

Mela et al, "Effect of low-dose mulberry fruit extract on postprandial glucose and insulin responses: A randomized pilot trial in individuals with type 2 diabetes"

## **SUPPLEMENTARY MATERIAL** (tables and figures in order of reference in manuscript)

### **Table S1.** Inclusion and exclusion criteria

Subjects who met the following criteria could be included in the study:

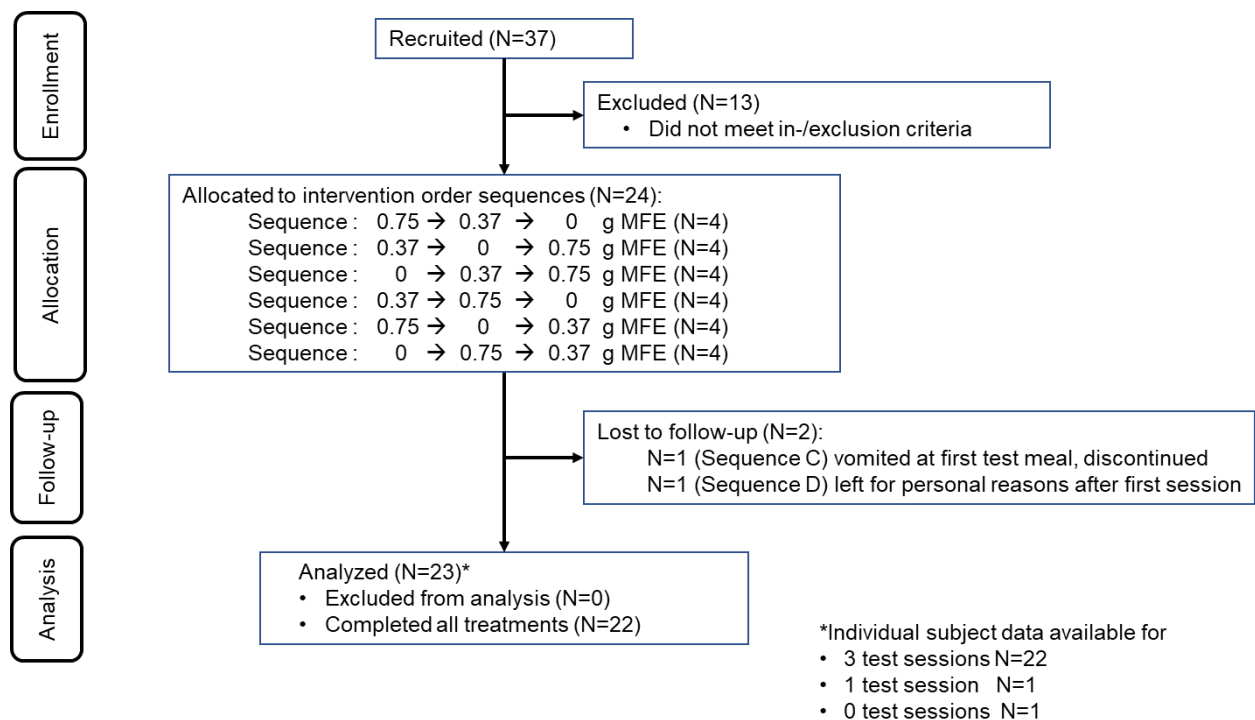
- Male and non-pregnant, non-lactating females with type 2 diabetes (confirmed by two independent measurements of HbA1c  $\geq 6.5\%$  but  $< 8.0\%$ ), who are either treatment naive (controlled solely through diet and exercise) or have not been treated with glucose lowering drugs for the preceding three months
- Age  $\geq 20$  and  $\leq 65$  years of age
- Body Mass Index (BMI) of  $\geq 18$  and  $\leq 35$  kg/m<sup>2</sup>
- Willing and able to give written consent to participate in the study
- HbA1c confirmed by two measurements as  $\geq 48$  mmol/mol (6.5%) and  $\leq 53$  mmol/mol (7.0%) or, at the discretion of the study physician, HbA1c  $> 53$  mmol/mol (7.0%) but  $< 63$  mmol/mol (8.0%)
- For subjects  $< 40$  years old, Type 1 diabetes ruled out by the study physician
- For patients with newly diagnosed hyperlipidaemia and not on medication: Lipid values of Total Cholesterol 200-350 mg/dL, LDL 100-170 mg/dL, HDL  $\geq 40$  mg/dL (males) or  $\geq 50$  mg/dL (females), Triglycerides  $< 199$  mg/dL
- Hemoglobin level within clinically acceptable range (males 12-17 gm/dL, females 11-15 gm/dL) as judged by the research physician
- Other routine blood chemistry parameters within normal range
- No medical conditions which might affect study measurement or measurement of HbA1c (e.g. chronic renal disease), as judged by the study physician
- Blood pressure up to 140/90, managed if relevant with lifestyle intervention and medications other than ACE (Angiotensin Converting Enzyme) inhibitors or ARBs (Angiotensin II Receptor Blockers)
- For subjects using other medications: Only medications which do not impact insulin sensitivity
- For subjects with hyperlipidemia: Use of statins if relevant
- Willing to comply to study protocol during the study
- Agreeing to be informed about medically relevant personal test-results by study physician
- Willing to refrain from drinking alcohol for at least one day before the blood withdrawal and study product administration
- Having accessible veins on arms as determined by examination at screening

