### Studies on patients with DM1

<table>
<thead>
<tr>
<th>Study name</th>
<th>Place, setting and time</th>
<th>Inclusion / Exclusion criteria</th>
<th>Characteristics</th>
<th>Intervention vs. Control Description with duration</th>
<th>Outcomes Primary and secondary</th>
<th>Results Longest follow-up period with intervention effects (IG vs. CG) with SD, 95%-CI or p value</th>
</tr>
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<tbody>
<tr>
<td>Malipa 2013 RCT</td>
<td>Zambia</td>
<td>DM1, 16-19 yrs</td>
<td>n=40 55% females 16-17 yrs: 35% 18-19 yrs: 65% Compliance: worse in IG 26.4 vs. 14.6 (p=0.001) Impact of diabetes: 20.5 Worries about diabetes: 20.5 Satisfaction with life: 20.5</td>
<td>IG (n=20): 1 meeting /wk over 8 wks CG (n=20): waiting list Duration: 8 wks</td>
<td>Compliance to treatment (Rating scale for compliance) Quality of life (impact and worries about diabetes, satisfaction with life)</td>
<td>After 2 months: Compliance: better in IG (11.0 vs. 30; p&lt;0.001) Impact of diabetes: better in IG (16.8 vs. 24.2; p=0.045) Worries about diabetes: better in IG (14.32 vs. 26.68; p&lt;0.001) Satisfaction with life: better in IG (28.5 vs. 12.5; p&lt;0.001)</td>
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<tr>
<td>Salem 2010 RCT</td>
<td>Egypt, urban 02/2009-11/2009</td>
<td>DM1 for ≥3 years, 12-18 yrs, HbA1c ≥7.5 % for ≥6 months no significant diabetic complications limiting exercise like, uncontrolled hypertension, diabetic ketoacidosis, severe hypoglycemia within the past 3 months, patients on lipid lowering therapy</td>
<td>n=196 61.7 % female age (yrs): 14.78 ± 2.31 HbA1c (%): 8.7±1.7 duration of diabetes (yrs): 4.6 ± 1.9</td>
<td>IG2 (n=73): attended exercise sessions three times/week vs. IG 1 (n=75): attended exercise sessions once times/week vs. CG (n=48): no exercise Duration: 6 months</td>
<td>glycemic control, plasma lipids values, blood pressure, severity and frequency of hypoglycemia, anthropometric measurements and insulin dose</td>
<td>Change over 6 months: HbA1c (%): Benefit for IG2 and IG1: 7.8 ± 1.0 vs. 8.1 ± 1.1 vs. 8.9 ± 1.3% (p=0.2)</td>
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<tr>
<td>Abdulrhman 2013 NCT01554566 Cross-over 01/2010 -</td>
<td>Egypt, urban, tertiary care</td>
<td>DM1, age &gt; 2 yrs, HbA1c&lt; 10 % no renal or hepatic impairment, coexisting</td>
<td>n=20 50 % females age (yrs): 11.3 ± 4.3 duration of diabetes (yrs): 4.7±14.5</td>
<td>IG/ CG (n=10): Honey consumption (0.5 ml/kg body weight per day) vs.</td>
<td>Primary: serum lipids, c-peptide Secondy: anthropometric measures (e.g. BMI), fasting and 2h-</td>
<td>After 12 weeks: (IG/CG vs. CG/IG): HbA1c (%): Benefit with CG/IG: 6.7±0.9 vs. 5.9±0.8 (p&lt;0.01) no differences in change in period 1: -</td>
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<td>Mohamad 2009</td>
<td>Egypt, urban</td>
<td>Type 1 Diabetes, age 17 to 20 yrs</td>
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<td>Longest follow-up period with intervention effects (IG vs. CG) with SD, 95%-CI or p value</td>
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<tr>
<td>van der Hoogt 2017</td>
<td>South Africa</td>
<td>DM1, age 4-17 yrs on insulin pump therapy, HbA1c&gt;9.6% for ≥3 months, BMI/age z-score -1 to &lt; 3, daily insulin use of &gt;0.5 u/kg, no remission of diabetes, smoking, coeliac disease, cystic fibrosis, diseases or medication that are associated with delayed gastric emptying or altered digestion, glucocorticoids, oral diabetic drugs, no acute illnesses</td>
<td></td>
<td>Change over 12 weeks</td>
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<tr>
<td>Elbarbary 2016</td>
<td>Egypt, urban</td>
<td>DM1, adolescents and adults who wished to fast the month of Ramadan with insulin pump for 26 months and attending the whole</td>
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<td>Longest follow-up period with intervention effects (IG vs. CG) with SD, 95%-CI or p value</td>
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### Study Details

