Prevencija nastanka ateroskleroze
- Arterinorm -
kroz mehanizam trostrukog delovanja

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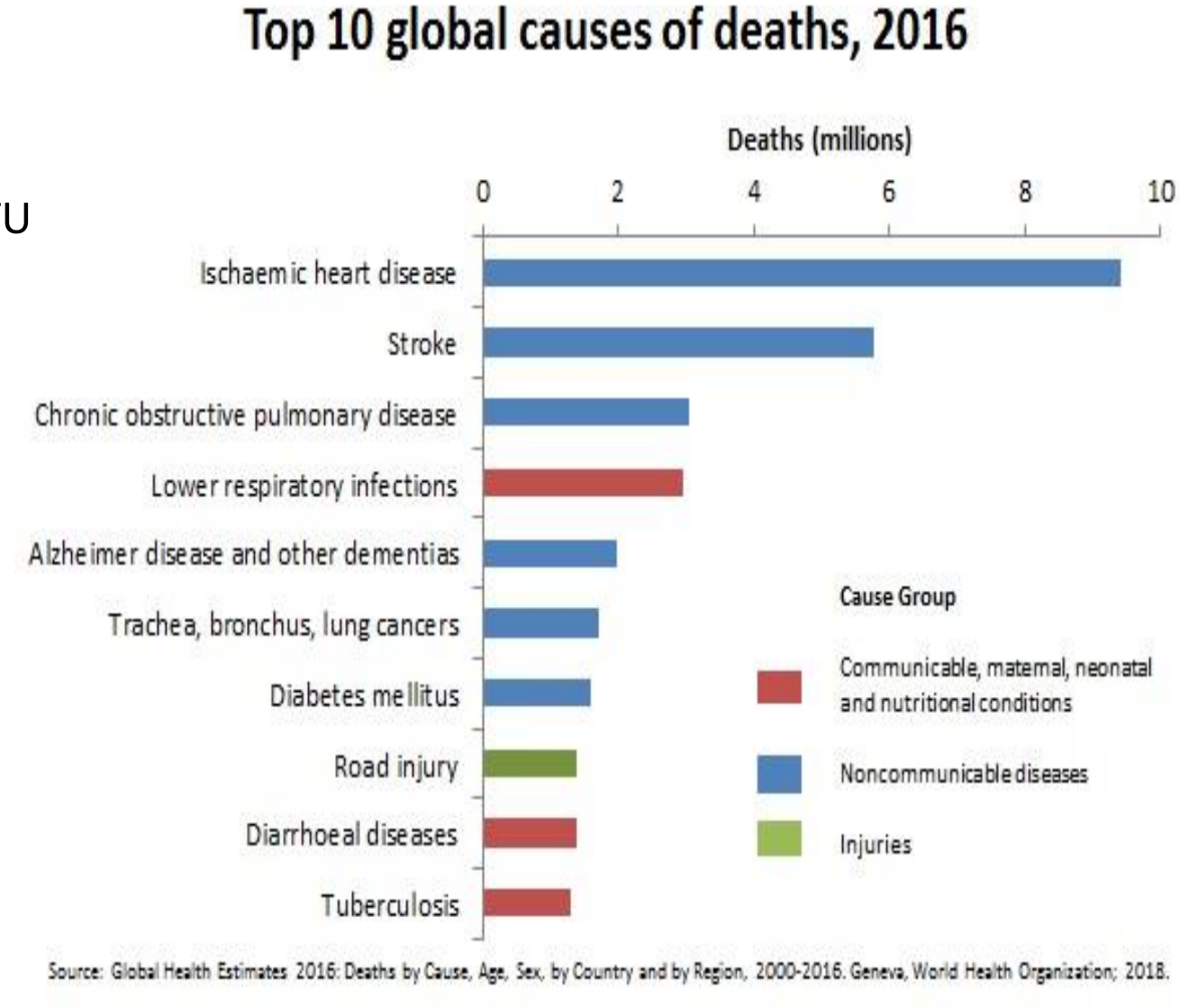
Institut za KVBV

SVET

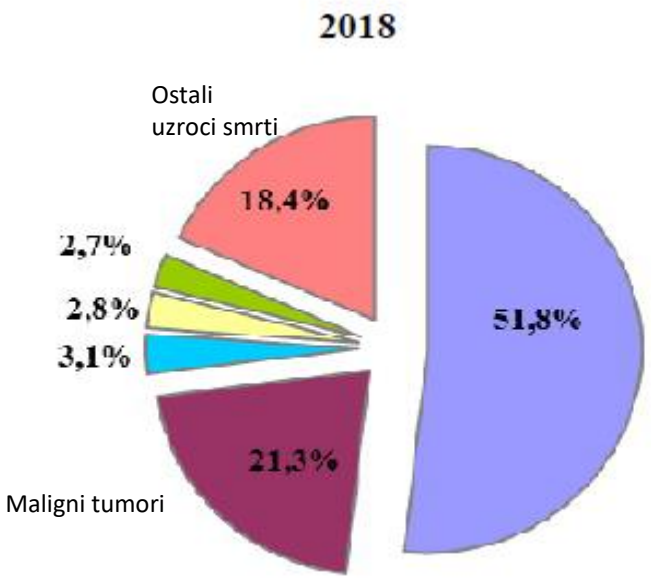
- KVB VODEĆI UZROČNIK SMRTNOSTI U SVETU
- SITUACIJA JE ISTA VEĆ 15 GODINA

15.2 milion od IBS i MU

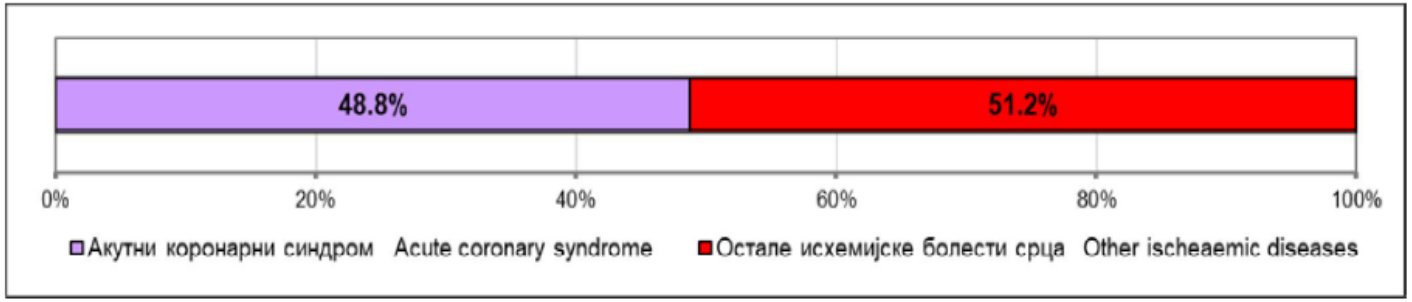


http://www.who.int/mediacentre/factsheets/fs310/en/

SRBIJA-epidemiologija, statistika



KV bolesti



Struktura umiranja (%) od ishemijskih bolesti srca, Republika Srbija, 2018.

Stopa mortaliteta (na 100.000 stanovnika) od vodecih nezaraznih bolesti, Republika Srbija, 2018.

