

# May Phytomedicines Play a Role in Cardiovascular Risk Reduction?

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## Abstract

C.F. suffered myocardial infarction despite low cardiovascular risk as defined by the Swiss Working Group on Lipids and Atherosclerosis (AGLA). C.F. wished replacement of his synthetic blood pressure lowering and antilipidemic medication by phytomedicines. A combination of standardized cocoa and black garlic extracts with coenzyme Q10 plus black seed oil with 30 mg thymoquinone in the daily dose normalized total cholesterol and maintained low blood pressure. However, the AGLA desired setpoint of LDL cholesterol (below 1.6 mmol/L) was not achieved. Since such low LDL cholesterol concentrations are not necessarily associated with less mortality, we agreed that C.F. continued with the phytomedicines because his quality of life was better than during the intake of the synthetic medications.

**Keywords:** agla cardiovascular risk score; myocardial infarction; cocoa–black garlic extract; coenzyme q10; black seed oil

## Abbreviations

**AGLA** : Swiss Working Group on Lipids und Atherosclerosis,

**CV** : Cardiovascular,

**HBMP** : Home blood pressure measurements,

**MI** : Myocardial infarction,

**Chol** : Cholesterol,

**CoQ10** : Coenzyme Q10

**SD** : Standard deviation

## Introduction

There is no doubt that among the herbal armamentarium cocoa [1], black garlic [2] and black seed and its oil [3] have a great impact on cardiovascular (CV) health [1-3]. However, for successful treatment of CV risk factors, an appropriate dose of the active principle in herbal medicinal products are required. Kuna Indians who consume about 900 mg of cocoa flavanols with their daily cocoa beverage do not suffer from

arteriosclerosis, hypertension or hyperlipidemia [1]. The daily flavanol dose was recalculated from the content of flavanol metabolites excreted in urine. If Kuna Indians move to America, getting rid of their cocoa beverage habit and eating fast food, their protection from CV risk is gone [1]. Odourless garlic with 2.7 mg of S-allyl-cysteine in the daily dosage has decreased arteriosclerosis, hypertension and hyperlipidemia [2]. The leading substance of black seed and oil, thymoquinone, should be given in a daily dose of 30 mg [4]. We report here a case with the replacement of synthetic CV medication by a mixture of standardized phytomedicines.

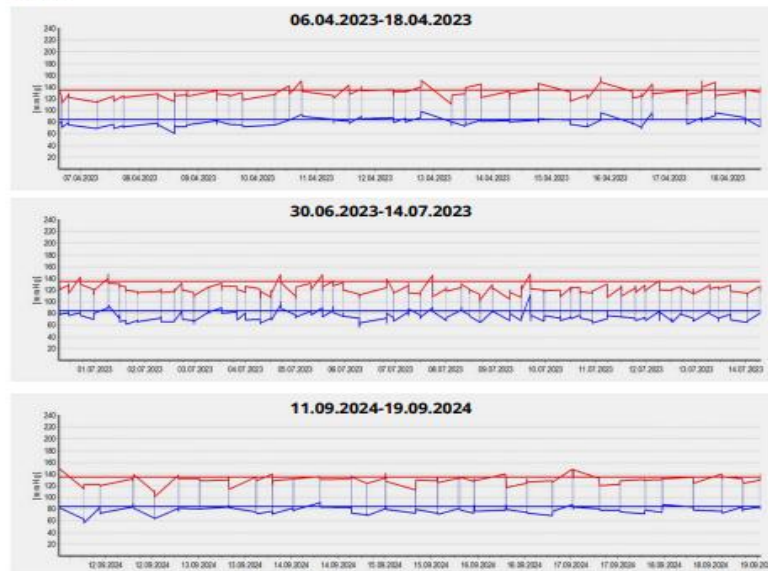
## Case History

In November 2022, male patient C.F. suffered a myocardial infarction (MI) despite his low AGLA (Swiss Working Group on Lipids and Atherosclerosis) CV risk score of 10% before the event and normal blood pressure (Figure. 1).