#### Mohamad 2009
- **RCT**
- **Setting:** Egypt, urban
- **Population:** Type 1 Diabetes, age 17 to 20 yrs
- **Inclusion / Exclusion criteria:**
  - No acute metabolic complications like diabetic ketoacidosis, hypoglycaemia, cardiovascular events, renal or acute infections
  - No acute illnesses
- **Characteristics:**
  - N=64
  - 30% female
  - Age (yrs): 19.9±6.8
  - HbA1c (%): 9.52±2.08
  - Fasting glucose (mg/dl): 228.7±13.5
  - BMI (kg/m²): 18.82±3.01
- **Intervention vs. Control:**
  - CG (n=27): camel milk (500 ml) + usual care vs. IG (n=27): usual care for diabetes (i.e. diet, exercise, insulin mixtard)
- **Duration:** 16 weeks
- **Outcomes:**
  - Postprandial glucose, HBA1c, serum lipid profile
  - Change over 12 weeks
    - HbA1c (%): Benefit for IG: 7.16±1.84 vs. 9.59±2.05
    - Fasting glucose (mg/dl): Benefit for IG: 227.2±17.7 vs. 98.9±16.2

#### van der Hoogt 2017
- **Cross-over RCT**
- **Setting:** South Africa
- **Population:** DM1, age 4-17 yrs on insulin pump therapy, HbA1c>9.6% for ≥3 months, BMI/age z-score -1 to < 3, daily insulin use of >0.5 u/kg, no remission of diabetes, smoking, coeliac disease, cystic fibrosis, diseases or medication that are associated with delayed gastric emptying or altered digestion, glucocorticoids, oral diabetic drugs, no acute illnesses
- **Intervention vs. Control:**
  - IG1 (n=22): 1 home-based low fat and protein meal vs. IG2 (n=22): 1 high fat and protein meal with identical carbohydrate content, two meals were consumed at dinner time (18:00) under parental supervision at least 1 day apart within one month
- **Duration:** 3 months
- **Outcomes:**
  - Primary: peak sensor glucose value post-meal, time to peak sensor glucose, time of first and largest correction bolus, total correction insulin, total meal insulin, additional insulin required, area under the sensor glucose response curve (AUC) (≥ 8 mmol/L), duration of elevated post-prandial glucose
  - Change over 12 weeks: Occurrence of hypoglycaemic events; 7 (32%) vs. 1 patients after IG1 vs. IG2

#### Medical device
- **Elbarbary 2016**
- **RCT**
- **Setting:** Egypt, urban
- **Population:** DM1, adolescents and adults who wished to fast the month of Ramadan with insulin pump for 26 months and attending the whole
- **Characteristics:**
  - N=73
  - 68.3% female
  - Age (yrs): 15.6±2.7
  - HbA1c (%): 7.65±0.9
  - BMI (kg/m²):
- **Intervention vs. Control:**
  - IG (n=25): sensor with low glucose vs. IG (n=25): sensor with low glucose during Ramadan fasting
- **Outcomes:**
  - Primary: hypoglycaemia
  - Other: glucose value, number of ‘full fasted days’, emergency hospital visit for diabetes-related
  - After 1 months:
    - Glucose value (mg/dl): 152.5±17.3 vs. 141.3±3.8 (p=0.9)
  - Complications: Number of hypoglycaemic excursions:
## Pharmacological Strategies

<table>
<thead>
<tr>
<th>Study name</th>
<th>Design</th>
<th>Setting Place, setting and time</th>
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<tr>
<td>Elbarbary</td>
<td>2018 NCT0292825 RCT</td>
<td>Egypt, urban</td>
<td>DM1, age: 9 - 18 yrs, ≥ 5 yrs disease duration, active diabetic nephropathy in the form of microalbuminuria, HbA1c ≤ 8.5 %</td>
<td>n=90 52.3 % female age (yrs): 12.8±3.1 HbA1c (%): 7.85±1.95</td>
<td>IG (n=45): 1 g/d carnosine vs. CG (n=45): control/placebo group</td>
<td>Patients in both groups received oral ACE-Is</td>
<td>Primary: change in tubular damage marker</td>
<td>3.68±1.62 vs. 6.7±2.1 (p=0.001)</td>
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<td>no infection, renal impairment due to other causes than diabetes, other diabetic complications, hypersensitivity to carnosine</td>
<td></td>
<td>suspension activation vs. CG (n=35): sensor without low glucose suspension activation Duration: 1 month</td>
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<td>Safety: any AE</td>
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<td>2020</td>
<td>Egypt, urban</td>
<td>DM1 on insulin therapy with &gt; 5 yrs of disease duration, 12-18 yrs, active nephropathy, HbA1c ≥ 8.5 %, no infections, renal impairment due to other causes than diabetes, other diabetic complications</td>
<td>n=80 55% female age (yrs): 15.4 ± 1.6 HbA1c (%): 7.95±0.5 fasting glucose (mg/dl): 114.5±21.8 duration of diabetes (years): 8.65 ± 2.65</td>
<td>both groups received oral angiotensin-converting-enzyme inhibitors (captopril)</td>
<td>after 12 wks: HbA1c (%):</td>
<td>Primary: Cystatin C diet, physical activity, and metformin dosage</td>
<td>7.5±0.6 vs. 8.0±0.6 Fasting glucose (mg/dl): 107.7±14.1 vs. 116.4±17 (p=0.131)</td>
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**Pharmacological Strategies**

