoenzymes involved in the digestion of proteins, and affect the improvement of the absorption of small peptides and amino acids is detected under the influence of protobiotic bacteria [59]. Current research data indicate that the use of prebiotics normalizes the digestion and absorption of carbohydrates at lead intoxication too. This is expressed in optimizing the activity of the enzymatic and transport systems of the carbohydrate assimilation in the small intestine in growing rats intoxicated with lead acetate.

It can be assumed, the increase in hydrolysis and absorption of carbohydrates in the small intestine caused by lead acetate intoxication, leads to a decrease of food substrate in the colon. In turn, a decrease of oligo- and disaccharidases in the colon limits the conditions for the growth and development of obligate bacteria in lead intoxicated growing rats. Disturbance in microbial homeostasis and concomitant microbial metabolism leads to additional endotoxemia and affects the function of the intestine and other body systems [13].

In the current observation the optimizing effect of inulin and lactulose is manifested in the normalization of the carbohydrate assimilation in the small intestine, which is increased after intoxication with lead acetate in growing rat. Gastrointestinal hormones such as ghrelin, peptide YY, serotonin and glucose-dependent insulin, which secretion are determined by the colon microbiota [1, 15, 33, 46, 56, 61, 62] can serve as intermediaries for the transmission of signals from microbiota to the carbohydrate hydrolytic systems of the host.

The results showed that in intoxicated with lead acetate rats the lactulose’s optimizing effect on the carbohydrate assimilation in the small intestine develops earlier than inulin’s one. Perhaps the more expressed effect of lactulose is due to the fact that the fermentation of the short-chain oligosaccharides to which lactulose belongs is faster than the long-chain ones to which inulin belongs. It results to earlier creation of conditions for the development of lactobacilli and bifidobacteria and the secretion of the metabolites necessary for the host organism in the colon [50, 51, 64].

Thus, the mechanisms by which various prebiotics normalize carbohydrate uptake in the small intestine, as well as blood glucose levels in lead poisoning, include the complex physiology of glucose homeostasis [52]. The systems responsible for the initial and final stages of digestion and absorption of carbohydrates, endogenous hormonal system [12, 28], including hormones produced by intestinal microflora, and [66] are taken place in this homeostasis.

So, we have shown that chronic intoxication with lead ions has a stimulating effect on the systems involved in cavity and membrane hydrolysis and transport
of carbohydrates in the small intestine, which leads to hyperglycemia in a growing organism. The "tension" of carbohydrate assimilation in the small intestine under influence of lead acetate can be removed by oral administration of prebiotics - inulin and/or lactulose.

So, the undigestible by the host organism inulin and lactulose take part in increasing of adaptation of the carbohydrate assimilation system in the small intestine during intoxication with lead ions in growing rats. The revealed property of prebiotics suggests the prospect of their use as physiologically acceptable additives to stabilize carbohydrate digestion and blood glucose levels during lead intoxication and, possibly, other heavy metals in the growing organism.

References


