The effect of red yeast rice on lipids, inflammatory markers and plasma glucose in subjects with mild hypercholesterolemia and mildly elevated plasma glucose

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Background

- Several large clinical trials have demonstrated that lowering cholesterol levels with statins reduces the incidence of cardiovascular events and mortality.
- Red yeast rice has been used in China for centuries as a food preservative, food colorant, and to make rice wine. E.g. the famous red Peking duck is coloured by red yeast rice. Red yeast rice contains small amounts of monakolin K. This is the same substance discovered by Endo in 1979 and later commercialised as the drug lovastatin (Mevacor, MSD).
- Several Chinese studies[1] and one American study[2] indicate that red yeast rice has a significant cholesterol lowering effect.
- A recent Chinese study[3] indicates that red yeast rice can significantly decrease the incidence of nonfatal myocardial infarction and deaths from coronary heart disease compared to placebo.
- Some reports have suggested an effect of red yeast rice on fasting plasma glucose by unknown mechanisms.

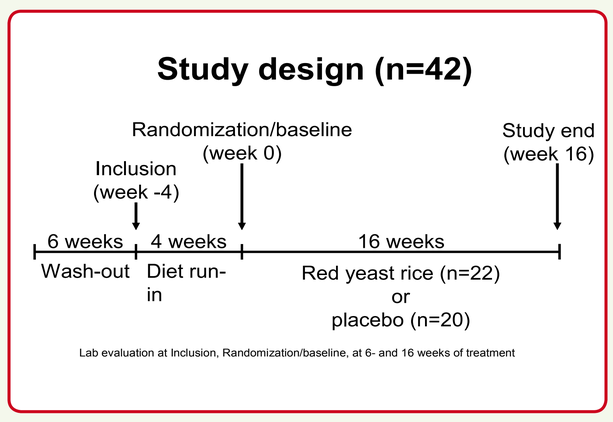
Objectives

- To evaluate in a European (Caucasian) population the effect of red yeast rice compared to placebo on lipids, inflammatory markers and plasma glucose markers in subjects with mild hypercholesterolemia and mildly elevated plasma glucose.

Methods

- A randomized double-blind placebo controlled study (figure 1)

Figure 1



- Primary endpoints: The effect of red yeast rice on fasting blood values of total-cholesterol (TOT-C), LDL-cholesterol (LDL-C), HDL-cholesterol (HDL-C), triglyceride (TG), apolipoprotein A1 (APOA1), and apolipoprotein B (APOB).
- Secondary endpoints: The effect of red yeast rice on fasting plasma glucose, glycosylated haemoglobin (HbA1c), and high sensitivity CRP

- Eligible subjects were men and women between 18 and 75 years with:
  - fasting 3.0 mmol/L < LDL-cholesterol < 6.0 mmol/L
  - fasting TG < 4.5 mmol/L
  - 5.5 < HbA1c% < 7.5 and/or fasting plasma glucose > 5.5 mmol/L
- The subjects (n = 42) were randomized and received either red yeast rice (**Hypocol®, Wearnes Biotech & Medicals Pte Ltd, Singapore**: 4 capsules / day = 2400 mg red yeast rice / day) (n=22) or placebo (n=20) for 16 weeks.
- Prior to inclusion patients already taking cholesterol lowering drugs underwent a 6 weeks wash out period.
- At inclusion all patients were instructed to follow a diet according to NCEP ATP III during a 4 week diet run in phase prior to randomization.
- Fasting serum lipids (TOT-C, LDL-C, HDL-C, TG, APOB and APOA1), safety parameters (CK, ASAT, ALAT, GT, creatinine, urea) and fasting plasma glucose were measured at inclusion (week -4), baseline/randomization (week 0), and after 6 and 16 weeks on treatment.
- Fibrinogen, high sensitivity CRP, TSH, insulin, and C-peptide were measured at inclusion, baseline/randomization and after 16 weeks on treatment.
- Blood pressure, weight, and waist circumference measurements were collected at first and last visit.
- Food questionnaire (Smart Diet®) was collected at first and last visit to allow measurement of any systematic dietary change.

