Kefir intake as adjuvant onto glycemic control in diabetic rats

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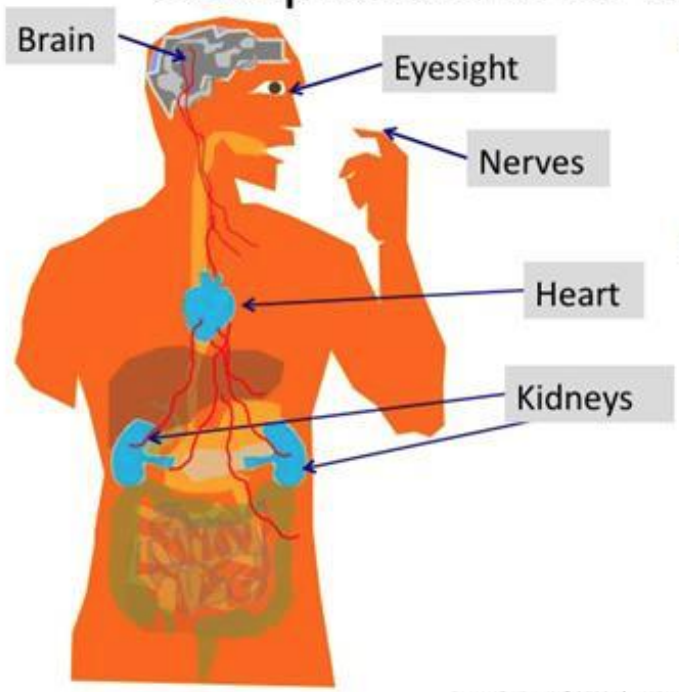
Outline

- Type I Diabettes Mellitus
- Kefir;
- Aim;
- Protocol;
- Oxidative stress;
- Results;
- Conclusion.

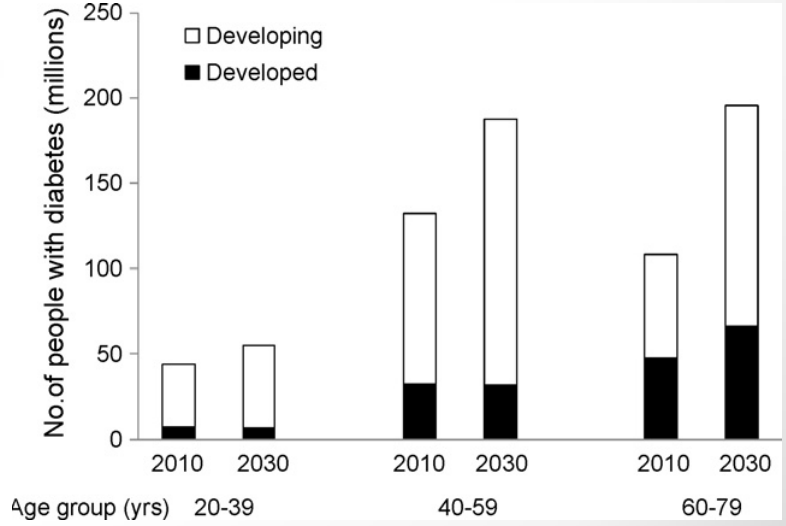
Diabetes Mellitus

Complications of Diabetes



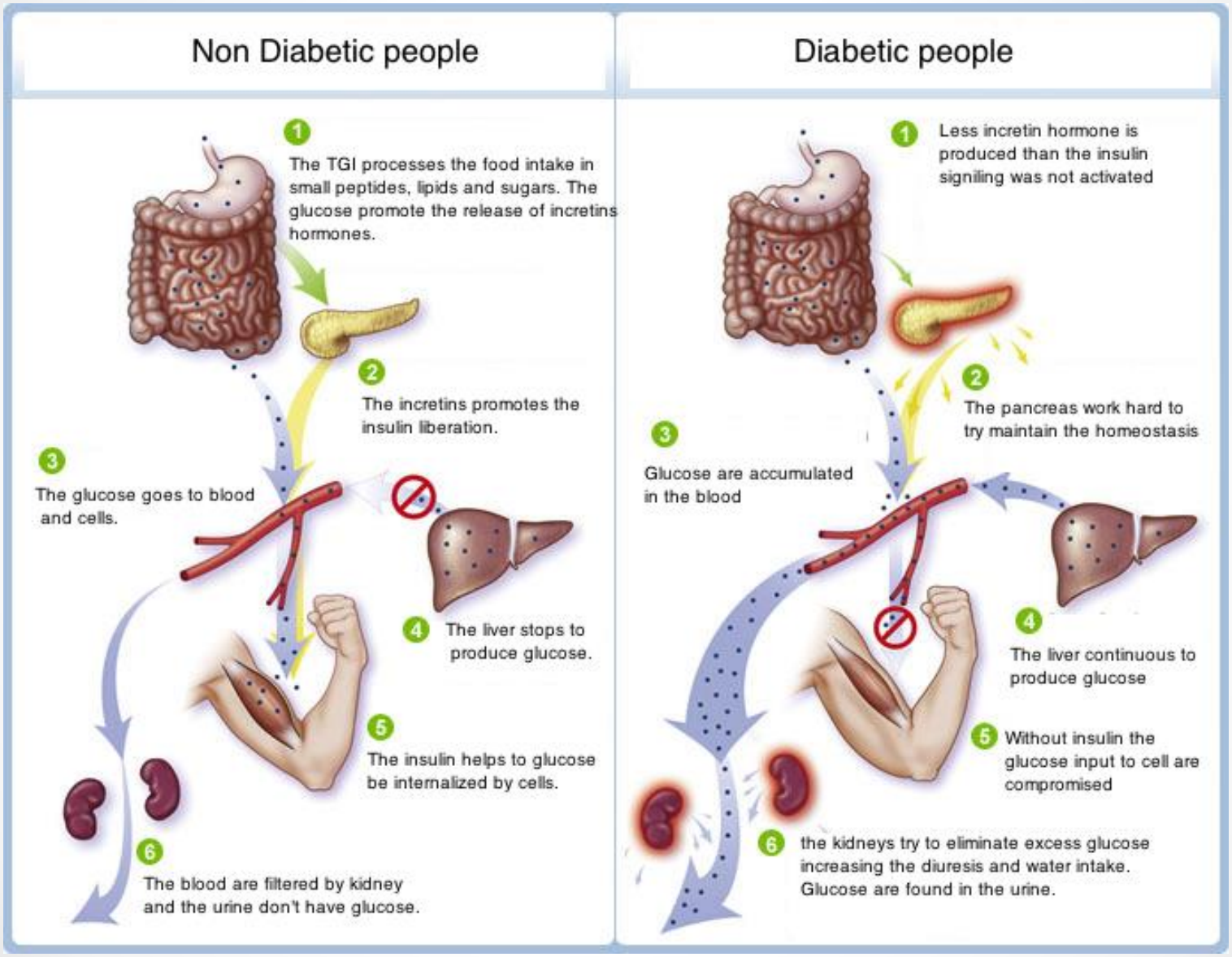
- Complications develop mainly because of high blood sugar levels over the years
- Diabetes increases the risk of getting:
  - heart problems
  - stroke
  - eye sight problems
  - kidney problems
  - foot problems
  - skin problems