Patient Fries, Caspar  
 Patienten-Nr. 154-B  
 Geburtstag 05.12.1946



SYS/DIA



**Total Evaluation 06.04.2023-18.04.2023**

109 Measurements

	Min.	Mean	Max.	SD	> Limit
SYS	111	129,3	156	9,5	22,9%
DIA	60	80,1	98	7,2	21,1%
PULS	51	66,0	89	10,2	0,0%
MAP	78	96,5	116	7,2	29,4%
PP	26	49,2	70	7,5	44,0%

**Total Evaluation 30.06.2023-14.07.2023**

169 Measurements

	Min.	Mean	Max.	SD	> Limit
SYS	100	122,1	147	9,0	8,3%
DIA	56	75,3	112	8,3	10,1%
PULS	53	66,5	97	8,3	0,0%
MAP	73	90,9	124	7,9	10,7%
PP	26	46,8	64	7,0	30,2%

**Total Evaluation 11.09.2024-19.09.2024**

93 Measurements

	Min.	Mean	Max.	SD	> Limit
SYS	101	129,4	149	8,3	17,2%
DIA	56	77,7	92	6,9	11,8%
PULS	50	62,3	75	5,8	0,0%
MAP	76	94,9	109	6,6	15,1%
PP	32	51,7	67	7,0	57,0%

**Figure 1:** Details of the home blood pressure measurements (SD standard deviation).

According to the AGLA guideline recommendations, the primary care physician started treatment with acetylsalicylic acid 100 mg, ticagrelor 2 x 90 mg, pantoprazol 40 mg, bisoprolol 1.25 mg, lisinopril 2.5 mg and atorvastatin 2 x 40 mg per day. Until January 2023, C.F. received 6 coronary stents. In January 2024, the statin was changed to ezetimibe/rosuvastatin 10/20 mg because of liver enzyme increase (Table 1)

C.F. consulted us in April 2023 because he wished to have replaced synthetic medication by phytomedicines. At that time, total cholesterol (Chol) was 3.6 nmol/L and LDL Chol 1.5 nmol/L (the ideal AGLA guideline setpoint would have been 1.4 nmol/L or lower). On April 6, we started with CardioascR, a proprietary cocoa-black garlic extract supplemented with coenzyme Q10 (CoQ10), 400 mg of flavanols, 942 mg

black garlic extract\* and 200 mg CoQ10/day. During the CardioascR treatment, total cholesterol increased to 5.3 nmol/L (upper range 5.6 nmol/L) but increased further into the pathological range until January 2024 (Table 1). So, we doubled the CardioascR dose and added 6 capsules of black seed oil with 3 mg of thymoquinone/day. Since serum total cholesterol increased to 5.7 nmol/L after a drop (5.3 nmol/L) and LDL Chol increased to 3.6 nmol/L in the follow-up until May 2024, we exchanged the black seed oil with an oil with 30 mg of thymoquinone per day. After that, serum total Chol stabilized in the normal range (Table 1) but LDL Chol did not reach the desired AGLA guideline set point of 1.6 mmol/L or below. We discussed this with C.F. who enjoyed the quality of life during the phytomedicine treatment. C.F. wished to continue with the herbal medication, although the AGLA guideline requirement was not fulfilled.

	m-d-yy	post MI			HBPM	HBPM						HBPM
	02-18-2022	11-09-2022	01-13-2023	01-27-2023	03-21-2023	10-30-2023	01-26-2024	02-06-2024	05-06-2024	06-21-2024	07-06-2024	09-13/25-20
Treatment		Atorvastatin 80mg/d Lisinopril 2.5 mg Bisoprolol 1.25 mg	Rosuvastatin 20 Ezetimib 10 mg		6 Cardiovasc on April 6		12 Cardiovasc + Nigella oil		12 Cardiovasc + Nigella forte oil			
	mmol/L	mmol/L	mmol/L	mmol/L	mmol/L	mmol/L	mmol/L	mmol/L	mmol/L	mmol/L	mmol/L	mmol/L
Total Cholesterol	4,5	4,5	3,4	3,6	3,2	5,3	<b>6,4</b>	5,3	<b>(5,7)</b>	5,1	5	4,6
HDL-Chol	1,1	0,97	0,99	1,2	1,3	1,6	1,5	1,5	1,6	1,4	1,3	1,3
LDL-Chol	2,8	3,3	1,7	1,9	1,5	3,1	<b>4,1</b>	3,2	3,6	3,3	3,1	3,4
Triglycerides	1,3	0,52	1,7	1	1	1,3	1,3	1,4	1,1	0,9	1,3	1,1
α-Lipoprotein			<b>289</b>	<b>221</b>	<b>254</b>	<b>222</b>						<b>235</b>
CRP		1,7	2,3	<5								
AGLA-CV-Score	9%	10%										
mm HG		115/72										
GOT	19		<b>124</b>	25	28	28						24
GPT	20		<b>223</b>	<b>229</b>	<b>87</b>	28						22
Gamma-GT	13			<b>282</b>	<b>100</b>	25						20
MI myocardial infarction												
	130 mmHg was inserted into the AGLA-Score because of the patient's normal blood pressure in the home blood pressure measurement (HBPM) profiles (Fig. 1)											