U Srbiji u proseku 36000 godišnje oboli MU i IM

1 događaj na svakih 15min

1 smrt na svakih sat vremena

Zdravstveno-statisticki godisnjak Republike Srbije, 2018, Batut

http://www.who.int/mediacentre/factsheets/fs310/en/

Registar za akutni koronarni sindrom u Srbiji 2012

Zdravstveno stanje i zdravstvene potrebe stanovništva Srbije. Beograd

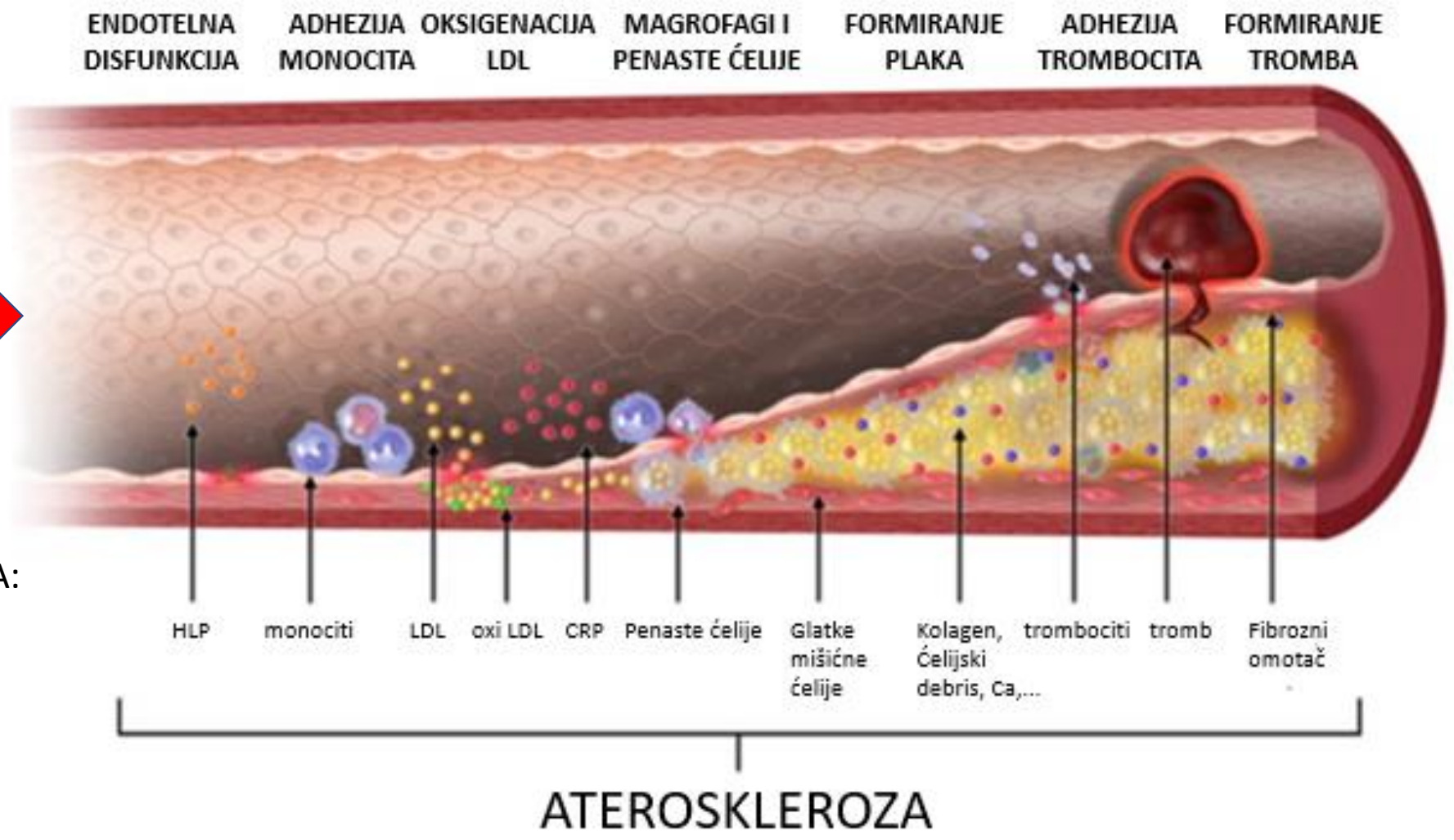
NACIONALNI VODIČ DOBRE KLINIČKE PRAKSE ZA DIJAGNOSTIKOVANJE I LEČENJE ISHEMIJSKOG MOŽDANOG UDARA

MEHANIZAM NASTANKA

1. DISLIPIDEMIJA
2. HIPERTENZIJA
3. PUŠENJE CIGARETA
4. HIPERGLIKEMIJA
5. OKSIDATIVNI STRES
6. HIPERHOMOCISTEINEMIJA
7. INFEKTIVNI AGENSI

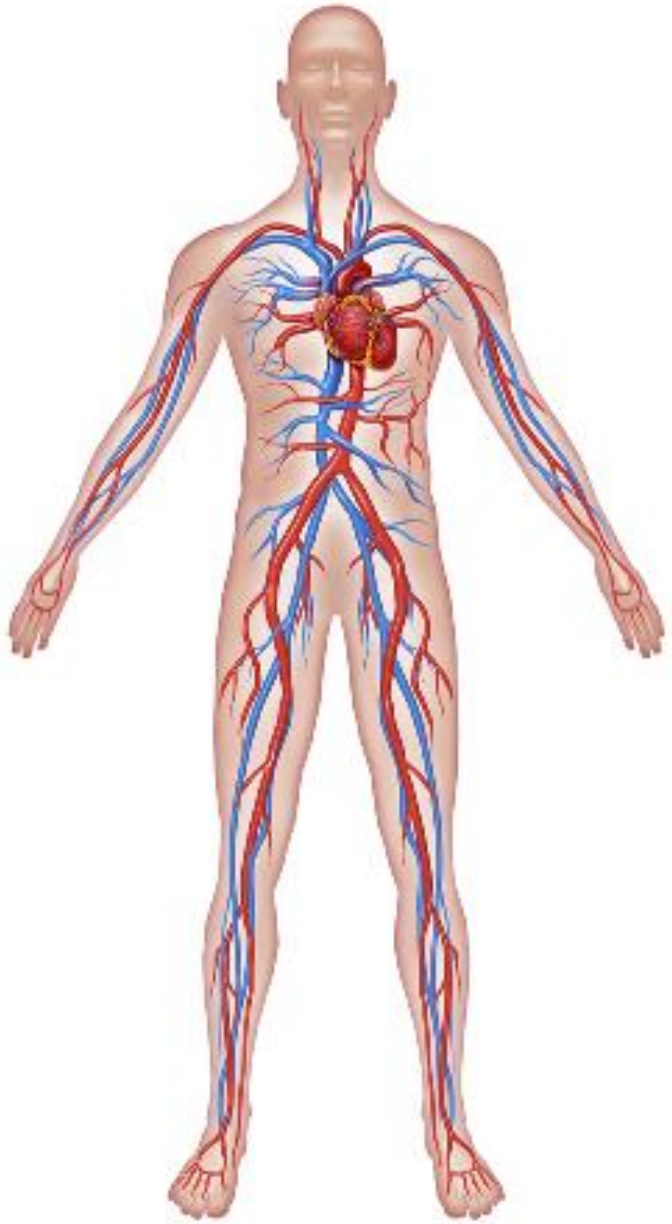
NEPROMENLJIVI FAKTORI RIZIKA:

- NASLEĐE
- POL
- GODINE



GENERALIZOVANI PROCES

- Lumenska opstrukcija
- Akutni koronarni sindrom
- Moždani udar ili tranzitorni ishemijski atak
- Periferna arterijska bolest
- Visceralna ishemija
- Aneurizma aorte



- Smatra se da je u većine ljudi oko **85. godine života** oko 60% koronarne cirkulacije prekriveno aterosklerotičnim plakovima, i to pod uslovom da u toku života nisu prisutni faktori rizika.
- U prisustvu faktora rizika kao što je **dislipidemija** takve promene na koronarnim krvnim sudovima se dostižu negde u **42. godini života**.

Nacionalni vodič dobre kliničke prakse, Lipidski poremećaji, 2012.

- Poremećaji lipida imaju fundamentalni značaj za aterogenezu
- Povišene vrednosti LDL holesterola, predstavljaju glavni faktor rizika.

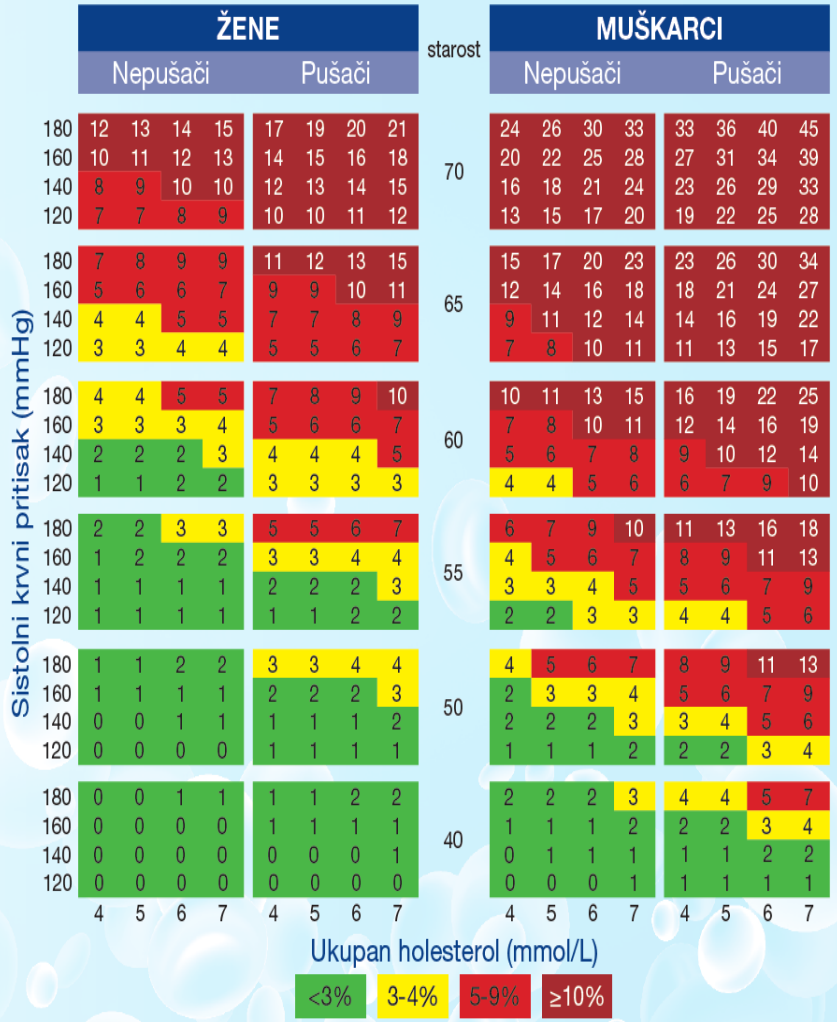
„For each 1 mmol/L reduction in LDL-C, major vascular events (MI, CAD death, or any stroke or coronary revascularization) are reduced by 22%, major coronary events by 23%, CAD death by 20%, total stroke by 17%, and total mortality by 10% ‚over 5 years“.