Image: R. Kousar & M.Mayhew, Australian Community Centre for Diabetes, 2011

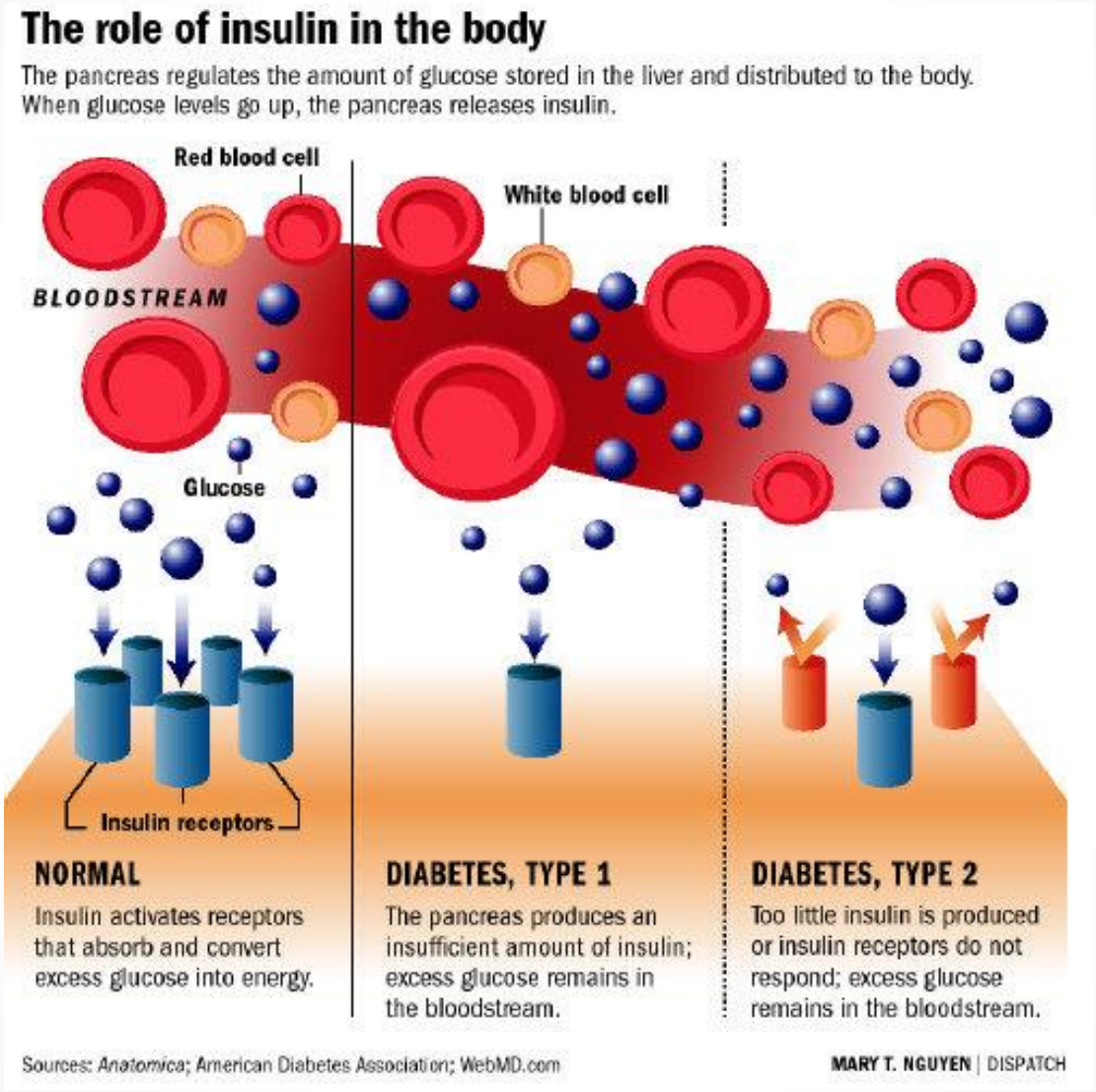


Source: http://www.conversationsforabetterworld.com/symptoms-of-diabetes-in-kids/