Exclusion criteria:

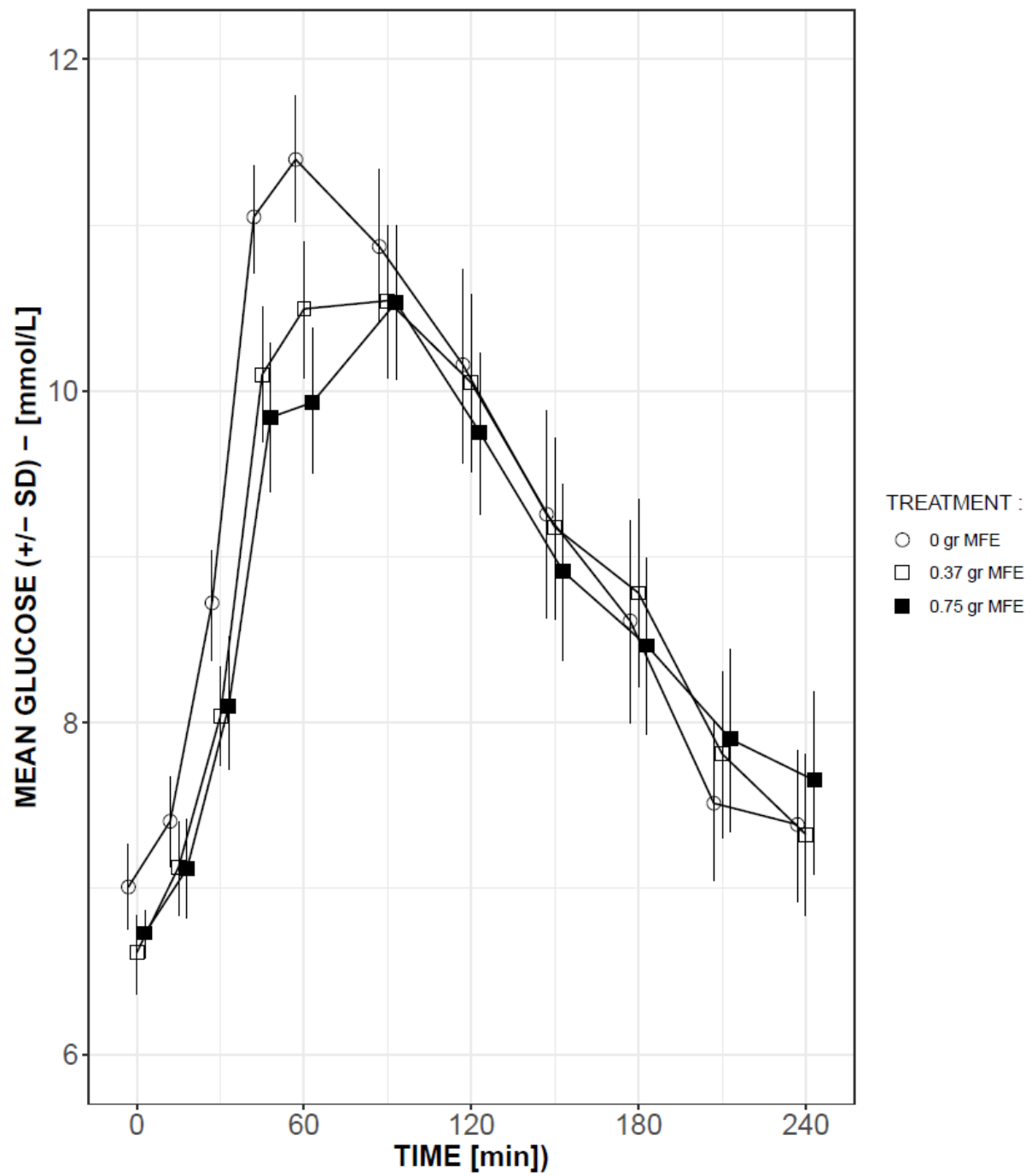
- Being an employee of Unilever or Hindustan Lever Ltd. or the study site
- Use of tobacco products
- Consumption of alcoholic drinks daily, or more than 2 drinks in a day, or more than 8 drinks per week
- Participation in any other biomedical study 3 months before screening visit day of this study and/or participating in any other biomedical study during the screening period.
- Reported work in night shifts (between 23.00 and 6.00 hrs)
- Chronic medication other than those allowed in the inclusion criteria
- Reported weight loss/gain  $\geq 10\%$  of body weight in the 6 months preceding screening
- Blood donation for 2 months prior to screening
- Urine analysis indicating drug abuse

