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Effects of Cardiozym™ Supplementation on Lipid Profile and Cardiovascular Risk in Patients at Risk for Cardiovascular Disease

A Retrospective Chart Review

ABSTRACT

INTRODUCTION

Numerous previous studies have examined the effects of dietary supplements on cardiovascular (CV) health, but there is limited research on the effects of combined nutraceuticals on lipid profile and CV risk.

OBJECTIVES

To investigate the effects of a novel nutraceutical product (Cardiozym™) containing red yeast rice (RYR, monacolin K), hydroxytyrosol (HT), and coenzyme Q10 (CoQ10) on lipid profile and CV risk.

METHODS

In this retrospective chart review, data were collected from the medical records of 38 patients at risk for cardiovascular disease (CVD) who were started on Cardiozym™. After 6 months of supplementation, the primary outcome was improvement in lipid profile and reduction in CVD risk as measured by the Framingham Risk Score (FRS). Health parameters and CV risk scores were compared between baseline and 6-month follow-up using a paired samples t-test. Linear mixed models adjusted for patient sex, age, weight, and use of antihypertensive medication were used to test the change in each parameter from baseline to follow-up.

RESULTS

Cardiozym™ had a significant beneficial effect on serum levels of total cholesterol, low-density lipoprotein cholesterol (LDL) and non-high-density lipoprotein cholesterol. Improvements in blood pressure levels were also observed. Significant associations were found between alcohol consumption and changes in mean LDL and triglyceride levels. After adjustment for age, sex, weight, and use of antihypertensive medications, significant reductions in mean FRS and 10-year CV risk were observed.

CONCLUSIONS

A 6-month Cardiozym™ supplementation based on RYR, HT and CoQ10 not only improved lipid profile in subjects at risk of CVD but also mitigated CV risk, highlighting its effectiveness as an intervention to promote heart health.

KEYWORDS

CV Disease, Red Yeast Rice, Hydroxytyrosol, CoQ10, Framingham Risk Score, Lipid profile, Blood Pressure.

INTRODUCTION

Cardiovascular disease (CVD) in its various forms remains the leading cause of morbidity and death worldwide, particularly in developing countries, accounting for approximately 32% of all deaths in 2022.[1] Over the past 40 years, there has been a dramatic decline in CVD mortality, accompanied by major advances in the management and prevention of CVDs through pharmaceutical interventions, lifestyle modifications, and dietary supplements.[2]

Dietary supplements have received considerable attention as a potential adjunctive therapy in the management of various CVDs. Several research studies have examined the effects of dietary supplements on cardiovascular (CV) health, but the results have been inconsistent. For example, multivitamin supplementation has been shown to be ineffective in reducing the risk of CVD or mortality in the absence of a clear nutrient deficiency.[3,4] On the other hand, other compounds have shown promising effects in improving cardiac function and lowering blood pressure (BP) and lipids.

Among these compounds, Red Yeast Rice (RYR) produced by yeast fermentation of white rice, has been shown to possess cholesterol-lowering effects provided by its major bioactive compound, monacolin K. According to a recent review, significant reductions in total cholesterol (TC) and low-density lipoprotein cholesterol (LDL) levels were observed in patients with mild to moderate hypercholesterolemia following RYR supplementation, while effects on high-density lipoprotein cholesterol (HDL) and triglycerides (TG) were generally inconsistent.[5]

Coenzyme Q10 (CoQ10), a naturally occurring antioxidant, has been suggested to have cardioprotective effects due to its essential role in gene expression, energy metabolism and reduction of oxidative stress. Recent evidence has shown that CoQ10 supplementation prevents the oxidation of LDL and its accumulation in arteries, and reduces vascular stiffness and hypertension in patients with CVD.[6,7] More specifically, it significantly decreased TC and increased HDL levels without affecting TG and LDL levels.[8,9]