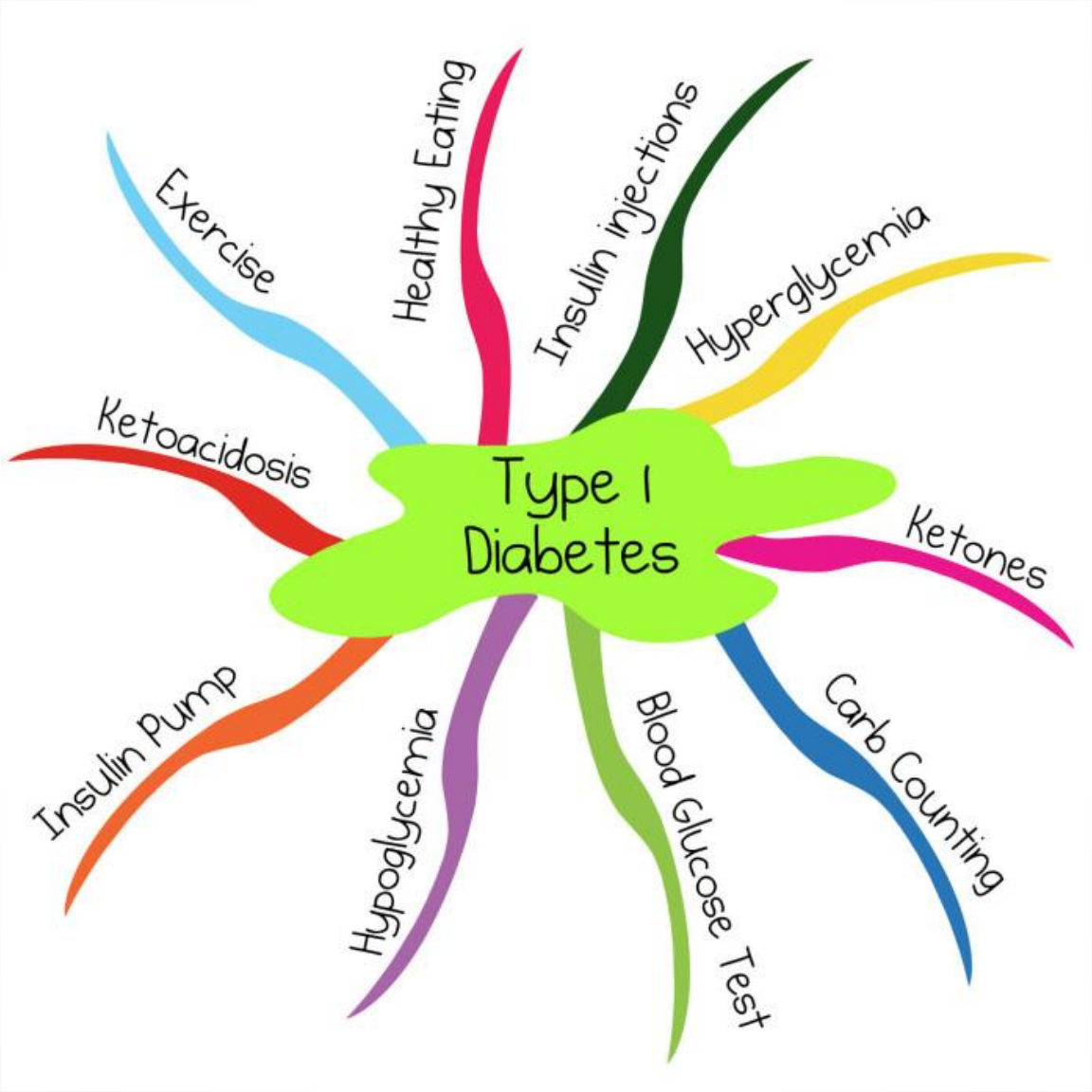
Source: Shaw, 2010



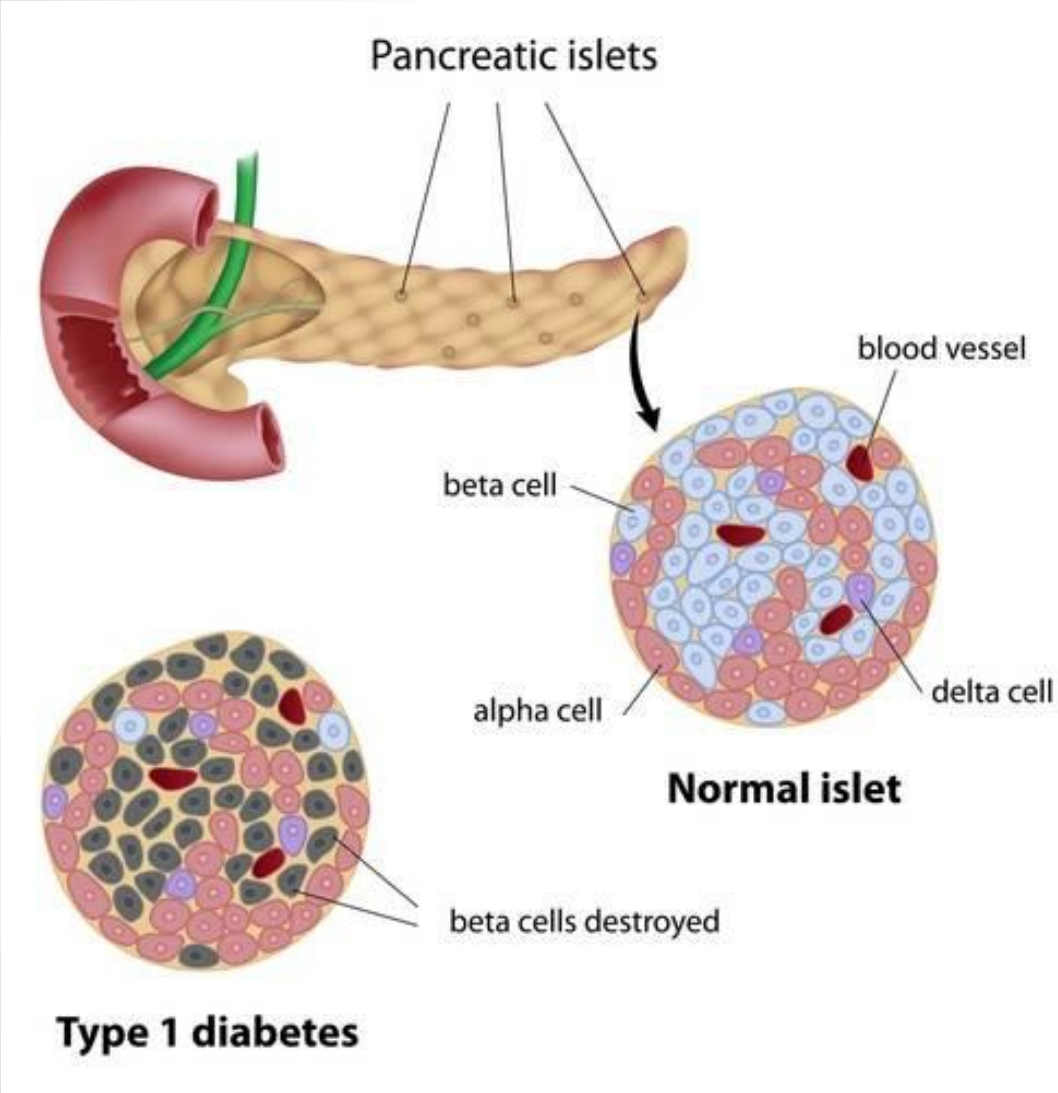
http://controlaradiabetes.pt/entender-a-diabetes/o-que-acontece-na-diabetes-tipo-2

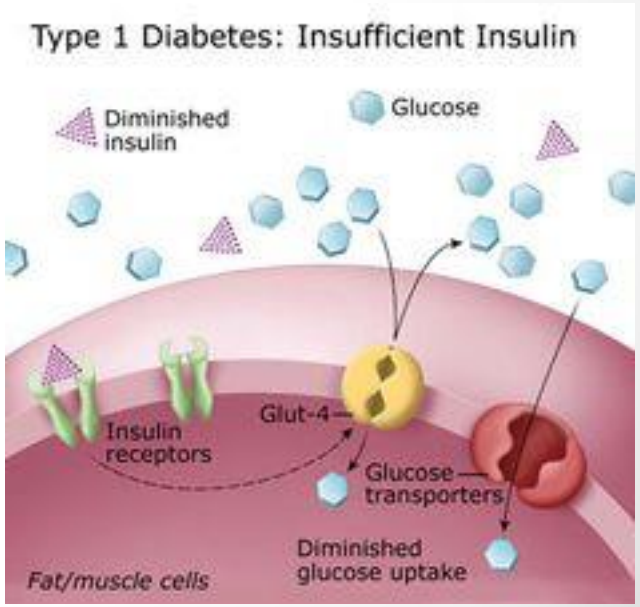


Source: https://alissajhunt.wordpress.com/category/diabetes/type-1-juvenile-diabetes/page/2/



