Reversal Effects of Probiotic Supplementation on a High Glucose Diet in Caenorhabditis elegans Model

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Abstract

With an increasing glycemic index associated with the Western diet, it comes to no surprise that obesity, diabetes, and heart disease are on the rise. Shortened lifespan is associated with these diseases and consumption of a high sugar diet. The benefits probiotics provide on shortened lifespan induced by a high glucose diet and the effects of probiotics in combination of cranberry extracts in the model system Caenorhabditis elegans were investigated. When C. elegans was supplemented with each probiotic strain, lifespan extension was observed. Reversal of glucose induced shortened lifespan and lifespan extension in combination of cranberry extracts was strain dependent.

Introduction

The “Western Diet,” prominent among developed nations, often refers to a diet rich in meat proteins and refined sugars. With an increasing glycemic index observed in Western society, it comes to no surprise that obesity, diabetes, and heart disease are on the rise. The Centers for Disease Control and Prevention describes obesity as an epidemic, affecting more than 35% of U.S. citizens. Shortened lifespan and increased susceptibility to pathogens are associated with these diseases and linked to increased consumption of foods high in sugar. In order to reverse these observed effects, the healthful benefits probiotics provide on immune system stimulation, restoration of shortened lifespan induced by a high glucose diet, and the beneficial effects of probiotics in combination of cranberry extracts in the model system Caenorhabditis elegans were investigated. An exciting benefit of implementing C. elegans in such studies is the innate immunological response and aging pathways homology in humans. By targeting these pathways, C. elegans provides an economical model system with application in humans. Here, we investigated the effects probiotics have on high glucose diet in C. elegans. Consistent with previous studies, when C. elegans was supplemented with each probiotic strain, lifespan extension was observed. Interestingly, the reversal of glucose induced shortened lifespan and the extension of lifespan in combination of cranberry extracts was strain dependent. The impact that probiotics have on the reversal of detrimental effects associated with a high glucose diet, including protection against known pathogens and immunological response pathways targeted by probiotics, is currently under investigation.

Specific Aims

1. Determine each probiotic’s effect on lifespan.
2. Determine if probiotics have the ability to reverse the detrimental effects of a high glucose diet.
3. Determine if the probiotics in combination with cranberry extracts (CBE) further extend lifespan.

Table 1. Lifespan of N2 worms on high glucose diet and probiotics at 25°C. N2 lifespan was shortened with all strains when supplemented with glucose. Lifespan restoration was observed in Lactobacillus delbrueckii, Bacillus subtilis, and Bacillus coagulans. Worms fed Lactobacillus plantarum exhibited an extreme decrease in lifespan when supplemented with 2% D-glucose. Data shown are representative of one round of lifespan assays.

<table>
<thead>
<tr>
<th>Diet</th>
<th>Mean±SE (Days)</th>
<th>P-value</th>
<th>% Decrease of Lifespan</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ld+2% glucose</td>
<td>14.693±0.300</td>
<td>&lt;0.05</td>
<td>15.70%</td>
</tr>
<tr>
<td>Bc+2% glucose</td>
<td>16.136±0.130</td>
<td>&lt;0.05</td>
<td>26.7%</td>
</tr>
<tr>
<td>Bs+2% glucose</td>
<td>15.359±0.106</td>
<td>&lt;0.05</td>
<td>20.6%</td>
</tr>
<tr>
<td>E. coli</td>
<td>15.706±0.398</td>
<td>&lt;0.05</td>
<td>13.6%</td>
</tr>
<tr>
<td>C. fermentum</td>
<td>15.994±0.499</td>
<td>&lt;0.05</td>
<td>10.7%</td>
</tr>
<tr>
<td>L. delbrueckii</td>
<td>16.670±0.468</td>
<td>&lt;0.05</td>
<td>3.1%</td>
</tr>
</tbody>
</table>

Table 2. Lifespan of N2 worms fed on probiotics and CBE diet at 25°C. N2 lifespan was increased with all strains when supplemented with CBE except L. plantarum. Lifespan extension was observed in Lactobacillus delbrueckii, Lactobacillus fermentum, Bacillus subtilis, and Bacillus coagulans. Data shown are representative of one round of lifespan assays.

<table>
<thead>
<tr>
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<th>Mean±SE (Days)</th>
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<th>% Decrease of Lifespan</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ld+2mg/mL CBE</td>
<td>14.061±0.099</td>
<td>&lt;0.05</td>
<td>12.8%</td>
</tr>
<tr>
<td>Bc+2mg/mL CBE</td>
<td>14.693±0.300</td>
<td>&lt;0.05</td>
<td>5.30%</td>
</tr>
<tr>
<td>Bs+2mg/mL CBE</td>
<td>15.245±0.190</td>
<td>&lt;0.05</td>
<td>13.6%</td>
</tr>
</tbody>
</table>

Future Directions & Significance

Insulin, a hormone involved in regulating metabolism and absorption of glucose in mammals, and the homolog IGF-1 have been shown to regulate lifespan in many organisms and is involved in other cellular processes such as stress response. The FOXO transcription factor-GDF-11 signaling pathway and decreased activity of heat shock transcription factor HSF-1 reduced the rate of tissue aging, resulting in increased lifespan. The DAF-16 and HSF-1 transcription factor may be inhibited by a high-glucose diet. A downstream gene encoding a glycerol channel app-1 was also involved in lifespan reduction induced by a high glucose diet. In mammals, adipose tissue is repared by insulin. We intend to target these pathways to determine their involvement in probiotic-mediated restoration of lifespan.

Our findings may also have implications in prevention and/or cure of obesity related diseases such as type 2 diabetes, tumor formation and heart disease. Studies could be further carried out in a higher organism such as mice. Because of the pathway homology including insulin/IGF-1-mediated signaling (IIS) pathway, p38 kinase pathway, and other immunological/stress response pathways between C. elegans and humans, these findings may be of high human health importance. In addition these findings may lead to relatively inexpensive and highly accessible prevention or treatment for infection.

Acknowledgments

Cranberry extracts were obtained from DECAS.

References