Current research has also highlighted the potential CV benefits of hydroxytyrosol (HT), a compound found in extra virgin olive oil with potent antioxidant and anti-inflammatory properties. According to a recent review, HT supplementation induced significant reductions in TC, LDL, and TG levels, while increasing HDL levels and preventing LDL particles stemming from oxidative damage.[10,11] Lower BP levels were also observed after HT supplementation.[10]

Combinations of these compounds are also available, but few studies have demonstrated their beneficial effects in combination therapy. D'Addato et al. reported that a combination of monacolin, CoQ10, HT and berberine improved the lipid pattern in hypercholesterolemic patients by reducing LDL and TG levels.[12] In hypertensive and hypercholesterolemic patients with metabolic syndrome, a formulation of RYR and CoQ10 reduced TC, TG, LDL, serum glucose, and BP, without affecting HDL levels.[13] In addition, a systematic review and meta-analysis of randomized controlled clinical trials of a nutraceutical combination including red yeast extract (monacolin K), CoQ10, in addition to folic acid, astaxanthin, policosanols, and berberine demonstrated improved serum levels of TC, TG, both HDL and LDL, and fasting blood glucose (FBG), without beneficial effects on BP.[14]

These studies highlight the beneficial effects of different combinations on lipid profile and BP levels in different patient populations. However, no previous studies have evaluated the effects of such combinations in terms of CV risk. Therefore, this study was designed to evaluate the effect of 6 months of Cardiozym™, a combined therapy of RYR, CoQ10 and HT, on patients' lipid profile, FBG, HbA1C and BP. In addition, the study aimed to evaluate the effect of Cardiozym™ on patients' CV risk using the Framingham Risk Score (FRS) and the 10-year risk of CVD, thereby adding valuable insights to the existing body of knowledge in the field of CV health.

METHODS

STUDY DESIGN AND SETTINGS

A retrospective chart review was performed in Malta between August 2020 and December 2022 and included patients initiated on Cardiozym™, a combination of RYR (200 mg, of which monacolin K 10 mg), CoQ10 (100 mg), and HT (5 mg), to evaluate the effects of Cardiozym™ administration. Data were extracted from patients' medical records at a baseline time point corresponding to the initial visit and at a follow-up time point 6 months after baseline.

STUDY PARTICIPANTS

Patients aged 20 years and older at risk for CVD and atherosclerosis or with a family history of CVD, atherosclerosis, and sudden death were enrolled. Patients with an indication for lipid-lowering therapy and those with borderline dyslipidemia were also included. Those with borderline dyslipidemia had an LDL between 130 mg/dl and 159 mg/dl. At-risk patients were those with an LDL > 160 mg/dl. Patients who had previously received statins and were intolerant of their treatment were also included in the study.

Exclusion criteria were patients under 20 years, familial hypercholesterolemia, allergy or contraindication to any of the components of Cardiozym™, pregnancy, active CVD, or a history of myocardial infarction (MI). Patients treated with statins or other lipid-lowering agents, such as fibrates or ezetimibe, and those taking lipid-lowering supplements were excluded from the study.

DATA COLLECTION AND OUTCOME MEASURES

Data from both the baseline and follow-up visits were extracted from patients' medical records using a case report form (CRF). At baseline, data collected included demographic information (age, sex, occupation), weight and height, and medical history (CVD, hypertension, diabetes, chronic kidney disease [CKD], cancer, and family history of CVD). In addition, the data collected included the lipid profile (TC, LDL, HDL, TG, non-HDL), FBG and HbA1C, BP measurements (systolic [SBP], and diastolic blood pressure [DBP]), lifestyle factors (smoking, alcohol consumption, menopause), and current medication use for antihypertensive drugs, corticosteroids, antiplatelet agents, and Framingham risk calculation. At the second visit, changes in any of the baseline characteristics were recorded.

The FRS was calculated for the total patient population based on the following coronary risk factors: age, sex, smoking, TC (mg/dl), HDL (mg/dl), SBP, and antihypertensive intake. The 10-year % risk of CVD in percentage was calculated using the Framingham score calculator and classified into three categories as low risk (< 10%), intermediate risk (10–20%), and high risk (> 20%) for developing CHD in the coming 10 years.