2019 ESC/EAS Guidelines for the management of dyslipidaemias

Nacionalni vodič dobre kliničke prakse, Lipidski poremećaji, 2012.

SCORE tabela

10-godišnjeg rizika za fatalno kardiovaskularno oboljenje u populaciji sa visokim kardiovaskularnim rizikom[1]



[1]*2019 ESC/EAS Guidelines for the management of dyslipidaemias*

Table 5 Intervention strategies as a function of total cardiovascular risk and untreated low-density lipoprotein cholesterol levels

	Total CV risk (SCORE) %	Untreated LDL-C levels					
		<1.4 mmol/L (55 mg/dL)	1.4 to <1.8 mmol/L (55 to <70 mg/dL)	1.8 to <2.6 mmol/L (70 to <100 mg/dL)	2.6 to <3.0 mmol/L (100 to <116 mg/dL)	3.0 to <4.9 mmol/L (116 to <190 mg/dL)	≥4.9 mmol/L (≥190 mg/dL)
Primary prevention	<1, low-risk	Lifestyle advice	Lifestyle advice	Lifestyle advice	Lifestyle advice	Lifestyle intervention, consider adding drug if uncontrolled	Lifestyle intervention and concomitant drug intervention
	Class[a]/Level[b]	I/C	I/C	I/C	I/C	IIa/A	IIa/A
	≥1 to <5, or moderate risk (see *Table 4*)	Lifestyle advice	Lifestyle advice	Lifestyle advice	Lifestyle intervention, consider adding drug if uncontrolled	Lifestyle intervention, consider adding drug if uncontrolled	Lifestyle intervention and concomitant drug intervention
	Class[a]/Level[b]	I/C	I/C	IIa/A	IIa/A	IIa/A	IIa/A
	≥5 to <10, or high-risk (see *Table 4*)	Lifestyle advice	Lifestyle advice	Lifestyle intervention, consider adding drug if uncontrolled	Lifestyle intervention and concomitant drug intervention	Lifestyle intervention and concomitant drug intervention	Lifestyle intervention and concomitant drug intervention
	Class[a]/Level[b]	IIa/A	IIa/A	IIa/A	I/A	I/A	I/A
	≥10, or at very-high risk due to a risk condition (see *Table 4*)	Lifestyle advice	Lifestyle intervention, consider adding drug if uncontrolled	Lifestyle intervention and concomitant drug intervention	Lifestyle intervention and concomitant drug intervention	Lifestyle intervention and concomitant drug intervention	Lifestyle intervention and concomitant drug intervention
	Class[a]/Level[b]	IIa/B	IIa/A	I/A	I/A	I/A	I/A
Secondary prevention	Very-high-risk	Lifestyle intervention, consider adding drug if uncontrolled	Lifestyle intervention and concomitant drug intervention	Lifestyle intervention and concomitant drug intervention	Lifestyle intervention and concomitant drug intervention	Lifestyle intervention and concomitant drug intervention	Lifestyle intervention and concomitant drug intervention
	Class[a]/Level[b]	IIa/A	I/A	I/A	I/A	I/A	I/A

CV = cardiovascular; LDL-C = low-density lipoprotein cholesterol; SCORE = Systematic Coronary Risk Estimation.
[a]Class of recommendation.
[b]Level of evidence.

CILJNE VREDNOSTI ZA LDL za prevenciju KV oboljenja

Very-high-risk	People with any of the following: Documented ASCVD, either clinical or unequivocal on imaging. Documented ASCVD includes previous ACS (MI or unstable angina), stable angina, coronary revascularization (PCI, CABG, and other arterial revascularization procedures), stroke and TIA, and peripheral arterial disease. Unequivocally documented ASCVD on imaging includes those findings that are known to be predictive of clinical events, such as significant plaque on coronary angiography or CT scan (multivessel coronary disease with two major epicardial arteries having >50% stenosis), or on carotid ultrasound. DM with target organ damage,[a] or at least three major risk factors, or early onset of T1DM of long duration (>20 years). Severe CKD (eGFR <30 mL/min/1.73 m^2). A calculated SCORE ≥10% for 10-year risk of fatal CVD. FH with ASCVD or with another major risk factor.
High-risk	People with: Markedly elevated single risk factors, in particular TC >8 mmol/L (>310 mg/dL), LDL-C >4.9 mmol/L (>190 mg/dL), or BP ≥180/110 mmHg. Patients with FH without other major risk factors. Patients with DM without target organ damage,[a] with DM duration ≥10 years or another additional risk factor. Moderate CKD (eGFR 30—59 mL/min/1.73 m^2). A calculated SCORE ≥5% and <10% for 10-year risk of fatal CVD.
Moderate-risk	Young patients (T1DM <35 years; T2DM <50 years) with DM duration <10 years, without other risk factors. Calculated SCORE ≥1 % and <5% for 10-year risk of fatal CVD.
Low-risk	Calculated SCORE <1% for 10-year risk of fatal CVD.

< 1,4 mmol/L

< 1,8 mmol/L

< 2,6 mmol/L

< 3,0 mmol/L

2019 ESC/EAS Guidelines for the management of dyslipidaemias

ASCVD = atherosclerotic cardiovascular disease; ACS = acute coronary syn- drome; BP = blood pressure; CABG = coronary artery bypass graft surgery; CKD = chronic kidney disease; CT = computed tomography; CVD = cardiovas- cular disease; DM = diabetes mellitus; eGFR = estimated glomerular filtration rate; FH = familial hypercholesterolaemia; LDL-C = low-density lipoprotein cho- lesterol; MI = myocardial infarction; PCI = percutaneous coronary intervention; SCORE = Systematic Coronary Risk Estimation; T1DM = type 1 DM; T2DM = type 2 DM; TC = total cholesterol; TIA = transient ischaemic attack

TERAPIJSKI IZBOR

		EFIKASNOST U SNIŽENJU TC	NEŽELJENA DEJSTVA
HDR	Mediteranska dijeta	15-20%	**NEMA**
	Redovna fizička aktivnost		
	Odvikavanje od loših navika		
SUPLEMENTACIJA PREPOZNATA OD ESC, EAS, EACPR	Fitosteroli	20-30%	**NEMA**
	Monakolin K		
	Polikozanoli		
	Biljna vlakna		
	Protein soje		
	Riblje ulje		
MEDIKAMENTI	inhibitori HMG -Co A reduktaze – statini	50-80%	**15%** *-Bol u mišićima* (rabdomioliza) *-oštećenje jetre* *-povećana učestalost novonastalog DM* *-demencija*
	Fibrati		
	CEPT inhibitor- ezetimib		
	PCSK inhibitori (evolokumab)		
	sekvestranati žučnih kiselina		
	derivati nikotinske kiseline -niacin i niaspan		
	omega 3 nezasićene masne kiseline		

ARTERINORM

JEDINSTVENI PROIZVOD NA TRZISTU koji reguliše

3 ključna mehanizma za nastanak aterosleroze.

