**Insulinotropic effects of milk proteins**

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**Background**

The progression of the metabolic syndrome proceeds through a step-wise deterioration of metabolic events where deterioration of insulin sensitivity appears to have a key role in a "vicious circle" of hyperinsulinaemia/hyperglycaemia and insulin resistance. Food factors inducing low postprandial glycaemic and insulin responses, and improving insulin sensitivity might thus be advantageous.

**Whey proteins**

Recent data suggest that certain proteins and protein-containing foods e.g. milk, particularly whey proteins, may exert insulinotropic effects without a concomitant postprandial hyperglycaemia. Equi-carbohydrate meals of lactose and different food proteins cause a significantly higher insulin response following a whey meal compared with other animal (cod) and vegetable (gluten) proteins (Figure 1). The key mechanism for protein-induced hyperinsulinaemia is not fully known, but it seems to involve both stimulation of glucose-dependent insulinotropic polypeptide (GIP) and a rapid response of several amino acids.

**Amino acids**

It is well known that amino acids act as insulin secretagogues similar to glucose. When testing a drink containing glucose and the five amino acids that increase the most after a whey meal (valine, leucine, isoleucine, threonine and lysine), the postprandial glycaemia and insulinemia was well mimicked (Table 1). The amino acid load was adjusted to mimic the postprandial amino acid pattern of those amino acids following a whey meal (Figure 2). Therefore, it could be concluded that whey causes hyperinsulinaemia by inducing a rapid response of specific amino acids.

**Use of whey as insulinogenic agent**

Subjects with diet-treated type 2 diabetes were served a high glycaemic breakfast and a subsequent lunch without (reference meal) or with supplementation of whey. Breakfast and lunch meals supplemented with whey, as opposed to a protein equivalent amount of ham, increased insulin response by 31 % and 57 % following breakfast and lunch, respectively. The whey supplementation reduced glycaemia at lunch by 21 % (P<0.05), and reduced glycaemic excursions from fasting value over the course of the day (0-7 h) by 12 % (P<0.05). In addition was the postprandial GIP responses increased following whey ingestion.

**Conclusions**

- Specific food proteins and amino acids can be used in tailoring foods with specific effects on postprandial insulinaemia.
- Enclosure of whey in high-glycaemic meals facilitates blood glucose regulation in type 2 diabetics, indicating a therapeutic role of certain proteins in individuals with diminished insulin secretory capacity.

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**Table 1** - Nutrient composition of and insulinaemic response after drinks containing free amino acids or whey protein

<table>
<thead>
<tr>
<th>Glucose</th>
<th>Leu</th>
<th>Ile</th>
<th>Val</th>
<th>Lys</th>
<th>Thr</th>
<th>Whey protein</th>
<th>Insulin AUC (0-90 min) (nmol<em>L⁻¹</em>min⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reference drink</td>
<td>25</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>10.6 ± 1.3³</td>
</tr>
<tr>
<td>Amino acid drink</td>
<td>25</td>
<td>2.2</td>
<td>1.1</td>
<td>1.1</td>
<td>1.6</td>
<td>1.4</td>
<td>13.9 ± 1.6b</td>
</tr>
<tr>
<td>Whey drink</td>
<td>25</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>18</td>
<td>17.0 ± 2.0b</td>
</tr>
</tbody>
</table>

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**Figure 1** – Postprandial serum insulin responses (AUC 0-90 min) after white wheat bread (WWB) and test meals based on food proteins served with lactose in healthy subjects.

**Figure 2** – Postprandial plasma amino acid responses (AUC 0-45 min)

**Figure 3** – Mean incremental changes in blood glucose in response to reference meals and test meals (with whey) in subjects with type 2 diabetes.