- Allergy to any food or cosmetics
- Pregnant or planning pregnancy during the study period
- Lactating or been lactating for 6 weeks before pre-study investigation and/or during the study period
- Intense exercise >10 h/week (defined as exercise which induces sweating and causes sufficient breathlessness to limit conversation)

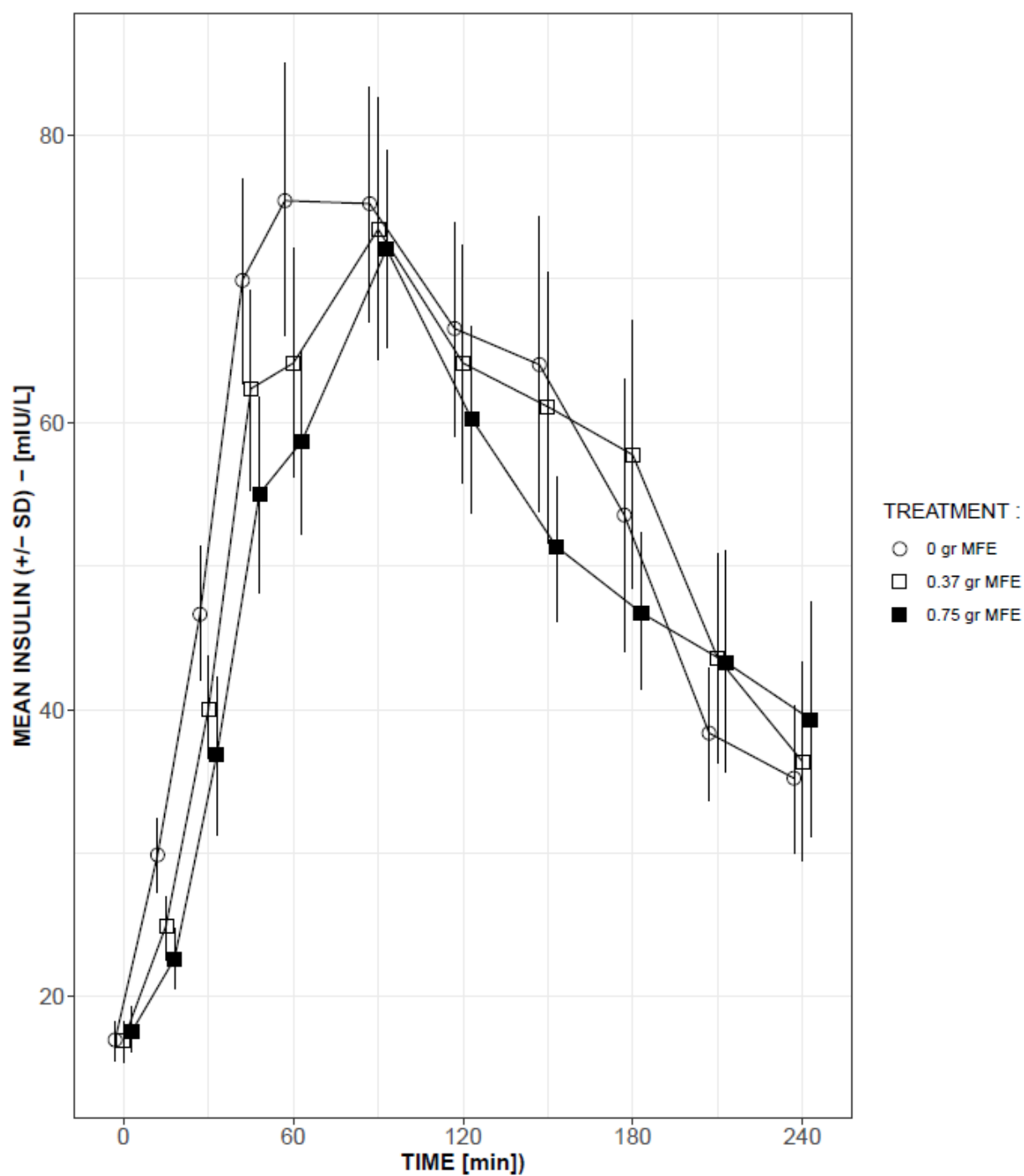
**Figure S1.** Consolidated Standards of Reporting Trials (CONSORT) subject flow diagram.