- **Elbarbary 2018**
  - RCT
  - NCT0292825
  - Egypt, urban
  - Setting: Place, setting and time
  - Population: Inclusion / Exclusion criteria
  - Characteristics
  - Intervention vs. Control Description with duration
  - Outcomes: Primary and secondary
  - Results: Longest follow-up period with intervention effects (IG vs. CG) with SD, 95%-CI or p value

- **Elbarbary 2020**
  - RCT
  - NCT03594240
  - Egypt, urban
  - Setting: Place, setting and time
  - Population: Inclusion / Exclusion criteria
  - Characteristics
  - Intervention vs. Control Description with duration
  - Outcomes: Primary and secondary
  - Results: Longest follow-up period with intervention effects (IG vs. CG) with SD, 95%-CI or p value

Elbarbary 2018: NCT0292825 RCT
- Egypt, urban
- DM1, age: 9 - 18 yrs, ≥ 5 yrs disease duration, active diabetic nephropathy in the form of microalbuminuria, HbA1c ≤ 8.5 %
- no infection, renal impairment due to other causes than diabetes, other diabetic complications, hypersensitivity to carnosine
- n=90 52.3 % female age (yrs): 12.8±3.1 HbA1c (%): 7.85±1.95
- IG (n=45): 1 g/d carnosine vs. CG (n=45): control/placebo group
- Patients in both groups received oral ACE-Is
duration: 1 month
- Primary: change in tubular damage marker
- Secondary: urinary albumin excretion (UAЕ), oxidative stress markers
- Safety: any AE
- Benefit for IG: 7.4 ±1.3 vs. 8.3±2.4
- change –9.88±7.12 vs. 3.89±2.28 (p=0.005)
- No adverse reactions were reported

Elbarbary 2020: NCT03594240 RCT
- Egypt, urban
- Setting: Place, setting and time
- Population: Inclusion / Exclusion criteria
- Characteristics
- Intervention vs. Control Description with duration
- Outcomes: Primary and secondary
- Results: Longest follow-up period with intervention effects (IG vs. CG) with SD, 95%-CI or p value

- no infection, renal impairment due to other causes than diabetes, other diabetic complications
- n=80 55% female age (yrs): 15.4 ± 1.6 HbA1c (%): 7.95±0.5 fasting glucose (mg/dl): 114.5±21.8 duration of diabetes (years): 8.65 ± 2.65
- both groups received oral angiotensin-converting-enzyme inhibitors (captopril)
- IG (n=40) oral vitamin B complex (B1,B6,B12) once daily vs.
- Primary: Cystatin C diet, physical activity, and metformin dosage
- after 12 weeks HbA1c (%): Benefit for IG: 7.5±0.6 vs. 8.0±0.6 Fasting glucose (mg/dl): 107.7±14.1 vs. 116.4±17 (p=0.131)

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<table>
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<td>CG (n=40): placebo</td>
<td>elevated liver enzymes, hyper-or hypothyroidism, hypertension, neoplasm, taking any vitamins or food supplements within 1 months before study start</td>
<td>Duration: 12 weeks</td>
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BMI: Body mass index; CG: Control group; CG/IG: Crossover from CG to IG; CI: Confidence interval; DM1: Type 1 diabetes; FPG: fasting plasma glucose; HbA1c: haemoglobin A1c; IG/CG: cross over from IG to CG; IG: intervention group; n: number of participants ;RCT: randomized controlled trial; SD: Standard-deviation; wks: weeks; yrs: years

**Supplementary Table 2**: Characteristics and results of studies on patients with DM1