Impact of IE fats on health

Post-prandial effects lipoprotein metabolism and plasma concentrations, glycemic control
Disclosure of interest

• Research funding
  – UK Food Standards Agency/Department of Health
  – Malaysian Palm Oil Board (mpob.gov.my)

• Member of Scientific Advisory Committee of the Global Dairy Programme
Available data

Small studies n<=16 - not RCTs


RCTs with n>16


Problems with previous studies

- Small numbers of subjects studied in many studies <16
- Study participants - healthy, young and predominantly female
- Lack of standardized test meal protocol
- Fats often contained a high proportion of high melting point fats >40°C
- No measure remnant particles (apolipoprotein B48)
Research on dietary fats

• Most research measures the effects of dietary fats in the fasting state

• Most of the time we are in the fed state (postprandial)
Exogenous Pathway

INTESTINAL CELL

FGA MAG

GOLGI

B48

CHYLOMICRON

LIVER

LYSOSOME

REMNANT

MUSCLE

NEFA

TAG

ADIPOCYTE

LIPOPROTEIN LIPLA

B48

HDL

E

C

E
Impaired postprandial lipaemia has adverse effects on lipoprotein metabolism by generating more atherogenic particles.
Effect of different chain length fatty acids on postprandial lipaema

Change in plasma triglycerides after test meal

Sanders et al Atherosclerosis 2000, 149: 413-420
Postprandial lipaemia

Area under curve

18:1cis  18:1trans  18:0  16:0  MCT  Low fat

Statistical significance of $F$ value $P < 0.0001$

Mean change in plasma TAG from fasting with 95%CI

- **3h**
  - Oleate: 0.75 mmol/l
  - Salatrim: 0.50 mmol/l
  - Cocoabutter: 0.25 mmol/l

- **6h**
  - Oleate: 0.25 mmol/l
  - Salatrim: 0.25 mmol/l
  - Cocoabutter: 0.25 mmol/l

SALATRIM meal decreased FVIIc and FVIIa

Randomized vs Unrandomized cacoabutter

Plasma TAG (mmol/L) vs Time (h)

Unrandomized CCB
Randomized CCB

Incremental area under curve

Diet x time effect P=0.003

Effect of randomization of palm oil on postprandial lipaemia

Solid fat index curve determined by NMR analysis

Temperature (°C)

Solids (%)
Study methodology

- An intake of at least 50g fat is needed to produce reproducible postprandial lipemia
- Characterise the test fat with regard to chemical composition and physical characteristics
- Meals high in fat and exercise should be avoided on the day before the test meal
- The test meal should be able to be consumed within 10 minutes
- Cannulation is preferred over repeated venepuncture
- Blood should be sampled up until a minimum of 6h up to 8h
- Participants should have access to sip water throughout the procedure
- Report incremental area under curve
- Conduct study double-blind if possible
Measurement of glucose and insulin responses

- 75-80g carbohydrate in test meal is equivalent to that use in an oral glucose tolerance test
- Glycemic index testing uses 50g
- Measure c-peptide as an index of insulin secretion
- Sample at 0, 15, 30, 60, 90, 120 min also at 45 min if feasible
- Consider measuring gut peptide GIP, GLP-1
Hypothesis

Fats with a high proportion of palmitic acid in the $sn$-2 position will decrease postprandial lipemia.
Outcome

- Primary outcome
  Sample size calculations were based on 90% power at $P=0.01$ to detect a 0.5 SD unit change in the area under the curve for plasma triglycerides which gave a sample size of 48
- Secondary outcomes were changes in apoprotein B48 and non-esterified fatty acids (NEFA) and insulin secretion and glucose
- Exploratory outcomes were postprandial changes in inflammatory cytokines, GIP and PYY
Study design

• A randomized cross-over design conducted at 2 centres (London and Maastricht)

• The study was conducted double-blind
Participants and setting

- Healthy men and women recruited in two centres
  - Maastricht n=24
  - London n=26

Cross-over design with treatment allocation according to a Latin square design

Participants and investigators were blinded to the treatment allocation
Muffin and milkshake test meal