**Figure S2.** Plasma glucose response over 4 hours following consumption of mulberry fruit extract (MFE) added to boiled rice.



**Figure S3.** Serum insulin glucose response over 4 hours following consumption of mulberry fruit extract (MFE) added to boiled rice.



**Table S2.** Plasma glucose response over 3 hours following consumption of mulberry fruit extract (MFE) added to boiled rice.

Intervention	N	Mean glucose +iAUC <sub>3hr</sub> (lower, upper 95% CI), min·mmol/L	Mean % difference, MFE vs control (lower, upper 95% CI)
Control	21	448 (380, 529)	
Control + 0.37 g MFE	22	454 (396, 521)	1.3 (-13.0, 18.0)
Control + 0.75 g MFE	20	385 (307, 485)	-14.1 (-32.5, 9.2)

**Table S3.** Plasma glucose response over 4 hours following consumption of mulberry fruit extract (MFE) added to boiled rice.

Intervention	N	Mean glucose +iAUC <sub>4hr</sub> (lower, upper 95% CI), min·mmol/L	Mean % difference, MFE vs control (lower, upper 95% CI)
Control	21	487 (406, 583)	
Control + 0.37 g MFE	22	511 (442, 591)	4.9 (-10.5, 23.1)
Control + 0.75 g MFE	20	440 (349, 555)	-9.6 (-29.0, 9.8)

**Table S4.** Serum insulin response over 3 hours following consumption of mulberry fruit extract (MFE) added to boiled rice.

Intervention	N	Mean insulin tAUC <sub>3hr</sub> (lower, upper 95% CI), min·mIU/L	Mean % difference, MFE vs control (lower, upper 95% CI)
Control	21	9625 (8155, 11358)	
Control + 0.37 g MFE	22	9040 (7670, 10654)	-6.1 (-15.4, 4.2)
Control + 0.75 g MFE	20	8009 (6782, 9460)	-16.8 (-25.2, -7.4)

**Table S5.** Serum insulin response over 4 hours following consumption of mulberry fruit extract (MFE) added to boiled rice.

Intervention	N	Mean insulin tAUC <sub>4hr</sub> (lower, upper 95% CI), min·mIU/L	Mean % difference, MFE vs control (lower, upper 95% CI)
Control	21	11763 (10023, 13805)	
Control + 0.37 g MFE	22	11339 (9672, 13294)	-3.6 (-11.9, 5.5)
Control + 0.75 g MFE	20	10175 (8665, 11949)	-13.5 (-21.1, -5.1)

**Table S6.** Maximum glucose level (C<sub>max</sub>) over 4 hours following consumption of mulberry fruit extract (MFE) added to boiled rice.

Intervention	N	Mean Cmax (lower, upper 95% CI), mmol/L	Mean % difference, MFE vs control (lower, upper 95% CI)
Control	21	11.5 (10.9, 12.1)	
Control + 0.37 g MFE	22	10.9 (10.4, 11.5)	-4.9 (-10.2, 0.6)
Control + 0.75 g MFE	20	10.7 (10.1, 11.2)	-7.3 (-12.5, -1.7)

**Table S7.** Glucose swing (C<sub>max</sub>-C<sub>min</sub>) over 4 hours following consumption of mulberry fruit extract (MFE) added to boiled rice.

Intervention	N	Mean glucose swing (lower, upper 95% CI), mmol/L	Mean difference, MFE vs control (lower, upper 95% CI), mmol/L
Control	21	4.6 (3.9, 5.3)	
Control + 0.37 g MFE	22	3.8 (3.2, 4.5)	-0.8 (-1.4, -0.2)
Control + 0.75 g MFE	20	3.6 (2.9, 4.2)	-1.1 (-1.7, -0.4)

**Table S8.** Pooled urine glucose concentration over 4 hours following consumption of mulberry fruit extract (MFE) added to boiled rice, change vs baseline.

Intervention	N	Mean urine glucose at baseline (lower, upper 95% CI), µg/ml	Mean pooled urine glucose post-meal (lower, upper 95% CI), µg/ml	Change in mean pooled urine glucose post-pre meal (lower, upper 95% CI), µg/ml	Mean difference in change from control (lower, upper 95% CI), µg/ml
Control	22	4.0 (2.5, 5.5)	24.4 (15.5, 33.3)	20.4 (11.9-28.9)	
Control + 0.37 g MFE	22	4.3 (3.8, 4.8)	23.5 (21.5, 25.5)	19.2 (15.2, 23.1)	-1.2 (-9.2, 6.8)
Control + 0.75 g MFE	20	4.2 (2.7, 5.7)	24.9 (16.2, 33.6)	20.7 (12.1, 33.2)	0.3 (-11.7, 12.0)