Source: http://www.thetribuneregister.com/new-system-for-type-1-diabetics/2760/

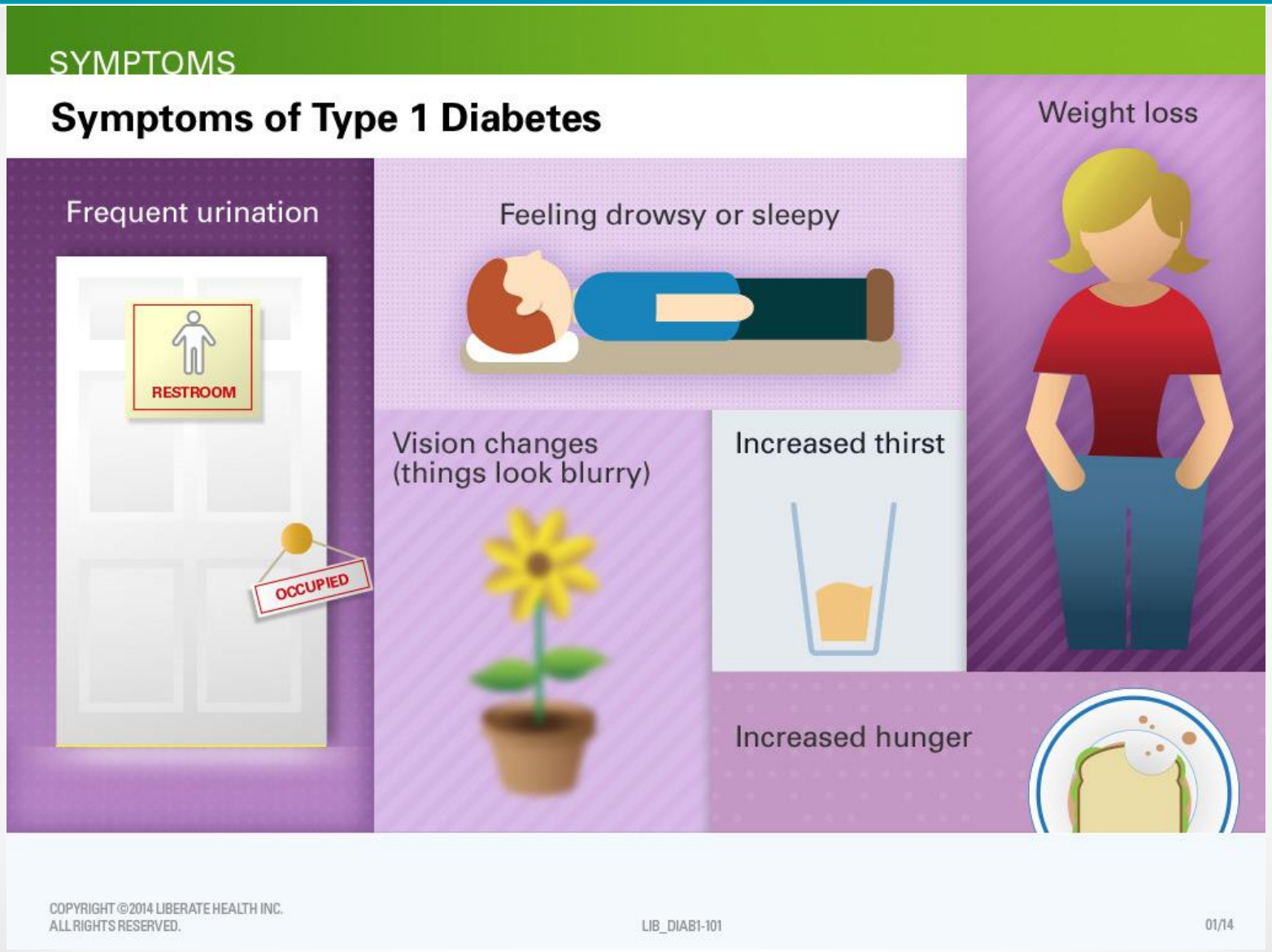




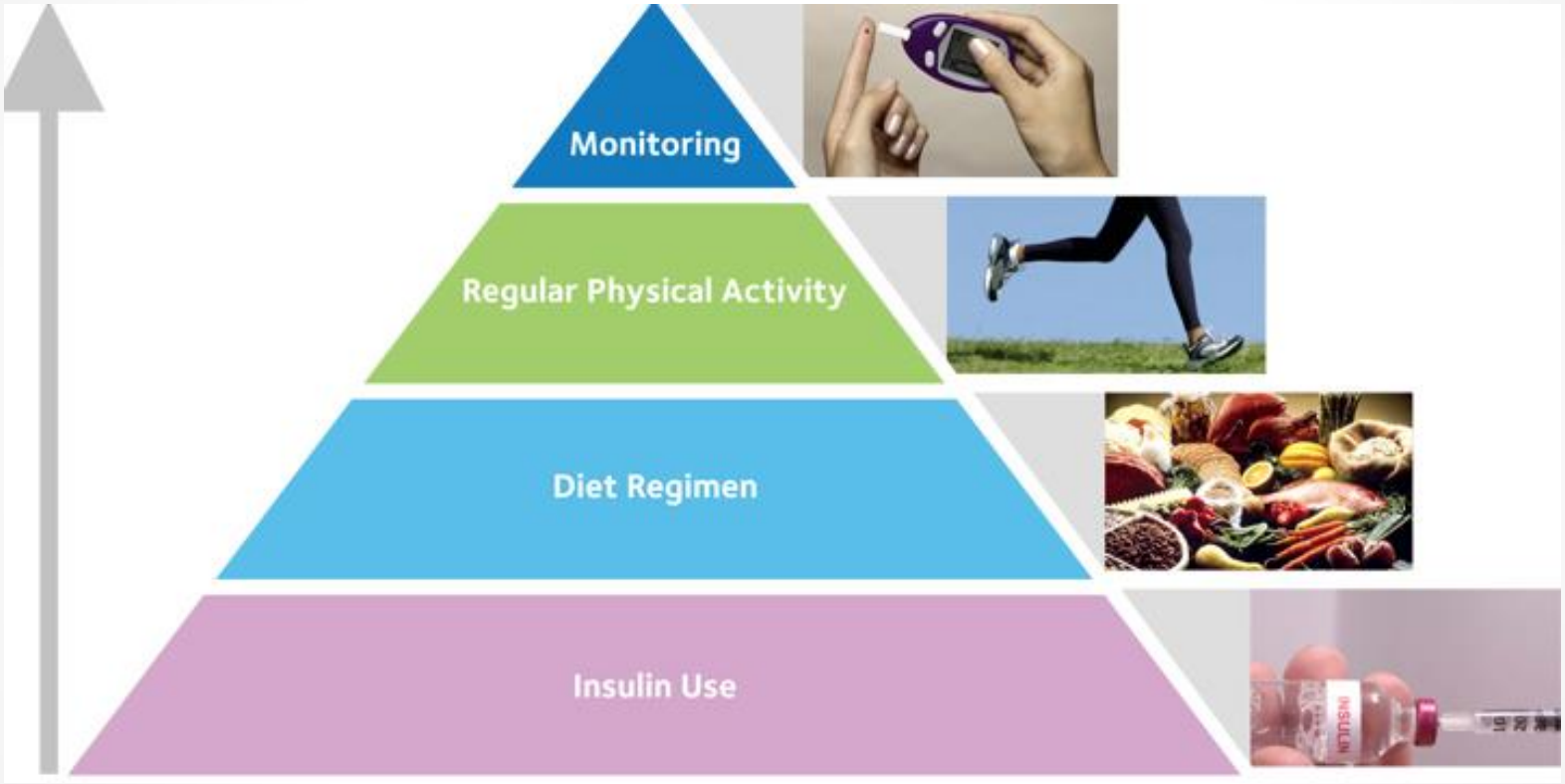
Source: http://www.123rf.com/photo_11271329_pancreatic-islet-normal-and-type-1-diabetic.html

Source: http://dtc.ucsf.edu/types-of-diabetes/type1/understanding-type-1-diabetes/how-the-body-processes-sugar/blood-sugar-other-hormones/

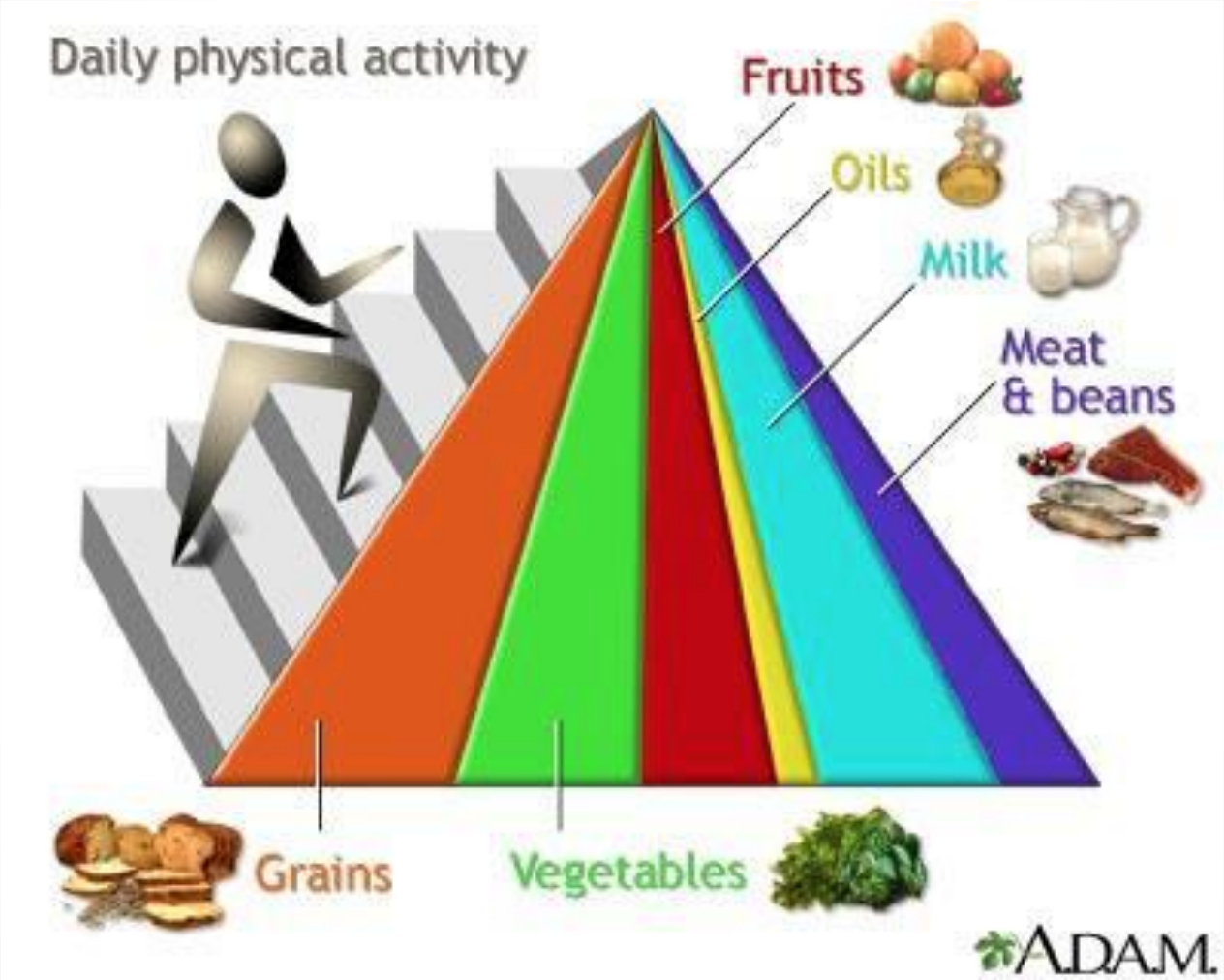
SYMPTOMS



Source: http://liberatehealth.us/liberate_condition/diabetes-2/diabetes/



Source: https://www.diabeticpick.com/blog/difference-between-diabetes-type-1-and-2/

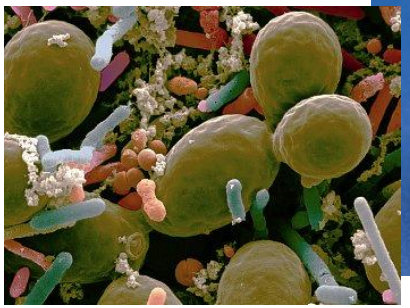


Source: http://www.nytimes.com/health/guides/specialtopic/weight-management/dietary-management.html

Kefir

- Kefir is a fermented milk that contains a complex symbiotic mixture of Lactic Acid Bacteria (LAB) and Molds.