The study was an observational analysis of pre-existing medical records and did not involve direct contact with participants. However, each patient was assigned a unique identification number for this study to maintain the confidentiality and privacy of the data collected.

STATISTICAL METHODS

To summarize patient characteristics, means with standard deviations and frequencies with percentages were used to describe continuous variables and categorical variables, respectively. Two-tailed paired sample t-tests were used to compare changes from baseline for variables including lipid profile parameters and CV parameters. Separate multivariate linear regression models were used to evaluate the association between patient age, sex, weight, smoking and alcohol consumption and the change in LDL, TG, FBS, SBP, FRS, and the 10-year risk of CVD between baseline and follow-up. Baseline to follow-up changes in TC and LDL levels, SBP, FRS, and 10-year risk of CVD were evaluated using linear mixed models adjusting for age, sex, weight, and the use of antihypertensive medications.

A p-value <0.05 was considered statistically significant. All statistical analyses were performed using Stata v17.0 software.

RESULTS

PATIENT CHARACTERISTICS AT BASELINE AND FOLLOW-UP

Data from 38 patients were collected and analyzed. A summary of patient characteristics at baseline is shown in Table 1. The mean (standard deviation [SD]) age of the patients was 50.60 (11.38) years, and 63% were female. Common CVD risk factors included hypertension treated with antihypertensive drugs (21.1%), family history of CVD (50%), and sudden death (7.9%). At follow-up, patients' mean (SD) body weight decreased from 75.90 (12.13) to 72.34 (15.48), and an increase in medication use was observed (53% to 63.2%). Corticosteroids were checked because this is a medicine that could affect atherosclerosis; hence, it could be a confounding factor for the risk of CVD.

CHANGE IN HEALTH PARAMETERS AND CARDIOVASCULAR RISK BETWEEN BASELINE AND FOLLOW-UP

Table 2 shows the health parameters and indicators of CVD risk of patients started on Cardiozym™ at baseline and at 6-month follow-up. When comparing health parameters between baseline and 6 months after Cardiozym™ intake, we found that there was a statistically significant decrease in TC, LDL, non-HDL, SBP and DBP. A small, significant increase in FBG was observed, while there was no significant change in TG and HbA1C levels. Only 16 patients had records of their HbA1C, so this was reported before and after the initiation of Cardiozym™. Regarding CVD risk parameters, there were significant reductions in both FRS and 10-year CVD risk between baseline and follow-up.

The relationship between changes in health (lipid profile, FBG, HbA1C levels and BP measurements) and cardiovascular disease risk parameters after 6 months of Cardiozym™ use and age, sex, weight, smoking, and alcohol consumption is shown in Table 3. Significant associations were found between alcohol consumption and change in mean LDL levels (coefficient = -56.68, 95% CI: -99.46 to -13.90, p = 0.011) and change in mean TG (coefficient = -18.88, 95% CI: -4.46 to -33.20, p = 0.012). No significant associations were found between changes in the other health parameters, including both FRS and 10-year CV risk, and any of the independent variables studied.

The linear mixed models adjusted for age, sex, weight, and antihypertensive medication use showed statistically significant reductions in mean TC (coefficient = -40.3, 95% CI: -49.7 to -31.1, p < 0.001) and LDL (coefficient = -38.3, 95% CI: -47.1 to -29.5, p < 0.001) between baseline and follow-up visits. In addition, significant reductions in mean SBP (coefficient = -1.98, 95% CI: -2.93 to -1.03, p < 0.001), mean FRS (coefficient = -1.79, 95% CI: -2.73 to -0.85, p < 0.001), and 10-year cardiovascular risk (coefficient = -1.89, 95% CI: -2.96 to -0.81, p < 0.001) were observed between the two visits.