**Table 1:** Visits, treatment and laboratory values before and after the myocardial infarction.

\*The garlic extract was tested at the University of Aachen for its antioxidative effect, which was 10 times higher than that of the aged garlic extract tested in clinical studies [5].

### Side headings/Subheadings

Phytomedicines for CV risk reduction

### Discussion & Conclusion

The case report indicates that in individual cases, the AGLA CV Score is not a reliable predictor of high CV risk. C.F. suffered MI despite a low AGLA risk of 10% and when it happened was classified as high CV risk patient [6] and was given treatment according to the AGLA guidelines. When the patient wished to receive herbal replacement for this treatment, we started with a combined cocoa and black garlic extract supplemented by CoQ10 and, according to the patient's total cholesterol, increased the dose of active principle or added other options (Table 1). Dose-finding studies are now required to evaluate the optimum dose of the individual components, including CoQ10 [7].

CoQ10 is one of the dietary antioxidants with a high tolerability and safety profile [8-10]. By adding 120 mg CoQ10 to 1200 mg of odourless black garlic extract, vessel elasticity and endothelial function had improved compared to placebo [11] and arterial calcification assessed by computer tomography and the proinflammatory marker C-reactive protein had decreased [12]. In patients with chronic heart insufficiency and impaired left ventricular ejection rate, a dose of >100 mg CoQ10 daily over 6 months reduced CV mortality by 55% [13]. Especially patients with hyperlipidemia and diabetes mellitus profited from an additional 100 or 200 mg CoQ10 [14]. A systematic review and meta-analysis including 12 studies (650 patients) suggested that the CoQ10 primary prevention in diabetic patients was caused by the CoQ10-induced decrease of total and LDL Chol [15].

Future studies must clarify why about 30 percent of the population or more do not respond to odourless garlic extract with a decrease of CV risk factors [16]. It may well be that a genetic Chol disorder is one of the reasons. Likewise, non-response to cocoa extract has been observed [17, 18] and also to black seed preparations [19]. In a systematic review, the impact of black seed (oil) on blood pressure was lower than that known from black garlic and cocoa preparations [20]. Unfortunately, the articles

did not state the thymoquinone content in the daily dosages. We suppose that a daily dose of 30 mg of thymoquinone is a potent and safe CV risk-lowering medicine and/or drug enhancer for other phytomedicines [4]. This should be elucidated in further studies. It also remains to be shown in which signaling pathways are involved in the mechanism of action to which extent supplemental CoQ10 might increase the responsiveness to the phytomedicine mixture in non-responders.

In a retrospective cohort study over a median follow up of almost 6 years, the lowest LDL Chol group (< 1.8 nmol/L) had a higher risk of all-cause, CV disease and cancer mortality compared to the reference group gained from data on CV mortality validated in another independent cohort (LDL Chol 3.1 - < 3.6 nmol/L, 21). This had already been observed by Penson et al. [21] who showed in addition that low hs-CRP appeared to be associated with reduced risk of incident CV disease and mortality in a high-risk population. The low hs-CRP values in the case of C.F. did not indicate an associated inflammatory process. However, the "lipid paradox" that too low level of LDL Chol do not always confer protective effects on mortality outcomes in the population with high CV risk does not oppose continuing with the phytomedicines at least as long as the LDL Chol remains in the range of 2.6 to 3.6 nmol/L. The beneficial effect of LDL Chol below 1.6 nmol/L is not yet proven beyond doubt [22]. The number of patients to be treated for one patient to profit from intensive LDL Chol lowering treatment is very high [6] and may not outweigh the inferior quality of life. In contrast to colchicine as co-treatment for LDL Chol reduction [23], standardized cocoa-black garlic extracts with CoQ10 and black seed oil were well tolerated and adverse events are not expected.

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