- The main microorganisms are:
  - *Lactobacillus,*
  - *Lactococcus,*
  - *Leuconostoc,*
  - *Streptococcus,*
  - *Kluyveromyces,*
  - *Saccharomyces,*
  - *Torula.*

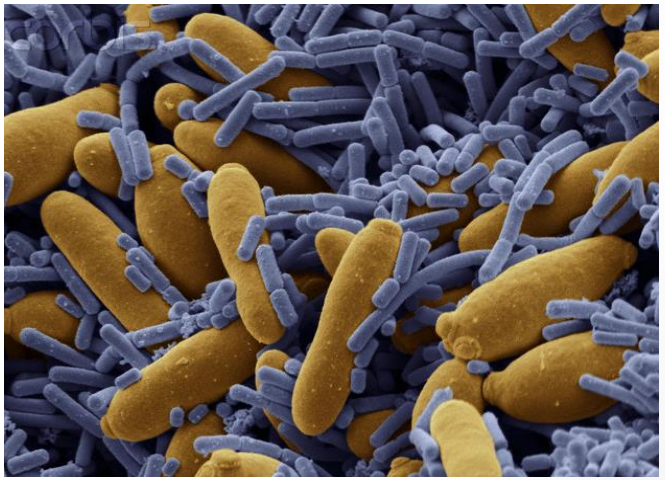


Kefir properties

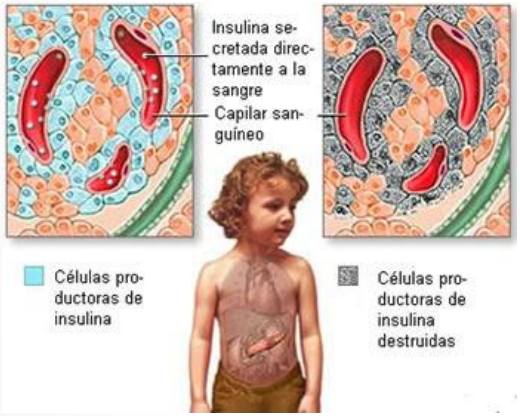
Kefir is known for **providing benefits** to human health through its **anti-inflammatory, immune-stimulatory and antioxidant properties**.

AIM

This study aimed at assessing the effects of **Kefir** on **oxidative stress and restoration of NO and in immunemodulation** in diabetic animals.