The linear mixed models adjusted for age, sex, weight, and the use of antihypertensive drugs, showed statistically significant reductions in mean cholesterol levels (coefficient = -40.3, p < 0.001, 95% CI: -49.7 to -31.1) and LDL levels (coefficient = -38.3 p < 0.001, 95% CI: -47.1 to -29.5), and mean SBP (coefficient = -1.98, p < 0.001, 95% CI: -2.93 to -1.03), between the initial visit and the follow-up visit (Table 4).

CHANGE IN CARDIOVASCULAR RISK BETWEEN BASELINE AND FOLLOW-UP

At baseline, the average FRS was 11.87 ± 5.37. Based on the FRS, the predicted 10-year CV risk was found to be 4.74 ± 5.82. Overall, 86.8%, 10.5%, and 2.6% of patients initiated on Cardiozym™ were at low, intermediate, and high risk of CVD according to FRS categorization. Following the 6-month administration of Cardiozym™, there was a significant overall decrease in both FRS (p<0.001) and 10-year CV risk (p<0.001), as shown in Table 2.

After adjusting for age, gender, weight, smoking and alcohol consumption, no significant associations were found between changes in both FRS and 10-year CV risk and any of the variables. However, adjusting for age, gender, weight, and the administration of antihypertensive medications in the linear mixed models' analysis, significant reductions in mean FRS (coefficient = -1.79, $p < 0.001$, 95% CI: -2.73 to -0.85) and 10-year CV risk estimates (coefficient = -1.89, $p < 0.001$, 95% CI: -2.96 to -0.81) were observed between the two visits (Table 4).

DISCUSSION

In the present study, in patients at risk for CVD, we showed that 6 months of Cardiozym™ treatment significantly reduced TC, LDL, and non-HDL levels. The study also showed a statistically significant reduction in both SBP and DBP. In addition to these improvements in various health parameters, significant reductions from baseline to follow-up were observed in mean FRS and consequently in 10-year CV risk.

While numerous previous studies have demonstrated the lipid-lowering effects of RYR,[15-17] HT,[10,18] and CoQ10[9,19-21] in monotherapy, only a limited number of studies have examined their synergistic effects. In this regard, our results contributed to this field by demonstrating their combined effect on the reduction of TC, LDL, and non-HDL levels, similar to the results of other studies.[22-23]

Our study reported a statistically significant decrease in both SBP and DBP over the 6-month supplementation period, even after adjustment for antihypertensive medication. However, in literature, the effects of combinations of RYR, HT, or CoQ10 on BP were variable. While data from one study[13] reported a similar trend, indicating that RYR and CoQ10 co-therapy led to a significant reduction in BP, another recent systematic review and meta-analysis showed no beneficial effects of a similar combination on BP.[14] These discrepancies may be due to differences in patient characteristics such as medical conditions, different formulations used, intervention protocol and duration, as well as assessment methods and study designs.

In terms of CVD risk reduction, our results are comparable to those of studies of RYR, CoQ10, or HT as monotherapy, showing a reduction in CV risk. According to some studies, RYR formulations were effective in reducing metabolic syndrome risk and preventing CVD.[24,25] Others showed that CoQ10 supplementation reduced CVD risk in diabetic patients by lowering CVD risk-related indices such as TC and LDL.[21] Notably, none of these studies examined the synergistic effects of the components of Cardiozym™ or assessed CVD risk using the FRS, as in our study. Therefore, direct comparisons with the results of our study are challenging. Overall, by shedding light on the effects of these components, our study highlights Cardiozym™ as an intervention with promising implications for CV health management. It is important to note that while these results are encouraging, the relatively limited number of studies investigating the synergistic effects of HT, CoQ10, and RYR combinations on CV risk underscores the need for further research, ideally including controlled trials with longer follow-up, to validate and refine our findings.

STRENGTHS AND LIMITATIONS

The novelty of our study was to investigate the synergistic effects of RYR, HT and CoQ10 administered in a single formulation to modulate lipid levels, BP, and CV risk. The use of the well-established FRS provides a quantitative measure of CV risk, increases the accuracy and consistency of the measurements, and strengthens the validity of our results. In addition, a wide range of health parameters, including lipid profiles, blood pressure and FRS, were systematically evaluated, providing a comprehensive overview of the impact of Cardiozym™ on CV health.