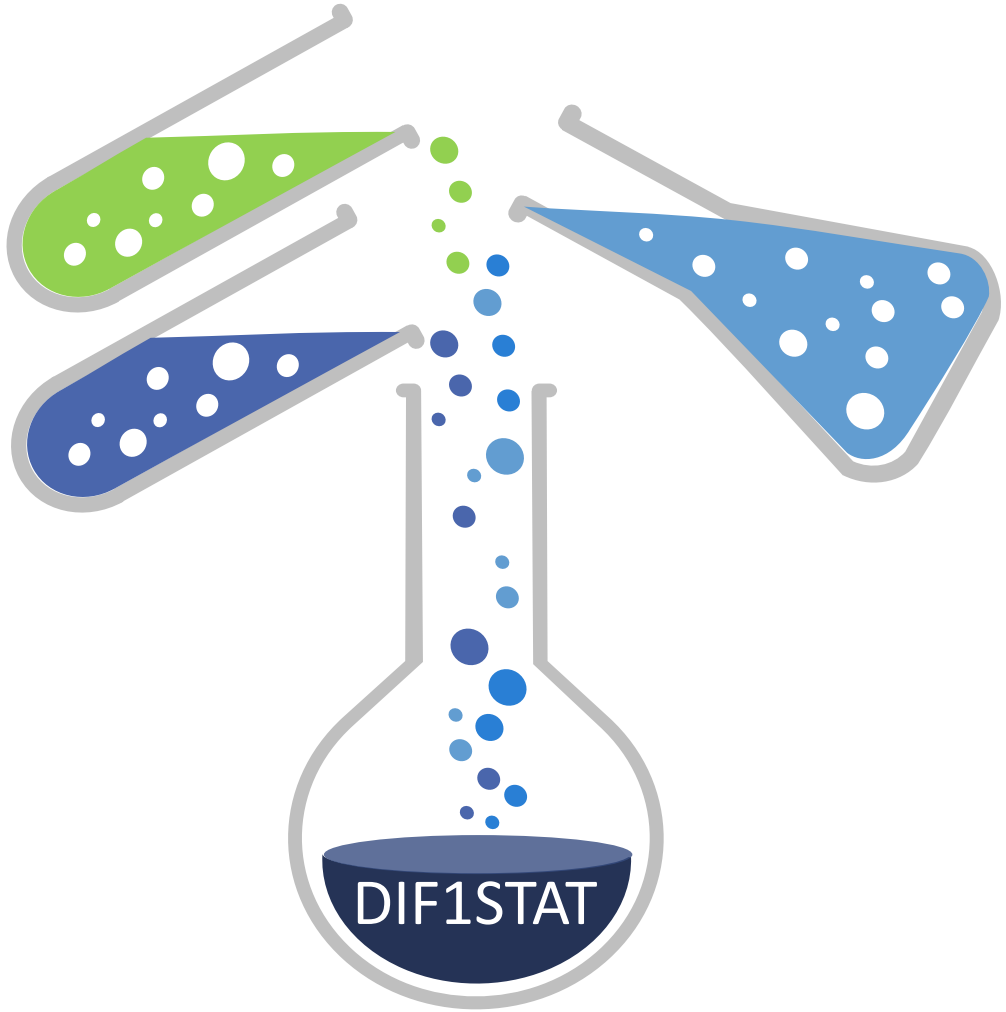
Ekstrakt fermentisanog crvenog pirinča (monascus purpureus), standardizovan na 1,5% **monakolina K**	200,0 mg	**Snižavaju nivo LDL holesterola, triglicerida i podižu nivo HDL holesterola u krvi**
Alifatični alkoholi dugog lanca (**polikozanol**), standardizovani na 60% oktakozanola	10,0 mg	
Vitamin B3 (niacin)	27,0 mg	
Folna kiselina	300,0 µg	**Snižavaju nivo homocisteina u krvi**
Vitamin B6	2,0 mg	
Vitamin B12	1,0 µg	
Vitamin E	20,0 mg	**Antioksidativna zaštita**
Ekstrakt čaja (Camellia sinensis) standardizovan na 40% polifenola	144,0 mg	

HIPOLIPEMIJSKI EFEKAT – **DIF1STAT**

SINERGIZAM BIOAKTIVNIH SUPSTANCI

POLIKOZANOLI

NIACIN

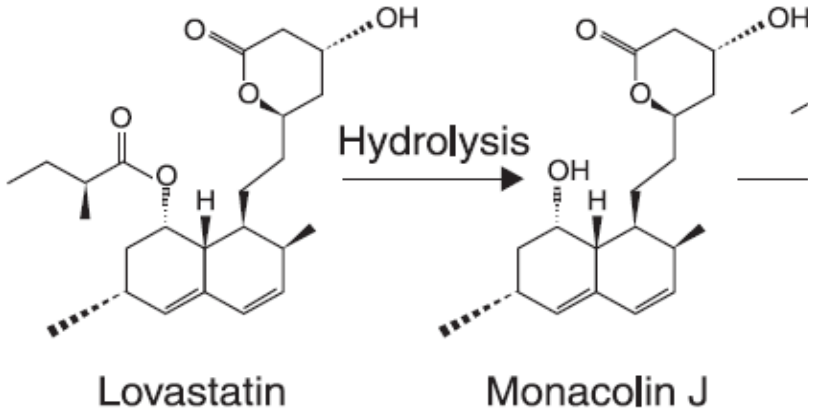


MONAKOLIN K

Fermentisani crveni pirinač

Monakolin K dobija se fermentacijom belog pirinča pomoću plesni Monascus purpureus

Deluje istim mehanizmom kao i sintetski statini, tako što blokira endogenu produkciju holesterola u jetri inhibicijom HMG Co reduktaze, ključni enzim u procesu sinteze holesterola.



Delotvornost **2,5-10 mg Monakolina K** dokazana je u više od 30 kliničkih studija dostupnih u bazi podataka PubMed.

Potvrda njegove efikasnosti je jasno definisana kroz aktuelne Evropske vodiče u lečenju dislipidemija 2019.

Uticaj promene zivotnog stila na nivo lipida

Table 8 **Impact of specific lifestyle changes on lipid levels**

	Magnitude of the effect	Level
Lifestyle interventions to reduce TC and LDL-C levels		
Avoid dietary trans fats	++	A
Reduce dietary saturated fats	++	A
Increase dietary fibre	++	A
Use functional foods enriched with phytosterols	++	A
Use red yeast rice nutraceuticals	++	A
Reduce excessive body weight	++	A
Reduce dietary cholesterol	+	B
Increase habitual physical activity	+	B
Lifestyle interventions to reduce TG-rich lipoprotein levels		
Reduce excessive body weight	+	A
Reduce alcohol intake	+++	A
Increase habitual physical activity	++	A
Reduce total amount of dietary carbohydrates	++	A
Use supplements of n-3 polyunsaturated fats	++	A
Reduce intake of mono- and disaccharides	++	B
Replace saturated fats with mono- or polyunsaturated fats	+	B
Lifestyle interventions to increase HDL-C levels		
Avoid dietary trans fats	++	A
Increase habitual physical activity	+++	A
Reduce excessive body weight	++	A
Reduce dietary carbohydrates and replace them with unsaturated fats	++	A
Modest consumption in those who take alcohol may be continued	++	B
Quit smoking	+	B

The magnitude of the effect (+++ = >10%, ++ = 5–10%, + = <5%) and the level of evidence refer to the impact of each dietary modification on plasma levels of a specific lipoprotein class.
HDL-C = high-density lipoprotein cholesterol; LDL-C = low-density lipoprotein cholesterol; TC = total cholesterol; TG = triglyceride.

2019 ESC/EAS Guidelines for the management of dyslipidaemias

ESC European Society of Cardiology
European Heart Journal (2020) **41**, 111–188
doi:10.1093/eurheartj/ehz455

ESC/EAS GUIDELINES

2019 ESC/EAS Guidelines for the management of dyslipidaemias: *lipid modification to reduce cardiovascular risk*

Primena monakolina K je opravdana kod pacijenata koji ne žele ili iz razloga pojave neželjenih dejstava ne mogu da koriste standardne statine. (15%)

7.5.2 Monacolin and red yeast rice (RYR)

In the only available RCT in patients with ASCVD, a partially purified extract of RYR reduced recurrent evens by 45%. A clinically relevant hypocholesterolaemic effect (up to a 20 % reduction) has been observed with RYR preparations providing a once daily dose of 2.5-10 mg monacolin K. Nutraceuticals containing purified RYR may be considered in people with elevated plasma cholesterol concentrations who do not qualify for treatment with statins in view of their global CV risk.

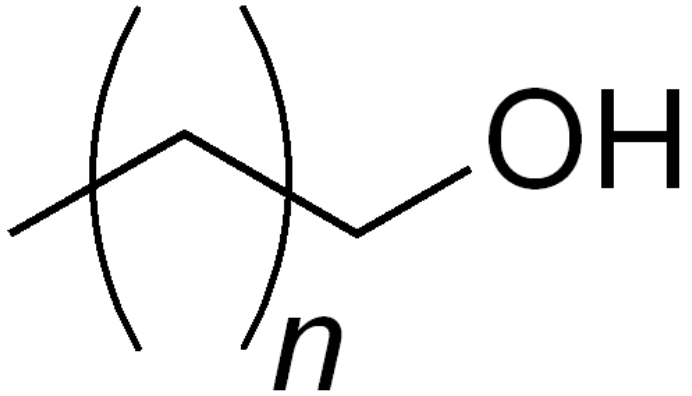
Polikozanoli

Polikozanol je prirodni ekstrakt biljnih voskova u kom dominira oktakozanol (izolovan iz šećerne trske).