STZ - diabetic induction 45 mg/kg iv

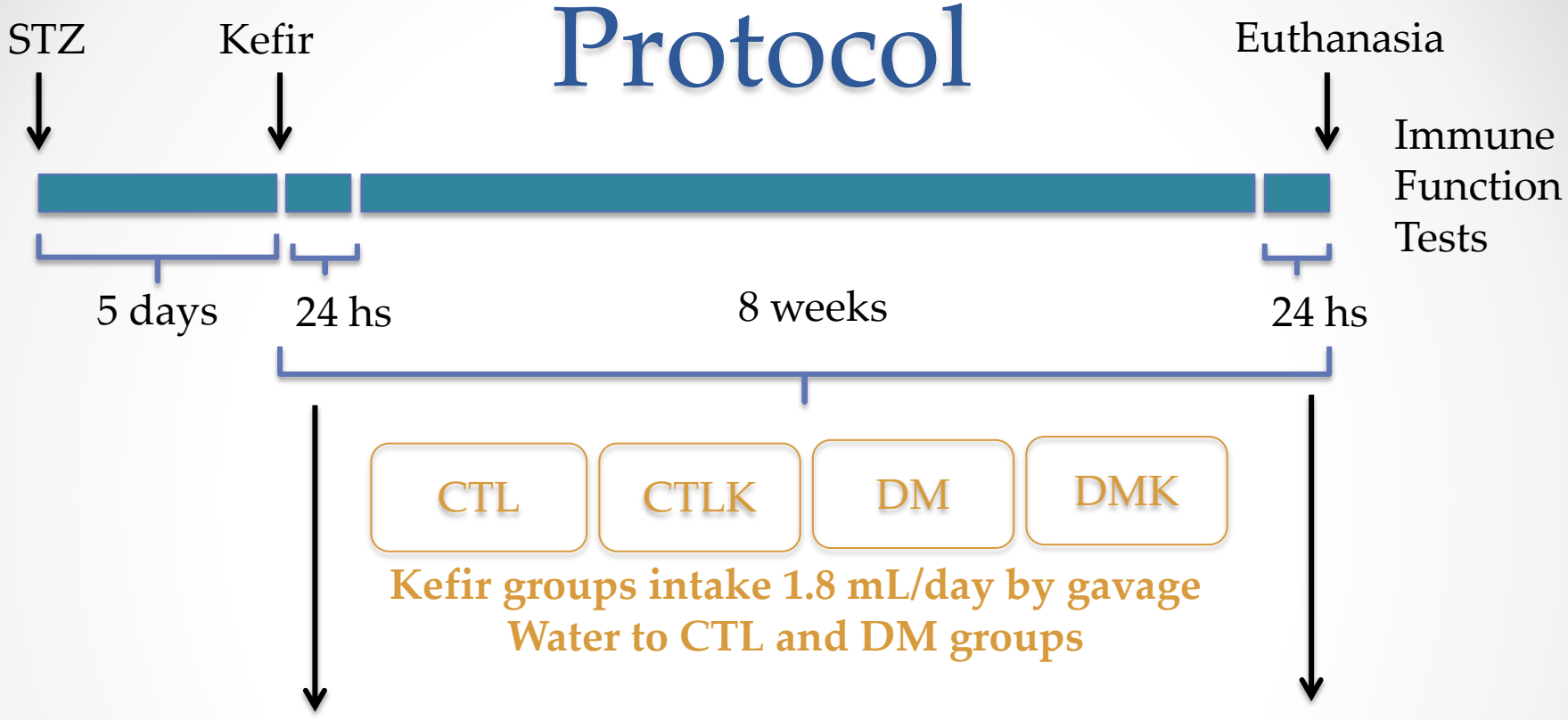


Kefir preparation

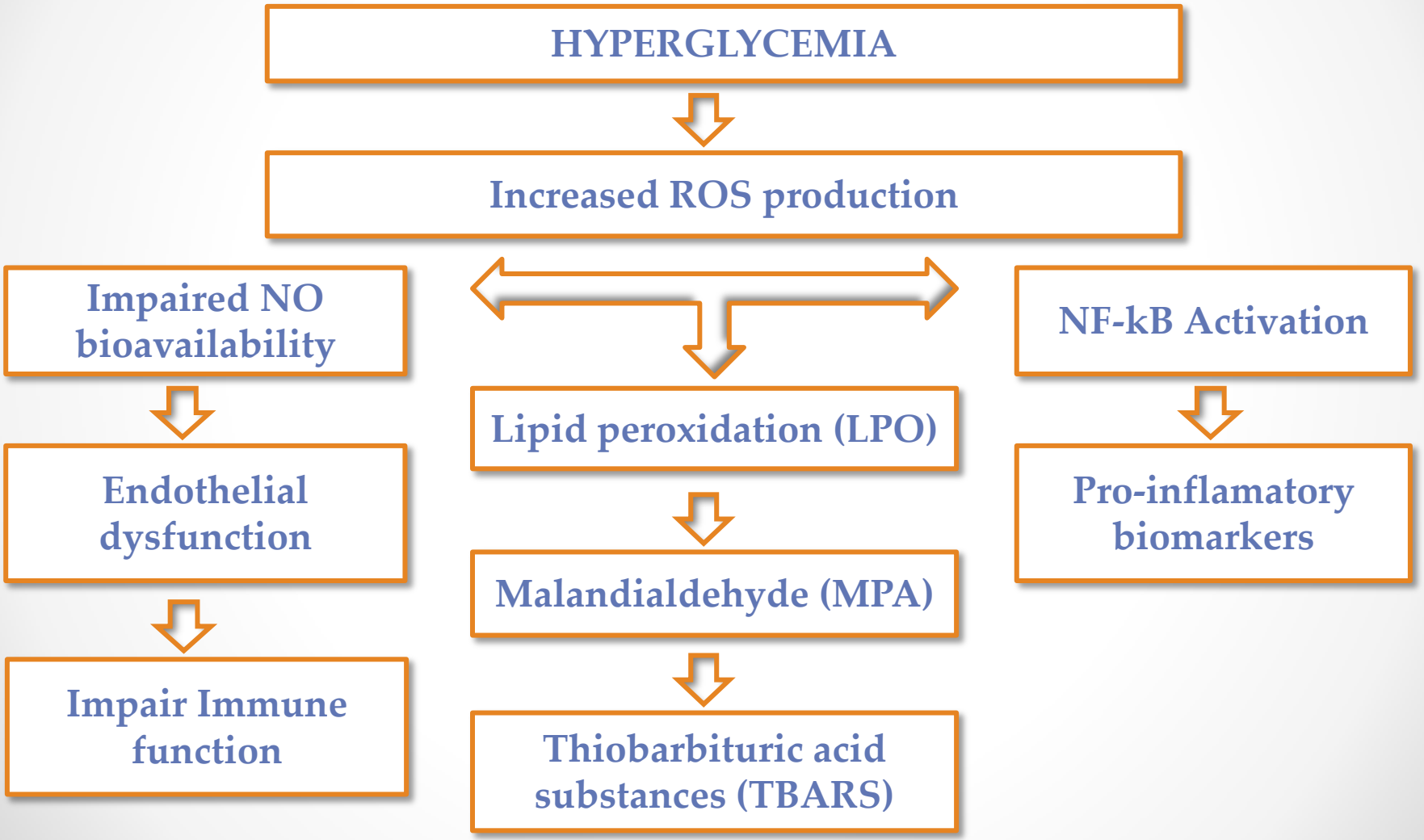
- Skimmed Milk
- 20mg/ 100mL Kefir DA Inoculation
- Fermentation until pH 4.6
- Cooling in ice bath
- Stiring(1min)
- Distribution in 50 mL cups
- Storing (4 °C)
- Kefir fermented milk

Source: https://www.nlm.nih.gov/medlineplus/ency/article/001214.htm

Protocol


STZ
Kefir
Euthanasia
Immune Function Tests
5 days
24 hs
8 weeks
24 hs
CTL
CTLK
DM
DMK
Kefir groups intake 1.8 mL/day by gavage
Water to CTL and DM groups
Water and Chow intake
Diuresis, Weight
Fasting Blood tolerance
Creatinine,Proteinuria,
Tbars, NO
Water and Chow intake
Diuresis, Weight
Fasting Blood tolerance
Creatinine,Proteinuria,
Tbars, NO

Oxidative Stress in DM



Punaro et al. 2014; Maciel et al. 2015

Metabolic profile

Parameters in experimental animals before treatment with Kefir

Parameters	CTL n=18	DM n=24
Water intake (mL/24 h)	30.0 ±0.9	80.2 ±4.9[c]
Chow intake (g/24 h)	19.1 ±0.4	23.9 ±0.9[c]
Diuresis (mL/24 h)	13.0 ±0.7	61.1 ±4.6[c]
Weight (g/24 h)	269.8 ±5.2	253.7 ±4.0[a]
Fasting blood glucose (mg/dL)	91.8 ±3.5	293.5 ±12.3[c]
NO plasmatic (µM)	89.7 ±12.2	58.9 ±9.0[a]
Excretion NO (µmol/24 h)	15.9 ±2.7	1.4 ±0.2[c]
TBARS plasmatic (nmol/mL)	3.03 ±0.06	3.17 ±0.06
Excretion TBARS (nmol/24 h)	86.9 ±5.3	192.4 ±10.4[c]
Urea plasmatic (mg/dL)	29.2 ±1.9	55.6 ±4.6[c]
Urea urinary (mg/dL)	7,556 ±444	2,403 ±129[c]
Creatinine plasmatic[y] (mg/dL)	0.28 ±0.02	0.33 ±0.01
Creatinine urinary[y] (mg/dL)	138.8 ±20.9	54.0 ±9.9[b]
Proteinuria (nmol/24 h)	11.2 ±0.6	21.4 ±1.0[c]

Values are expressed as means ± SEM. Student's unpaired *t* test.
[y]Corrected values per 100g weight; [a]$p<0.05$; [b]$p<0.01$; [c]$p<0.001$

Punaro et al. 2014

Metabolic profile

Metabolic profile, renal function, and oxidative stress of the groups after Kefir treatment.

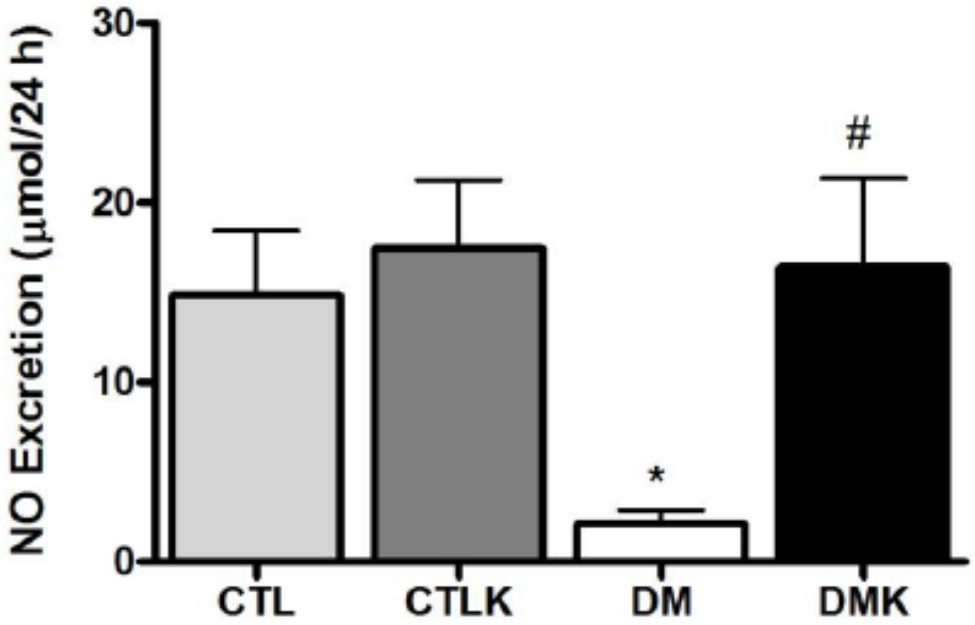
Variables	CTL	CTLK	DM	DMK
Water intake (mL/24 h)	24.8 ± 1.8	25.8 ± 3.7	124.4 ± 12.4[a]	94.1 ± 14.4[b,c]
Chow intake (g/24 h)	17.3 ± 0.6	19.1 ± 1.0	36.9 ± 2.0[a]	30.6 ± 2.3[b,c]
Diuresis (mL/24 h)	13.1 ± 1.0	13.7 ± 0.7	90.9 ± 9.0[a]	70.9 ± 9.4[b,c]
Weight (Δ)	67.5 ± 4.4	69.3 ± 1.6	25.3 ± 4.5[a]	35.3 ± 5.9[b]
Plasmatic urea (mg/dL)	31.9 ± 1.4	36.2 ± 2.5	58.5 ± 3.6[a]	47.6 ± 2.4[b,c]
Urinary urea (mg/dL)	8,691 ± 343	8,423 ± 229	2,006 ± 142[a]	2,996 ± 322[b,c]
Plasmatic creatinine (mg/dL)	0.71 ± 0.05	0.72 ± 0.04	0.75 ± 0.03	0.78 ± 0.05
Urinary creatinine (mg/dL)	131.7 ± 9.2	127.9 ± 4.5	33.2 ± 5.6[a]	34.8 ± 7.8[b]
Proteinuria (nmol/24 h)	10.4 ± 0.8	11.2 ± 0.7	25.5 ± 3.7[a]	21.0 ± 2.8[b]
Plasmatic NO (μM)	66.6 ± 4.3	77.8 ± 6.6	79.2 ± 5.0	76.5 ± 5.4
NO excretion (μmol/24 h)	14.9 ± 3.6	17.5 ± 3.8	2.1 ± 0.7[a]	16.4 ± 4.9
Plasmatic TBARS (nmol/mL)	3.32 ± 0.06	3.16 ± 0.08	3.79 ± 0.10[a]	3.58 ± 0.17
TBARS excretion (nmol/24 h)	81.6 ± 2.1	84.4 ± 4.3	300.4 ± 18.9[a]	248.9 ± 19.2[b,c]

Values are expressed as mean ± SEM. One-way ANOVA followed by Newman–Keuls Multiple Comparison post test. Control (CTL); control Kefir (CTLK); diabetic (DM); diabetic Kefir (DMK); $n = 9–12$/group.