However, several limitations of the study should be noted, including the observational nature of its design. Data were collected from patients' medical records, which did not allow

for an assessment of patient adherence to the prescribed dose of the supplement, in addition to the relatively small sample size, which may limit the generalizability of the findings. Another limitation was that patients' lifestyle modifications could have contributed to the positive outcomes. Future clinical trials with control groups, longer follow-up, and larger sample sizes are essential to extend our findings.

CONCLUSION

To our knowledge, this is the first study to evaluate the real-world use of Cardiozym™ in patients at risk for CVD. While our findings contribute to the existing body of knowledge on the effects of RYR and monacolin K, CoQ10 and HT on lipid profile, they provide valuable insights into the synergistic beneficial effects of this combination on CVD risk. Further comprehensive studies, ideally including controlled trials with longer follow-up, are essential to validate and refine our findings and ultimately contribute to a more holistic understanding of the role of Cardiozym™ in improving CV outcomes.

ABBREVIATIONS

BP: Blood Pressure
CI: Confidence Interval
CKD: Chronic Kidney Disease
CoQ10: Co-enzyme Q10
CV: Cardiovascular
CVD: Cardiovascular Disease
DBP: Diastolic Blood Pressure
CRF: Case Report Form
FBG: Fasting Blood Glucose
FRS: Framingham Risk Score
HDL: High-Density Lipoprotein
HT: Hydroxytyrosol
IRB: Institutional Review Board
LDL: Low-Density Lipoprotein
MI: Myocardial Infarction
RYR: Red Yeast Rice
SBP: Systolic Blood Pressure
SD: Standard Deviation
TC: Total Cholesterol
TG: Triglycerides

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Table 1. Baseline characteristics of patients initiated on Cardiozym™ (n=38).

	Baseline	Follow-up
	Mean (SD)	Mean (SD)
Age (years)	50.60 (11.38)	
Height (cm)	164.18 (8.52)	
Weight (kg)	75.90 (12.13)	72.34 (15.48)
	n (%)	n (%)
Sex		
Female	24 (63.0)	
Male	14 (37.0)	
Menopause	17 (71.0)	
Hormone replacement therapy	1 (6.0)	
Medication intake	19 (53.0)	24(63.2)
Antihypertensives	8 (21.1)	
Corticosteroids	0 (0.0)	
Smoking	4 (10.5)	4 (10.5)
Alcohol consumption	4 (10.5)	4 (10.5)
Relevant medical history		
Cardiovascular disease	0 (0.0)	
Cancer	1 (2.6)	
Diabetes	1 (2.6)	
Renal	0 (0.0)	
Hypertension	8 (21.1)	
Chemotherapy in the past two years	0 (0.0)	
Family History of CVD	19 (50.0)	
Family history of sudden death	3 (7.9)	

CVD: Cardiovascular Disease, SD: Standard deviation. Values are expressed as frequency and percentage except for age, height, and weight that are given as means and standard deviations.

Table 2. Health parameters and cardiovascular risk of patients initiated on Cardiozym™ at baseline and 6-month follow-up.

	Baseline	Follow-up	P-value
Lipid Profile			
Total cholesterol (mg/dL)	241.6 ± 29.7	201.2 ± 33.5	<0.001
LDL (mg/dL)	160.3 ± 30.8	122.0 ± 31.3	<0.001
HDL (mg/dL)	56.8 ± 14.1	57.4 ± 11.7	0.65
Triglycerides (mg/dL)	147.8 ± 93.7	132.9 ± 66.6	0.17
Non-HDL (mg/dL)	176.7 ± 49.4	146.2 ± 31.5	0.026
Fasting Blood Sugar	5.24 ± 0.77	6.19 ± 4.24	0.02
HbA1C (n=16)	5.47 ± 0.52	5.47 ± 0.45	0.96
Blood Pressure			
Systolic Blood Pressure (mm Hg)	126.92 ± 13.52	123.36 ± 9.05	0.02
Diastolic Blood Pressure (mm Hg)	78.21 ± 9.34	75.21 ± 6.11	0.03
Framingham Risk Score (FRS)	11.87 ± 5.37	9.92 ± 4.49	<0.001
10-Year Cardiovascular Risk (%)	4.74 ± 5.82	2.78 ± 3.59	<0.001
Cardiovascular Risk Category			
Low risk	33 (86.8%)	35 (94.6%)	
Intermediate risk	4 (10.5%)	1 (2.70%)	
High risk	1 (2.6%)	1 (2.70%)	