Imaju složeni mehanizam dejstva, najverovatnije dovode do ↓ **sinteze holesterola u jetri i ↑ LDL katabolizma u krvi**

Hipolipemijski efekti su dokazani u preko 60 kliničkih studija radjenih na 3000 bolesnika

Smatra se da ima i antiagregaciono dejstvo (20mg = 100mg ASA)



Reference:Singh DK, Li L, Porter TD. Policosanol inhibits cholesterol synthesis in hepatoma cells by activation of AMP-kinase. J Pharmacol Exp Ther 2006; 318(3):1020–6. Castano G, Mas R, Fernandez JC et al. Effects of policosanol in older patients with type II hipercholesterolemia and high coronary risk. J Gerontol. 2001;56:M186-M192.Gouni-Berthold I, Berthold HK. Policosanol: clinical pharmacology and therapeutic significance of a new lipid-lowering agent. Am Heart J. 2002;143:356-365.

AHJ

American Heart Journal

www.ahjonline.com

↓ TC 17%-21%

↓ LDL-C 21%-29%

↑ HDL-C 8%-15%

Policosanol: Clinical pharmacology and therapeutic significance of a new lipid-lowering agent

Ioanna Gouni-Berthold, MD,[a] and Heiner K. Berthold, MD, PhD[b] *Rotenburg an der Fulda and Bonn, Germany*

Background Policosanol is a mixture of higher primary aliphatic alcohols isolated from sugar cane wax, whose main component is octacosanol. The mixture has been shown to lower cholesterol in animal models, healthy volunteers, and patients with type II hypercholesterolemia.

Methods We reviewed the literature on placebo-controlled lipid-lowering studies using policosanol published in peer-reviewed journals as well as studies investigating its mechanism of action and its clinical pharmacology.

Results At doses of 10 to 20 mg per day, policosanol lowers total cholesterol by 17% to 21% and low-density lipoprotein (LDL) cholesterol by 21% to 29% and raises high-density lipoprotein cholesterol by 8% to 15%. Because higher doses have not been tested up to now, it cannot be excluded that effectiveness may be even greater. Daily doses of 10 mg of policosanol have been shown to be equally effective in lowering total or LDL cholesterol as the same dose of simvastatin or pravastatin. Triglyceride levels are not influenced by policosanol. At dosages of up to 20 mg per day, policosanol is safe and well tolerated, as studies of >3 years of therapy indicate. There is evidence from in vitro studies that policosanol may inhibit hepatic cholesterol synthesis at a step before mevalonate generation, but direct inhibition of the hydroxy-methylglutaryl–coenzyme A reductase is unlikely. Animal studies suggest that LDL catabolism may be enhanced, possibly through receptor-mediated mechanisms, but the precise mechanism of action is not understood yet. Policosanol has additional beneficial properties such as effects on smooth muscle cell proliferation, platelet aggregation, and LDL peroxidation. Data on efficacy determined by clinical end points such as rates of cardiac events or cardiac mortality are lacking.

Conclusions Policosanol seems to be a very promising phytochemical alternative to classic lipid-lowering agents such as the statins and deserves further evaluation. (Am Heart J 2002;143:356-65.)

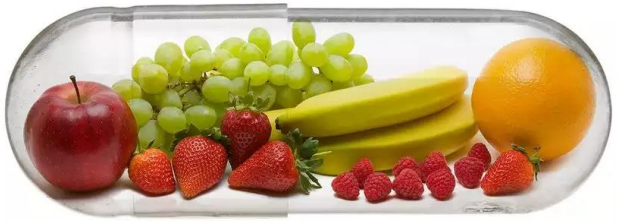
2019 ESC/EAS Guidelines for the management of dyslipidaemias: *lipid modification to reduce cardiovascular risk*

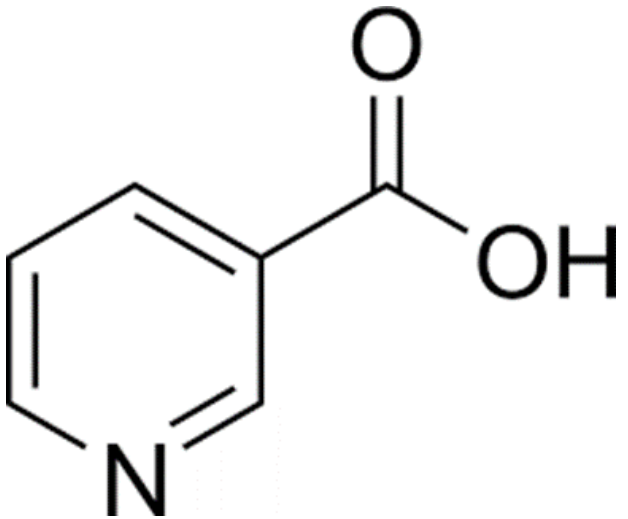
Niacin

Vitamin B3 ili nikotinska kiselina

Neophodan je za metabolisanje šećera, masti i proteina

- Dovodi i do redukcije ukupnog i LDL holesterola
- Snižava trigliceride
- **Najefikasnije povećava HDL holesterol**





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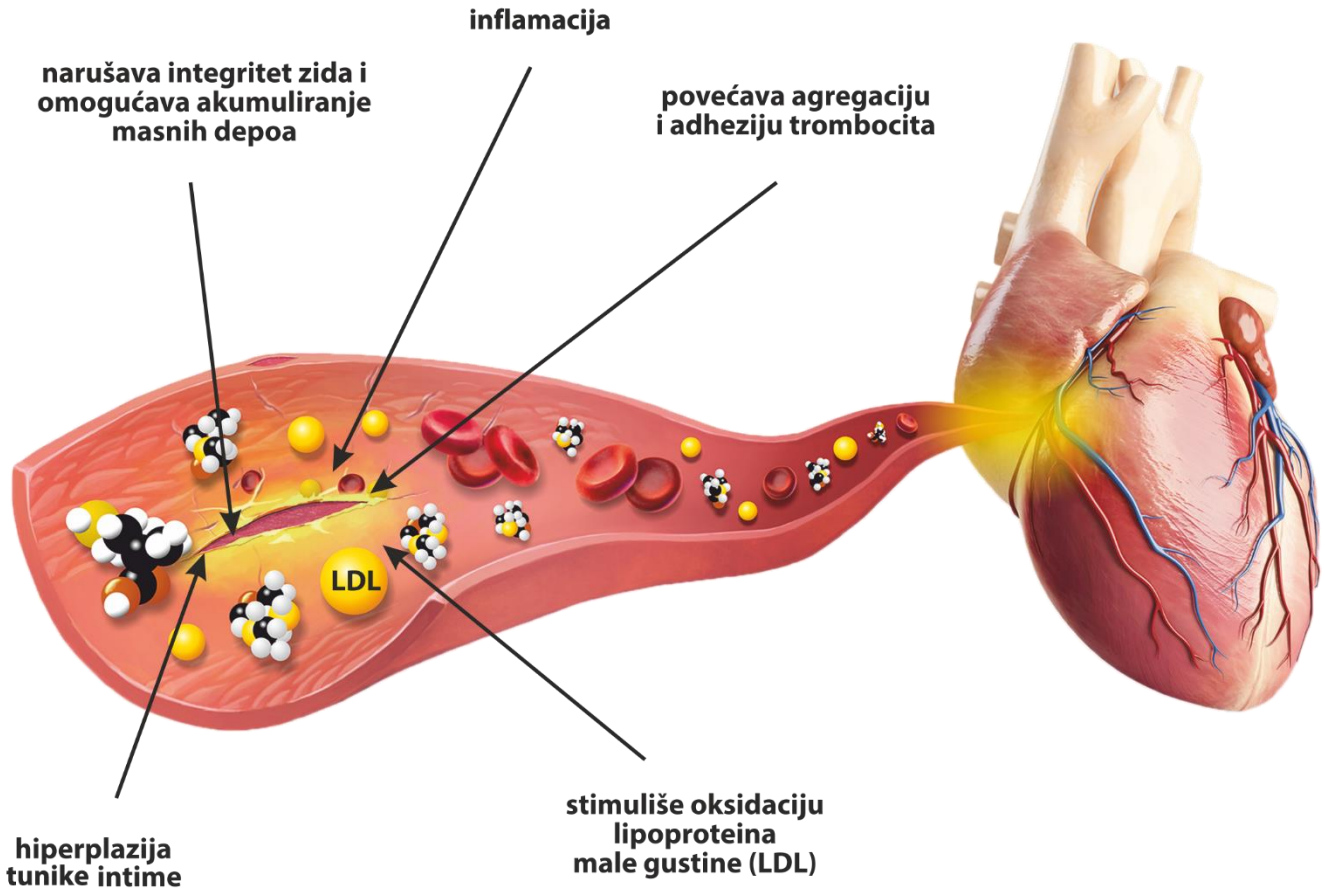
2019 ESC/EAS Guidelines for the management of dyslipidaemias: *lipid modification to reduce cardiovascular risk*