Results

- 40 persons (23 men and 17 women, mean age mean age 60 years) completed the study and were included in the data analysis.
- Data were assumed normal distributed. One-sample and paired-sample T tests were used for data analysis.
- Patients receiving red yeast rice experienced a significant cholesterol lowering effect for both total-cholesterol, LDL-cholesterol and APOB compared to placebo after 6 and 16 weeks on treatment (Table 1. Figure 2-4).
- Secondary endpoints, safety blood parameters, blood pressure measurements, weight and waist circumference measurements, and food questionnaire score did not differ between the two groups (Table 2).

Table 1. Lipid concentrations in treatment and control group. Table shows mean concentration ± standard deviation.

	Red yeast rice			Placebo		
	Baseline	6 weeks	16 weeks	Baseline	6 weeks	16 weeks
TOT-C	5.71 ± 0.73	4.72 ± 0.80[123]	4.76 ± 0.65[123]	5.86 ± 1.04	5.71 ± 0.88	6.17 ± 0.97
LDL-C	3.72 ± 0.77	2.88 ± 0.74[123]	2.82 ± 0.61[123]	4.15 ± 0.93	3.93 ± 0.80	4.29 ± 0.97
HDL-C	1.64 ± 0.39	1.67 ± 0.44	1.72 ± 0.43[3]	1.33 ± 0.36	1.37 ± 0.39	1.48 ± 0.40[3]
TG	1.02 ± 0.61	0.84 ± 0.40	0.91 ± 0.44	1.29 ± 0.88	1.42 ± 1.27	1.51 ± 1.52
APOB	0.99 ± 0.17	0.79 ± 0.18[123]	0.76 ± 0.13[123]	1.11 ± 0.27	1.05 ± 0.20	1.11 ± 0.21
APOA1	1.47 ± 0.23	1.50 ± 0.28	1.61 ± 0.31[3]	1.35 ± 0.25	1.35 ± 0.17	1.47 ± 0.27

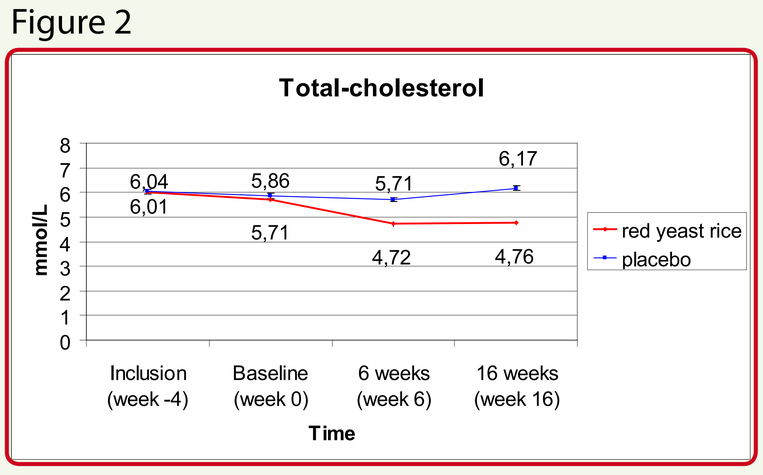
[1]Significant decrease from baseline to this visit in treatment group compared to control group (P<0.003)
[2]Significantly different from control group at same visit (P<0.001).
[3]Significantly different from baseline (P<0.045)

Table 2. Safety data and secondary endpoints in treatment and control group. Table shows mean concentration ± standard deviation.

	Red yeast rice			Placebo		
	Baseline	6 weeks	16 weeks	Baseline	6 weeks	16 weeks
CK	144 ± 63	134 ± 73	129 ± 48	131 ± 64	139 ± 70	121 ± 81
ASAT	31 ± 10	28 ± 5	35 ± 31	32 ± 11	31 ± 14	30 ± 16
ALAT	26 ± 13	28 ± 14	29 ± 19	35 ± 17	31 ± 12	30 ± 13
glucose	5.18 ± 0.95	5.21 ± 1.15	5.25 ± 1.36	5.49 ± 0.75	5.34 ± 0.76	5.20 ± 0.70
HbA1c	5.57 ± 0.28	Not measured	5.47 ± 0.24	5.64 ± 0.35	Not measured	5.56 ± 0.29
Hs-CRP	1.93 ± 2.45	Not measured	2.01 ± 2.82	3.51 ± 8.05	Not measured	1.64 ± 2.24