LDL: Low-Density Lipoprotein Cholesterol, HDL: High-Density Lipoprotein Cholesterol, HbA1C: Glycated Hemoglobin. Summary statistics are expressed as mean ± standard deviation for continuous variables, and as frequency (%) for categorical variables.

Table 3. Linear regression models for the association between age, sex, weight, smoking, alcohol consumption and change in health and cardiovascular disease risk parameters between baseline and after 6 months of Cardiozym™ use in patients included in the study.

		Coefficient	Lower 95% CI	Upper 95% CI	P-value
LDL	Age	0.35	- 0.78	1.49	0.53
	Sex	10.38	-15.83	36.59	0.427
	Weight	0.28	-0.77	1.34	0.6
	Smoking	28.75	-17.19	74.7	0.212
	Alcohol	-56.68	-99.46	-13.9	0.011*
Triglycerides	Age	0.67	-0.55	1.89	0.271
	Sex	4.5	-23.41	32.41	0.745
	Weight	-0.69	-1.75	0.37	0.196
	Smoking	-18.94	-60.22	22.34	0.357
	Alcohol	-18.88	-4.46	-33.20	0.012*
Fasting blood glucose	Age	0.67	-0.55	1.89	0.271
	Sex	4.5	-23.41	32.41	0.745
	Weight	-0.69	-1.75	0.37	0.196
	Smoking	-18.94	-60.22	22.34	0.357
	Alcohol	-18.88	-60.16	22.4	0.358
SBP	Age	0.075	-0.34	0.187	0.564
	Sex	2.065	-4.009	8.14	0.495
	Weight	-0.11	-0.36	0.13	0.36
	Smoking	3.97	-5.55	13.49	0.403
	Alcohol	8.16	-1.044	17.37	0.081
Framingham Risk Score	Age	-0.08	-0.16	0.008	0.075
	Sex	-1.45	-3.46	0.56	0.153
	Weight	0.019	-0.064	0.101	0.65
	Smoking	0.85	-2.37	4.06	0.59
	Alcohol	0.29	-2.94	3.52	0.858
10-Year Cardiovascular Risk	Age	-0.05	-0.15	0.053	0.340
	Sex	1.25	-1.076	3.58	0.283
	Weight	-0.028	-0.12	0.06	0.547
	Smoking	-0.99	-4.67	2.69	0.588
	Alcohol	1.25	-2.42	4.92	0.5

CI: Confidence interval; LDL: Low-Density Lipoprotein Cholesterol, SBP: Systolic Blood Pressure.
* A p-value <0.05 is considered statistically significant.

Table 4. Linear mixed models for the change in health and cardiovascular disease risk parameters between baseline and after 6 months of Cardiozym™ use in patients included in the study.

	Coefficient	Lower 95% CI	Upper 95% CI	P-value*
Total Cholesterol	-40.3	-49.7	-31.1	<0.001
LDL	-38.3	-47.1	-29.5	<0.01
SBP	-1.98	-2.93	-1.03	<0.001
Framingham Risk Score	-1.79	-2.73	-0.85	<0.001
10-Year Cardiovascular risk	-1.89	-2.96	0.81	0.001

CI: Confidence Interval; LDL: Low-Density Lipoprotein Cholesterol, SBP: Systolic Blood Pressure.
* A p-value <0.05 is considered statistically significant.