8.9 Nicotinic acid

Nicotinic acid has key action sites in both the liver and adipose tissue. In the liver, nicotinic acid inhibits diacylglycerol acyltransferase-2 resulting in decreased secretion of VLDL particles, which is also reflected in reductions of plasma levels of both IDL and LDL particles.[335] Nicotinic acid primarily raises HDL-C and ApoA1 by stimulating ApoA1 production in the liver.[335] Two large randomized trials with nicotinic acid—one with extended-release niacin[66] and one with niacin plus laropiprant[67]—have shown no beneficial effect and an increased frequency of serious adverse effects. No medication con-

HOMOCISTEIN - Samostalni faktor rizika za aterosklerozu



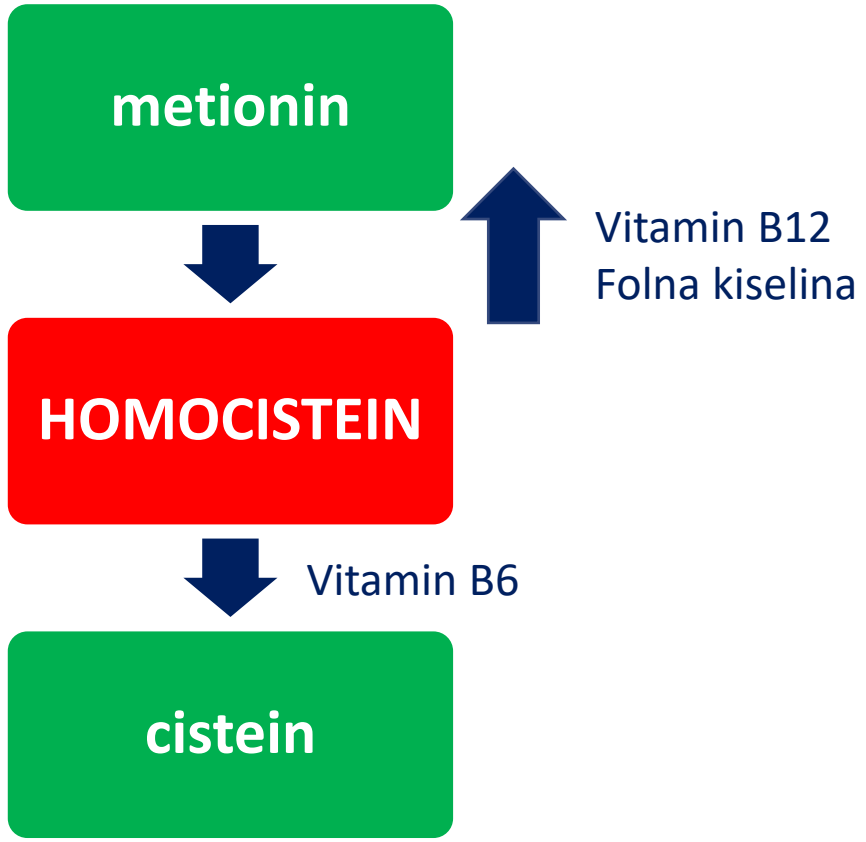
American Heart Association®

HOMOCISTEIN

Proizvodi se u organizmu

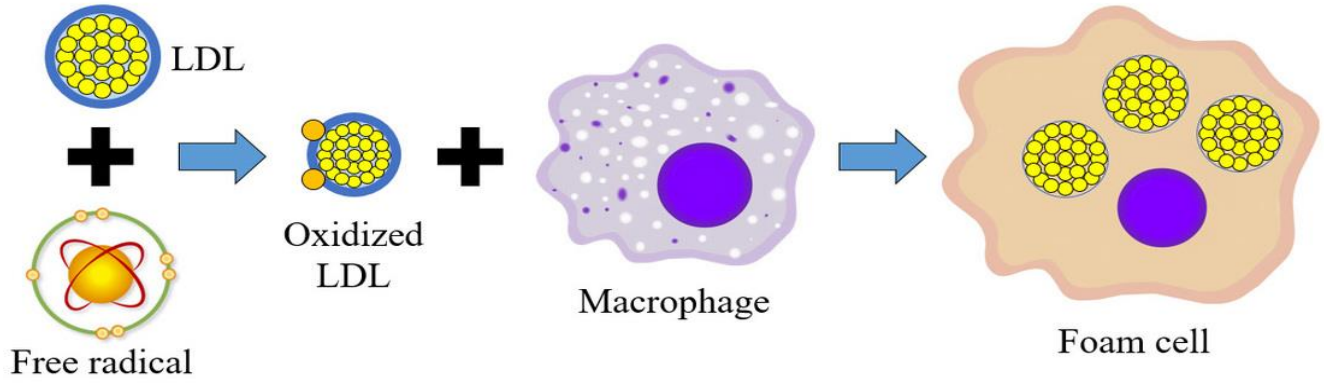
Nedostatak vitamina B6, B9 i B12 dovodi do zadržavanja viših koncentracija homocisteina u krvi

Povišene vrednosti homocisteina su samostalni faktor rizika za razvoj KVB



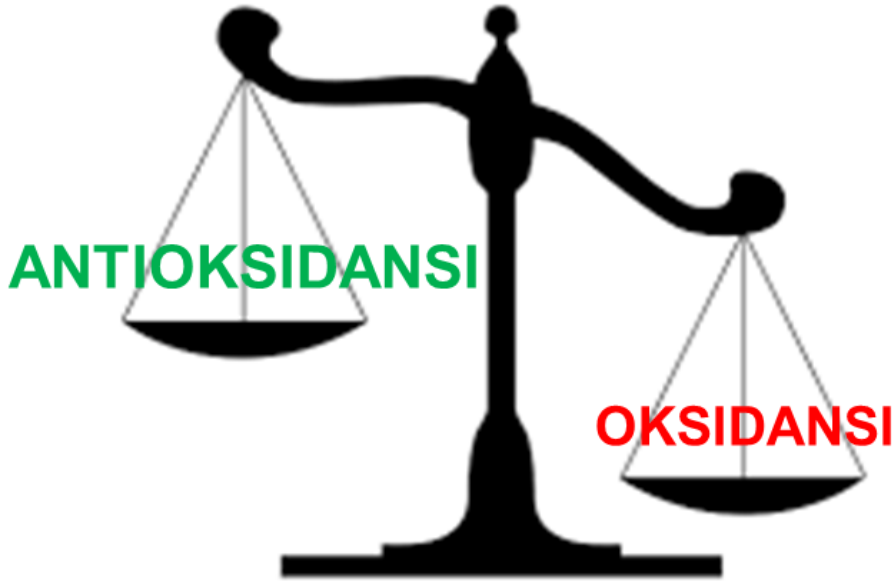
OKSIDATIVNI STRES

- Slobodni radikali i lipidna peroksidacija, prema brojnim studijama koje su do danas objavljene, predstavljaju glavni okidač za nastanak bolesti krvnih sudova tako što dovode do procesa ateroskleroze i **promena na endotelu krvnih sudova.**
- **Lipidna peroksidacija LDL-čestica** predstavlja jedan od glavnih procesa koji doprinose nastajanju arterogenog procesa.