<table>
<thead>
<tr>
<th>Test fats</th>
<th>SFA</th>
<th>MUFA</th>
<th>PUFA</th>
<th>sn-2 palmitic acid (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Native palm olein (PO)</td>
<td>45</td>
<td>42</td>
<td>12</td>
<td>13</td>
</tr>
<tr>
<td>Interesterified palm olein (IPO)</td>
<td>45</td>
<td>42</td>
<td>12</td>
<td>41</td>
</tr>
<tr>
<td>Lard</td>
<td>44</td>
<td>43</td>
<td>10</td>
<td>55</td>
</tr>
<tr>
<td>High oleic sunflower oil (HOS)</td>
<td>7</td>
<td>81</td>
<td>11</td>
<td>0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Energy (kcal)</th>
<th>Carbohydrate (g)</th>
<th>Fat (g)</th>
<th>Protein (g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>905</td>
<td>91</td>
<td>50</td>
<td>15</td>
</tr>
</tbody>
</table>
## Solid fat content of the test fats (%)

<table>
<thead>
<tr>
<th></th>
<th>Lard</th>
<th>Interesterified Palm Olein</th>
<th>High Oleic Sunfloweroil</th>
<th>Palm Olein (IV 56)</th>
</tr>
</thead>
<tbody>
<tr>
<td>10°C</td>
<td>49.7</td>
<td>52.7</td>
<td>0.0</td>
<td>33.2</td>
</tr>
<tr>
<td>20°C</td>
<td>35.9</td>
<td>30.1</td>
<td></td>
<td>4.4</td>
</tr>
<tr>
<td>25°C</td>
<td>27.5</td>
<td>20.5</td>
<td></td>
<td>0.7</td>
</tr>
<tr>
<td>30°C</td>
<td>15.7</td>
<td>12.4</td>
<td></td>
<td>0.0</td>
</tr>
<tr>
<td>35°C</td>
<td>6.2</td>
<td>7.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>40°C</td>
<td>4.4</td>
<td>4.5</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
STUDY PROTOCOL

Test meal (50g test fat & 85g CHO)

3h Standard lunch (low fat)

- 0, 60, 120, 180, 240, 300, 360, 420 & 480 min: plasma TAG, NEFA, PFA, cholesterol
- 180, 240 & 300 min: chylomicron TAG composition
- 0, 180 & 360 min: FVIIIa
- 0, 180, 240, 300 & 480 min: cytokines (IL-6, e-selectin, TNF-α)

Standard evening meal
Baseline measurements

Glucose, insulin, C-peptide, GIP, PYY, GLP-1
0, 15, 30, 60, 90, 120, 150, 180, 240, 300, 360, 420 and 480 min

TIME (h) 20.00 08.00 09.00 10.00 11.00 12.00 13.00 14.00 15.00 16.00 17.00
Postprandial changes in plasma non-esterified fatty acids (NEFA)

Meal x time interaction P=0.0001
Postprandial changes in apolipoprotein B48 concentrations

Meal x times P=0.006
Glucose-dependent insulinotropic polypeptide (GIP)

Meal x time $P<0.0001$

**Inset:**
- HOS
- PO
- IPO
- Lard

iAUC

Time (min)

GIP (ng/L)
Postprandial glucose no difference between treatments but significant gender effect $P<0.00001$
Other interesting observations

- Women showed much smaller increases in plasma triglyceride than men

- Women secreted more insulin and had lower postprandial blood glucose levels than men
Implications for long-term health/disease risk

- No evidence to indicate increased remnant concentrations following IE fats
- Decreased postprandial lipemia following higher melting points may have an advantage in terms of decreased postprandial activation of FVII
- Interesterified C16 fats do not differ from naturally occurring C16 fats with regard to postprandial effects on glucose homeostasis
Risk-benefit considerations

- **Benefit** - IE can replace TFA
- **Risk** - none identified for IE fats with regard to postprandial lipemia
Gaps and research needs

- There is a lack of information regarding the effects of interesterified shorter chain (C12-C14) fatty acids.
- Need for head to head comparison of stearic rich vs palmitic rich interesterified fats
- There is a lack of information regarding the effects of enzymically interesterified fats rich in stearic acid.
- Most studies have been conducted on healthy subjects in the normal body weight range. In view of the high prevalence of obesity and overweight and the growing burden of type 2 diabetes, there is a need to evaluate the effects of interesterified fats in the overweight/obese groups.
- There is emerging evidence that changing higher melting point fats as produced by interesterification may influence the secretion of gut peptides that are involved in hormonal signalling in postprandial period.