[a] $p < 0.001$ vs CTL.
[b] $p < 0.01$ vs CTLK.
[c] $p < 0.05$ vs DM.

Punaro et al. 2014

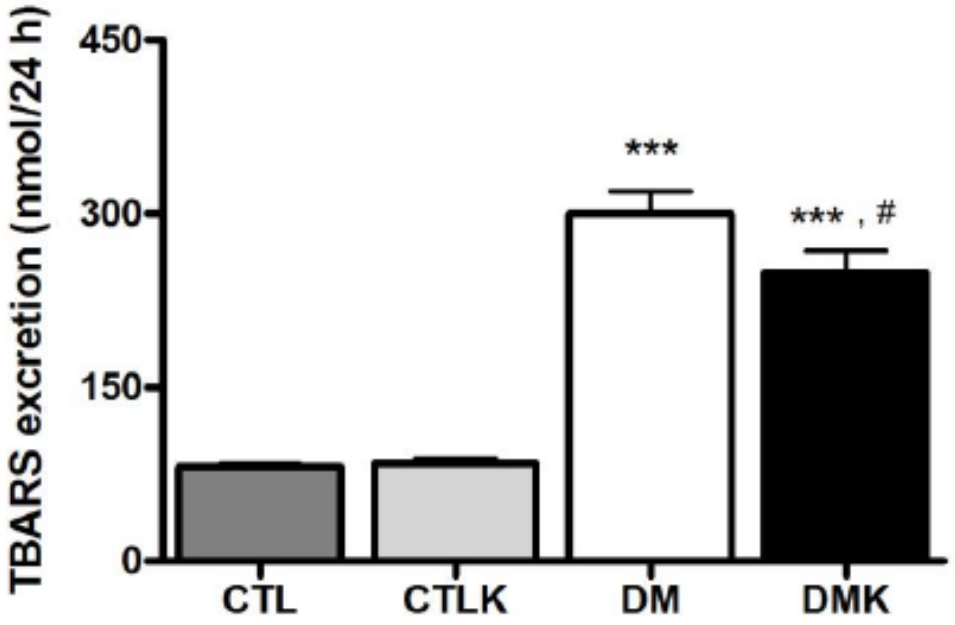
Oxidative Stress



Excretion of nitric oxide (NO) in all groups after 8 weeks of Kefir treatment. Control (CTL) n=9; control Kefir (CTLK) n=9; diabetic (DM) n=11; diabetic Kefir (DMK) n=12. Values are expressed as means ±SEM. One-away ANOVA followed by post test Student Newman Keuls. $^{*}p<0.05$ vs CTL; $^{\#}p<0.05$ vs DM.

Punaro et al. 2014

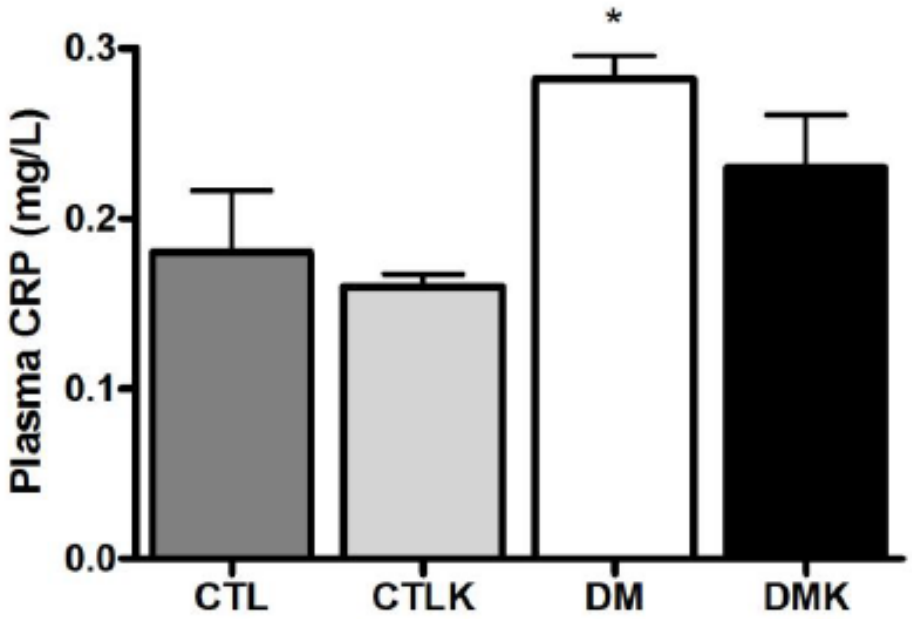
Oxidative Stress



Excretion of thiobarbituric acid reactive substances (TBARS) after 8 weeks of Kefir treatment. Control (CTL) n=9; control Kefir (CTLK) n=9; diabetic (DM) n=10; diabetic Kefir (DMK) n=12. Values are expressed as means ±SEM. One-away ANOVA followed by post test Student Newman Keuls. $^{***}p<0.001$ vs controls; $^{\#}p<0.05$ vs DM.

Punaro et al. 2014

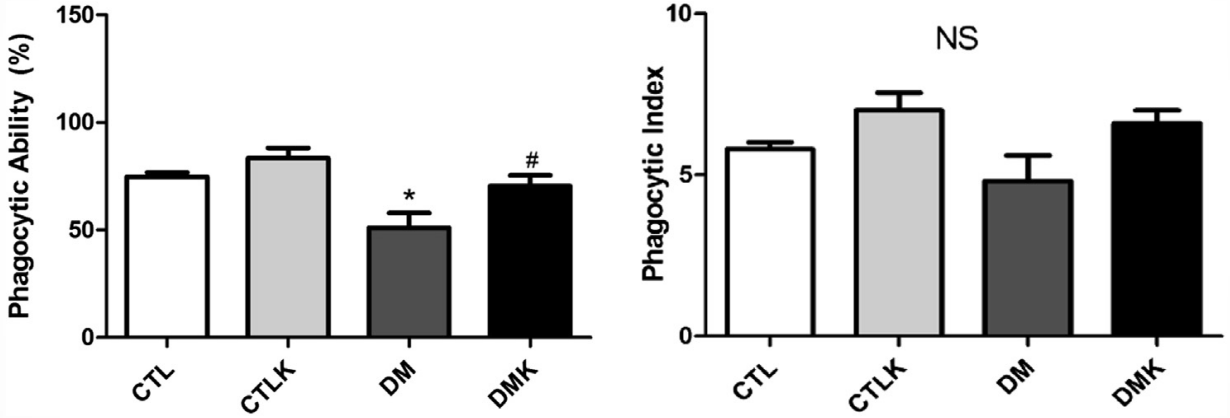
Inflammatory biomarker



Plasma C-reactive protein (CRP) levels after 8 weeks of Kefir treatment. Control (CTL) n=5; control Kefir (CTLK) n=5; diabetic (DM) n=6; diabetic Kefir (DMK) n=6. Values are expressed as means ±SEM. One-away ANOVA followed by post test Student Newman Keuls. * $p<0.05$ vs CTL.