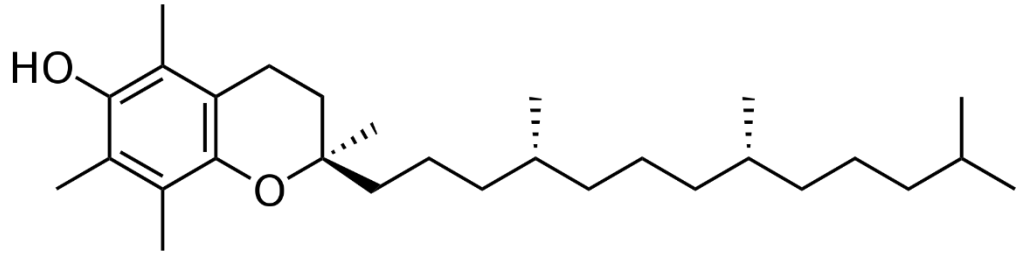
ANTIOKSIDATIVNA ZAŠTITA

Antioksidansi su biološki aktivne materije koje uklanjaju višak slobodnih radikala i na taj način sprečavaju razvoj oksidativnog stresa



VITAMIN E

- Snažan antioksidans
- Doprinosi zaštiti ćelija od oksidativnog stresa i pomaže očuvanje zida ćelijske membrane
- Sprečava oksigenaciju LDL čestica



POLIFENOLI

- Najzastupljeniji epigalo-katehin galat iz ekstrakta zelenog čaja
- Imaju jako antioksidativno dejstvo
- EGCG 25x jači od borovnice
- U studijama su pokazali i hipolipemijski efekat na LDL i ukupni holesterol

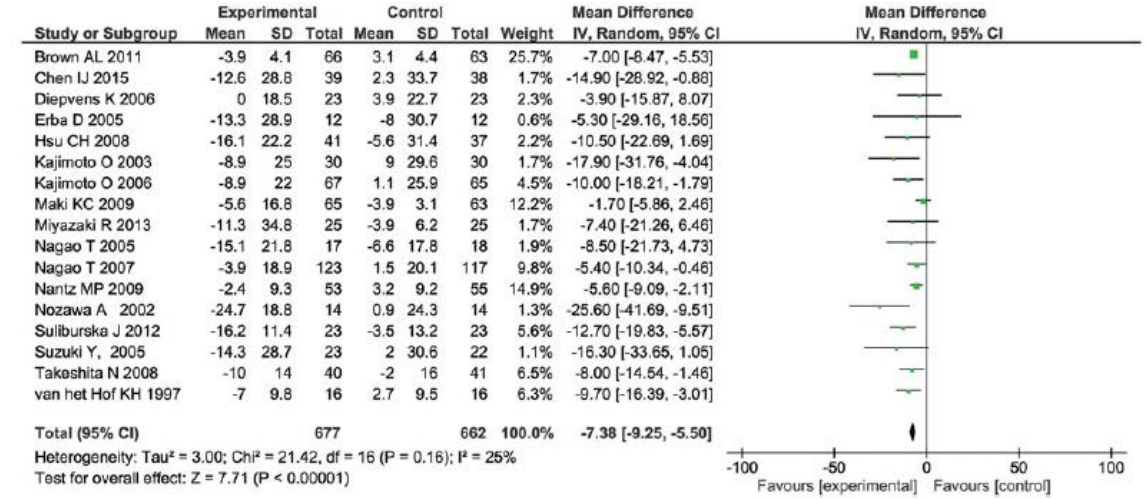


Figure 2. Meta-analysis of the effect of EGCG on LDL cholesterol compared with control arms. Sizes of data markers indicate the weight of each study in the analysis. WMD: weighted mean difference (the result was obtained from a random-effects model.

ARTERINORM

REGULACIJA LIPIDNOG STATUSA		
Monakolin K	Polikozanoli	Niacin

↓

↓ HOMOCISTEIN		
Folna kiselina	Vitamin B6	Vitamin B12

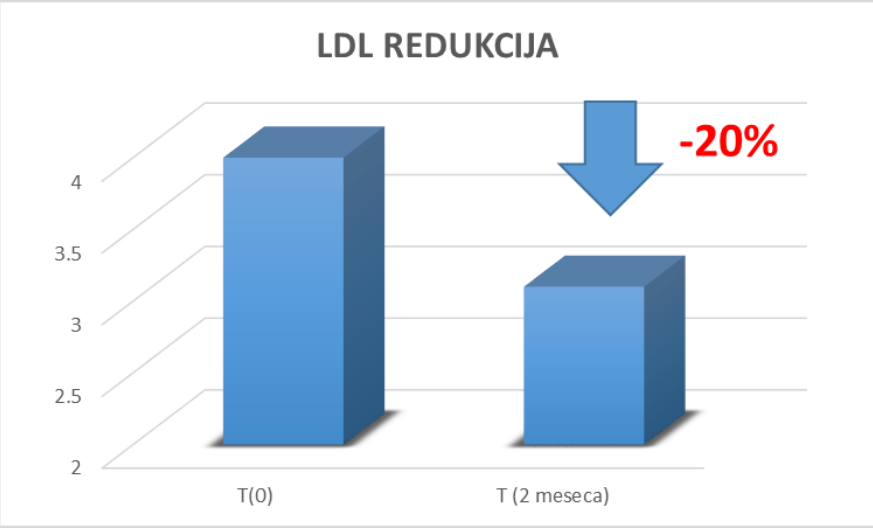
↓

ANTIOKSIDATIVNI EFEKAT	
Polifenoli	Vitamin E

ARTERINORM klinički dokazana

BRZA EFIKASNOST

- Nakon 2 meseca redukcija LDL holesterola za 20%
- Efekat jednak kao sa 20mg pravastatina



Antihyperlipidaemic effect of a *Monascus purpureus* brand dietary supplement on a large sample of subjects at low risk for cardiovascular disease: A pilot study

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Summary
Objectives: We planned to carry out a pilot study to evaluate the efficacy and safety as an antihypercholesterolemic agent of a brand dietary supplement made of *Monascus purpureus* titrated extract, octacosanols and niacin on 111 Caucasian patients with low cardiovascular disease risk (<20% by Framingham algorithms), comparing them with the antihypercholesterolemic effect of a low dosage of Pravastatin on 20 subjects with similar risk profile.
Results: In our study, the tested dietary supplement determined a significant decrease of Total Cholesterol (TC), Low Density Lipoprotein Cholesterol (LDL-C), and Triglycerides (TG) in moderately hypercholesterolemic subjects without clinically relevant change in liver and muscular toxicity markers. The reduction of LDL-C reached the 20%, and it is similar to that obtained with a well-known effective statin like Pravastatin.
Conclusions: Further long-term and double blind evaluation have to be carried out before to infer the observed results, however it appears that the studied dietary supplements could be a safe and efficacious antihypercholesterolemic agent for patients at low risk for cardiovascular diseases.

ARTERINORM klinički dokazana

DUGOROČNA PRIMENA PRUŽA DODATNE BENEFITE

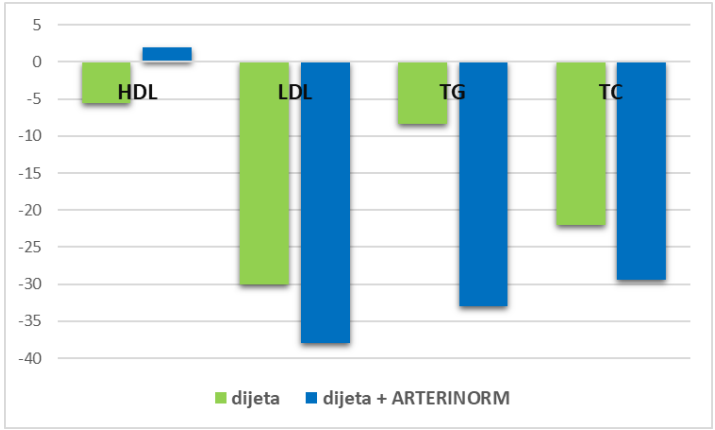
- Brža redukcija TC,LDL i TG
- Dugoročna primena najznačajnija za sniženje TG i povećanje HDL
- Bez pojave neželjenih efekata

Lipid/lipoproteins	Mean change (%) in group A 4 months (T1)	Mean change (%) in group B 4 months (T1)	*P* value	Mean change (%) in group A 8 months (T2)	Mean change (%) in group B 8 months (T2)	*P* value
TC	–7.6	–21.3	NS	–22	–29.4	NS
TG	–1.4	–6	NS	–8.4	–33	<0.001
HDLC	–2	–2	NS	–5.5	2	NS
LDLC	–10.3	–29	NS	–30	–38	NS
Non-HDLC	–9.13	–26	NS	–27	–37	NS

HDLC high density lipoprotein-cholesterol, *LDLC* low-density lipoprotein-cholesterol, *TC* Total cholesterol, *non-HDLC* non high density lipoprotein-cholesterol, *TG* triglycerides, *NS* not significant

Comparison between groups (Diet vs. Diet + Dif 1Stat)

Differences are calculated as follows Diet (group A) versus Diet plus Dif 1Stat (group B): T1 versus T1; T2 versus T2