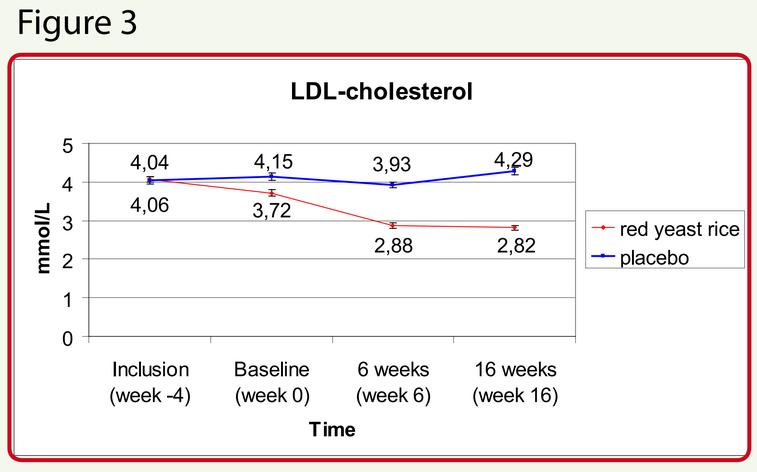
No significant difference (P<0.05) were seen between the groups

Figure 2



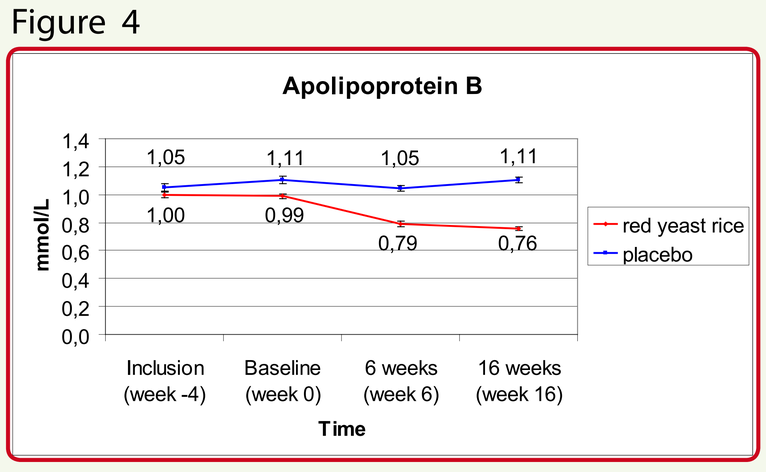
Mean reduction in total-cholesterol for patients receiving red yeast rice were 17.3% and 16.6% after 6 and 16 weeks of treatment, respectively. This was significant (P<0.001) different from placebo. Error bars show 95% confidence interval.

Figure 3



Mean reduction in LDL-cholesterol for patients receiving red yeast rice were 22.6% and 24.2% after 6 and 16 weeks of treatment, respectively. This was significant (P<0.001) different from placebo. Error bars show 95% confidence interval

Figure 4



Mean reduction in apolipoprotein B for patients receiving red yeast rice were 20.2% and 23.2% after 6 and 16 weeks of treatment, respectively. This was significant (P<0.003) different from placebo. Error bars show 95% confidence interval

Safety data

- No serious adverse events were reported.
- 9 minor adverse events (AE) were reported during the study, 2 of which lead to drop out. In the red yeast group 1 person dropped out of the study due to general discomfort, and 1 person reported increasing flatulence, 6 other AE's were very unlikely to be caused by study drug. 1 AE occurred in the placebo group.

Conclusion

- This study is the first to show a cholesterol lowering effect of red yeast rice in a European (Caucasian) population.
- The cholesterol lowering effect of the tested red yeast rice product is comparable to e.g. 20 mg Lovastatin or 40 mg of fluvastatin[4]

The famous red Peking duck is coloured by red yeast rice
Photo: Marina Oliphant

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References

1 Kou W., Z. Lu, Guo J. [Effect of xuezhikang on the treatment of primary hyperlipidemia]. (Chinese). Zhonghua Nei Ke.Za Zhi. 1997;36:529-31
2 Heber D., et al. Cholesterol-lowering effects of a proprietary Chinese red-yeast-rice dietary upplement. Am J Clin Nutr 1999;69:231-36.
3 Lu Z L. [China coronary secondary prevention study (CCSPS)]. (Chinese). Zhonghua Xin.Xue.Guan.Bing.Za Zhi. 2005;33:109-15.
4 Edwards J., Moore R. Statins in hypercholesterolemia: A dose-specific meta -analysis of lipid changes in randomized, double blind trials. BMC Family Practice 2003;4:

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