Punaro et al. 2014

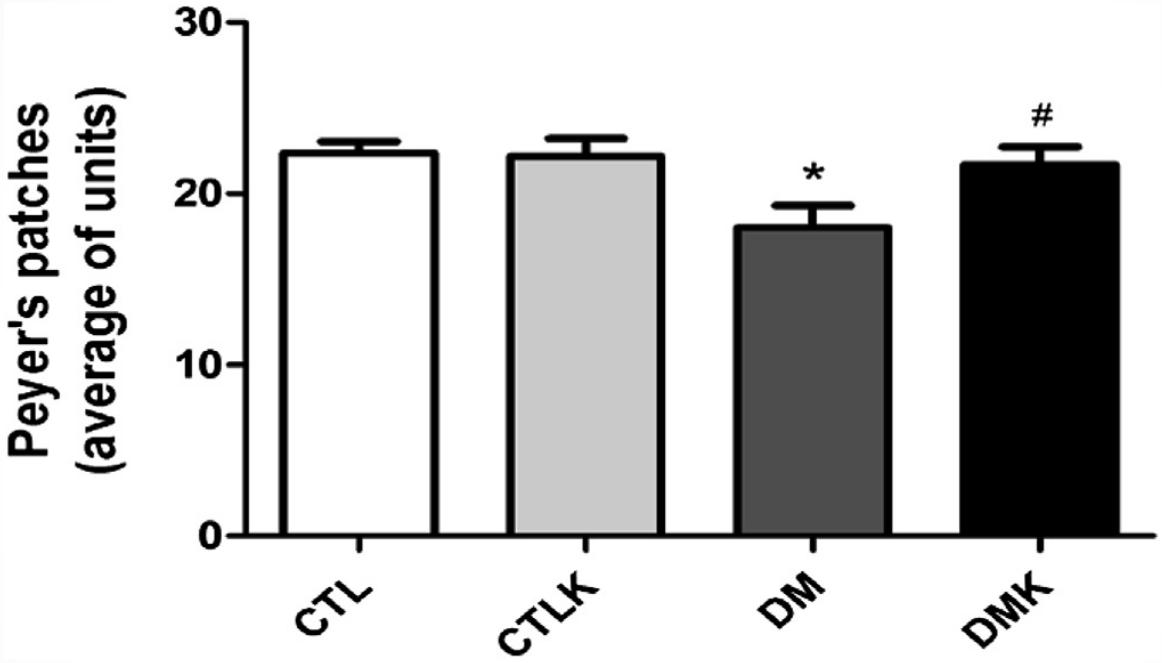
Phagocity Activity



Phagocytic ability and index of macrophages. Control (CTL); control Kefir (CTLK); diabetic (DM); diabetic Kefir (DMK), n = 5–8. ANOVA with Newman–Keuls Multiple Comparison post test. $p < 0.05$: *vs CTL; #vs DM; NS: non significant.

Maciel et al, 2015

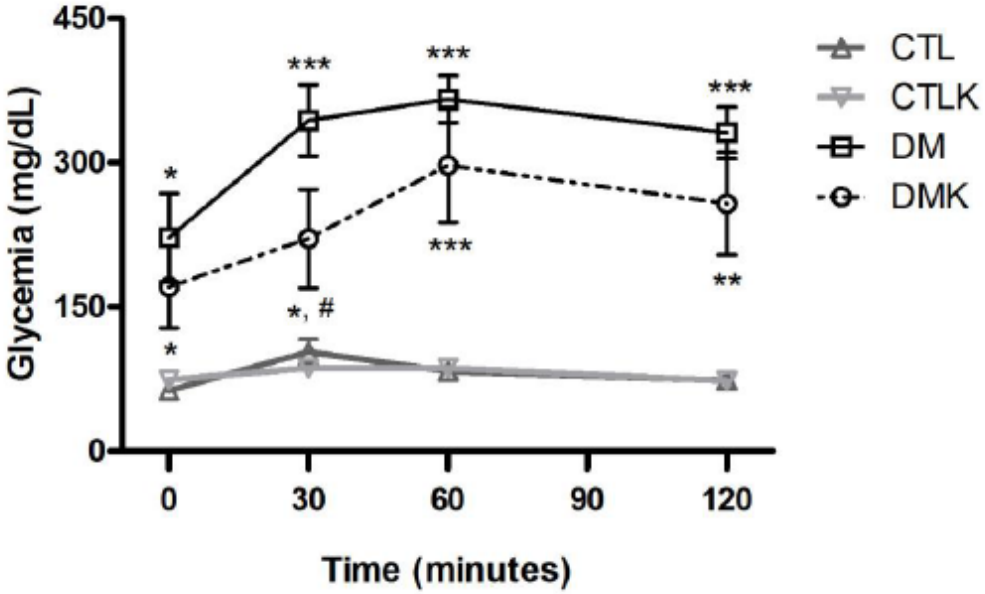
Peyer's Patchs



Peye'r patches (PP) in the small intestine. Control (CTL); control Kefir (CTLK); diabetic (DM); diabetic Kefir (DMK); n = 5–8. ANOVA with Newman–Keuls Multiple Comparison post test. $p < 0.05$: *vs CTL; #vs DM.

Maciel et al, 2015

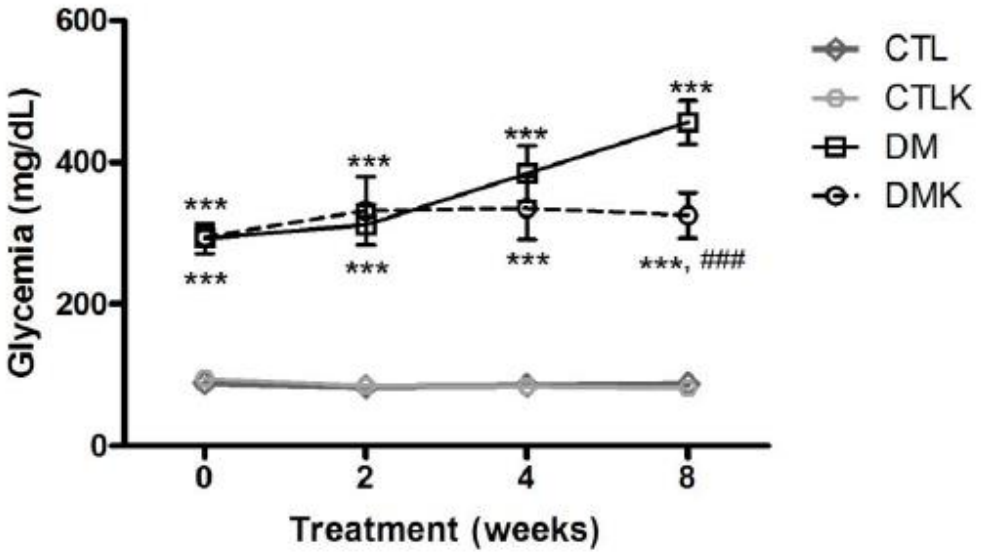
Oral Glucose Tolerance Test



Glycemia levels during oral glucose tolerance test (OGTT) after 8 weeks of Kefir treatment. Control (CTL) n=4; control Kefir (CTLK) n=5; diabetic (DM) n=6; diabetic Kefir (DMK) n=4. Values are expressed as means ±SEM. One-away ANOVA followed by post test Student Newman Keuls. $^{*}p<0.05$; $^{**}p<0.01$; $^{***}p<0.001$ vs controls; $^{\#}p<0.05$ vs DM.

Punaro et al. 2014

Glycemia levels



Glycemia levels in the 5th day after diabetes induction (0) and 2-4-8 weeks after Kefir treatment. Control (CTL) n=9; control Kefir (CTLK) n=9; diabetic (DM) n=12; diabetic Kefir (DMK) n=12. Values are expressed as means ± SEM. One-away ANOVA followed by post test Student Newman Keuls. $^{***}p<0.001$ vs controls; $^{\#\#\#}p<0.001$ vs DM

Punaro et al. 2014

Conclusion

The results obtained in this study show that **Kefir treatment significantly reduced** the progression of STZ-induced **hyperglycaemia, oxidative stress and** potentialize the **immune response modulatation** in rats.

Kefir may play a role in **slowing the metabolic changes** that contribute to DM as a non-pharmacological adjuvant improving the immunocompetence **to better control of glycaemia**, reducing or delaying the onset of complications associated with this disease.

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