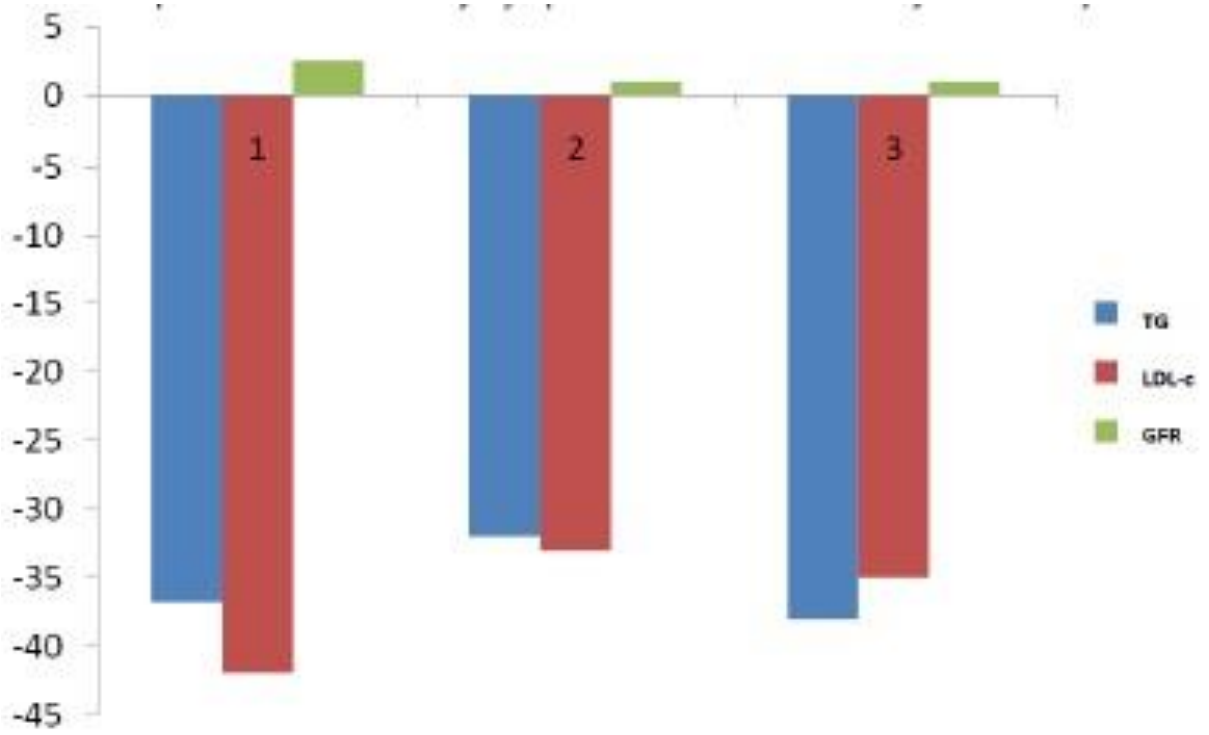


Combined Treatment with Dif1stat and Diet Reduce Plasma Lipid Indicators of Moderate Hypercholesterolemia More Effectively than Diet Alone: A Randomized Trial in Parallel Groups Lipids (2009) 44:1141–1148
DOI 10.1007/s11745-009-3368-5

ARTERINORM klinički dokazana

BEZBEDNOST

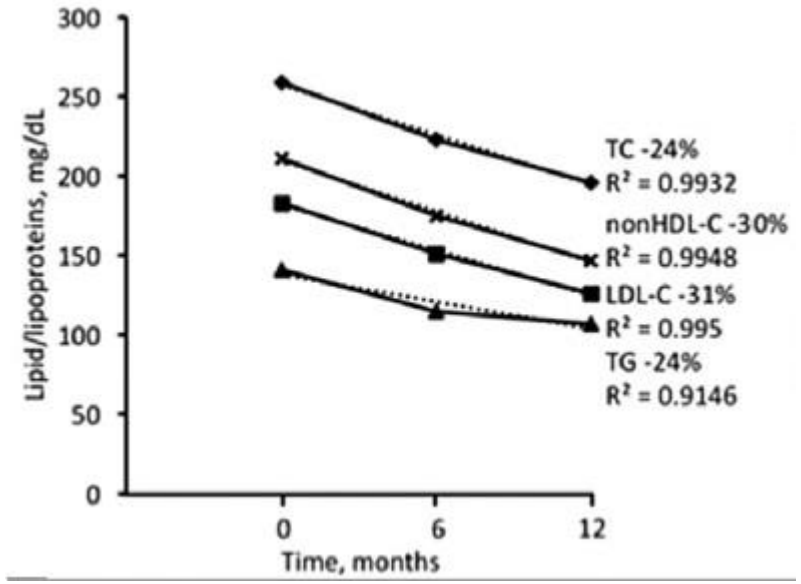
- Bez neželjenih efekata u praćenju **2 godine 1104 bolesnika** sa HBB



Efficacy and Safety of Dif1stat® for the Treatment of Secondary Dyslipidemia in Chronic Kidney Disease
September 2013, Vol. 7, No. 9, pp. 941-949 Journal of Life Sciences, ISSN 1934-7391, USA

ARTERINORM klinički dokazana

EFIKASNOST I BEZBEDNOST KOD PACIJENATA KOJI NETOLERIŠU STATINE ILI EZETIMIB



Mean changes in plasma ALT, AST, γ-glutamyl transferase, CK and glomerular filtration rate after 6 (T1) and 12 (T2) months treatment with diet plus MP.

Safety parameter (means)	Sampling time point					
	Male (T0)	Male (T1)	%Δ	Male (T2)	%Δ	p
Males						
ALT ± SD, UL	20 ± 8	19 ± 6	−5	18 ± 8	−10	ns
AST ± SD, UL	25 ± 6	24 ± 9	−4	21 ± 4	−16	ns
γ-GT ± SD, UL	17 ± 4	14 ± 5	−17	16 ± 3	−5.8	ns
CK ± SD, UL	195 ± 15	186 ± 21	−4.6	193 ± 32	−1.02	ns
GFR ± SD, mL/min/m^2	97.9 ± 0.06	97.8 ± 0.02	−0.1	97.2 ± 0.06	−0.7	ns
Cramp and myalgia	No	No	NA	No	NA	NA
Females						
ALT ± SD, UL	19 ± 6	16 ± 3	−15,7	17 ± 5	−10	ns
AST ± SD, UL	15 ± 4	14 ± 2	−6,7	13 ± 3	−13	ns
γ-GT ± SD, UL	16 ± 7	15 ± 2	−6,25	17 ± 4	6.25	ns
CK ± SD, UL	188 ± 18	175 ± 13	−7	168 ± 18	−10	ns
GFR ± SD, mL/min/m^2	98.2 ± 0.09	98.2 ± 0.08	0.2	98.4 ± 0.01	0.2	ns
Cramp and myalgia	No	No	NA	No	NA	NA

ALT, alanine aminotransferase; AST, aspartate aminotransferase; CK, creatine kinase; GFR, glomerular filtration rate; γ-glutamyl transferase (γ-GT); MP, Monascus purpureus; NA, not applicable; ns, not significant; p, result of unpaired T-test versus baseline; T, sampling time point (0 = baseline, 1 = 6 months, 2 = 12 months); %Δ, percent change in lab parameter compared to baseline.

Monascus purpureus for statin and ezetimibe intolerant heterozygous familial hypercholesterolaemia patients: A clinical study Atherosclerosis Supplements 30 (2017) 86e91

UPOTREBA

Jednom dnevno, najbolje pred spavanje, popiti jednu kapsulu.

Nakon perioda upotrebe od 3 meseca ovog proizvoda poželjno je proveriti nivo holesterola u krvi.

Bez glutena, mleka, laktoze i GMO.

Proizvod ne treba da uzimaju osobe preosetljive na neki od sastojaka proizvoda.

Proizvod nije namenjen deci, trudnicama i dojiljama.

Osobe na terapiji dislipidemija, pre upotrebe ovog proizvoda treba da se konsultuju sa svojim lekarom ili farmaceutom.

PREPORUČEN KOD PACIJENATA:

- Sa povišenim LDL holesterolom, trigliceridima ili ukupnim holesterolom
- Sa niskim HDL holesterolom u umerenom KV riziku
- Koji odbijaju ili netolerišu statinsku terapiju
- Kao dodatak statinskoj terapiji

- ✓PRIRODNA I BEZBEDNA STRATEGIJA ZA EFIKASNU KONTROLU LIPIDNOG STATUSA I PREVENCIJU KARDIOVASKULARNIH BOLESTI
- ✓KLINIČKI DOKAZANA ORIGINALNA FORMULA
- ✓TROSTRUKO DEJSTVO NA PREVENCIJU NASTANKA I RAZVOJA ATEROSKLEROZE

30 kapsula