Probiotics in the Management of High Cholesterol
The Gut-Heart Connection

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Joanna Scott-Lutyens
BA(Hons) DipION FdSc

Nutritional Therapist

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Aims

- A brief overview of good and bad cholesterol, and how both affect cardiovascular health.
- Discover how probiotics can help reduce cholesterol by harnessing the body's natural regulation system, and be used as part of CVD protocol
- Information on the research behind this.
- A quick discussion on how probiotics compare to other products on market

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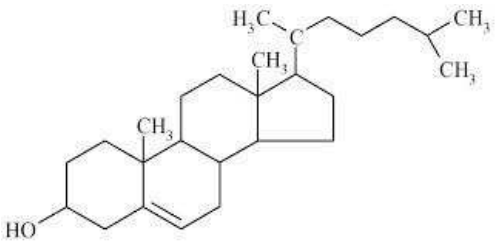
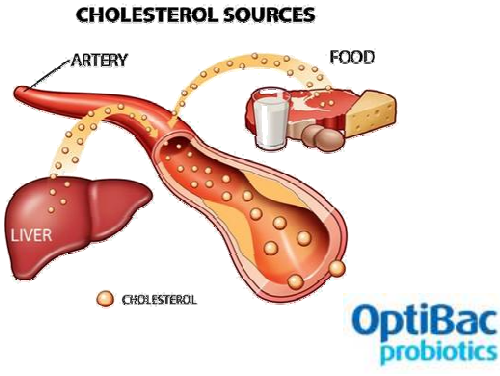
What is cholesterol?

- Waxy like substance
- Essential in the body
- Majority of cholesterol is produced by liver (80%)





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Why do we *need* cholesterol?

At least 6 reasons:

1. As a component of all cell membranes
2. To manufacture vitamin D
3. To manufacture steroid hormones
4. To manufacture bile salts
5. To repair blood vessels
6. For absorption & transportation of fat-soluble vitamins

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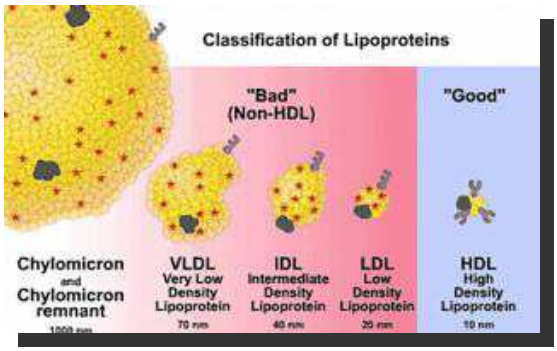
How is cholesterol transported in the body?

- Body binds fats to lipoproteins – these are a mix of lipid and protein - different densities = different properties
- High density lipoprotein (HDL = good)
- Low density lipoprotein (LDL = bad)



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What is a healthy cholesterol level?

- Varies depending on the doctor's opinion and general health of the patient

- TC: < 5 mmol/L (<4 for those at risk)
- LDL: < 3 mmol/L (<2 for those at risk)
- HDL: > 1 mmol/L (lower than this can increase risk)
- TC:HDL ratio < 4 (>6 is considered at risk)

http://www.nhs.uk/conditions/Cholesterol/Pages/Introduction.aspx
http://www.Heartuk.org.uk/

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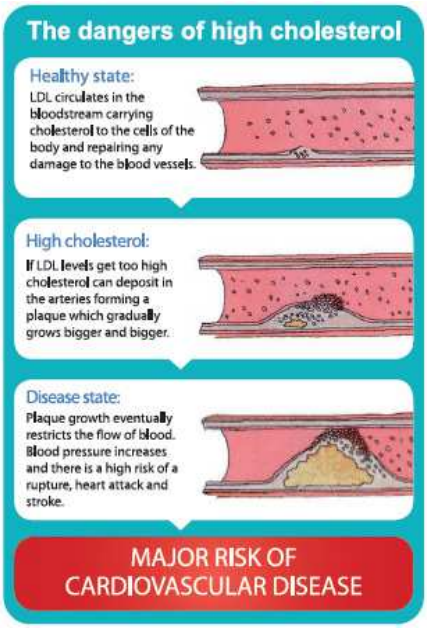
What are the issues with high cholesterol?

Atherosclerosis leading to:

High blood pressure, angina, heart attack, stroke

Plaque composition: cholesterol, white blood cells, fibrotic material, calcium, platelets

Consider: LDL, inflammation and immunity



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Inflammation or high cholesterol?

- LDL is more liable to be oxidised than HDL
- Oxidised cholesterol is more dangerous because it is:
  - more reactive
  - inflammatory
  - stimulates the immune system

- High cholesterol more of a concern in a patient with inflammation, is overweight, or has metabolic disease.

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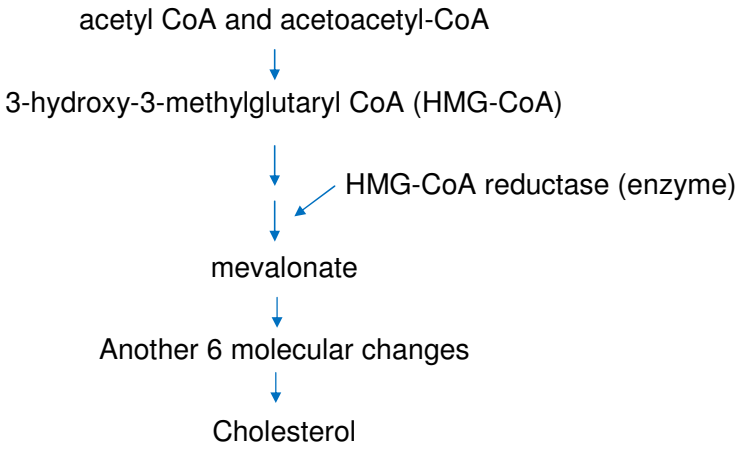
How cholesterol is naturally synthesised and regulated



- Rate of cholesterol synthesis highly responsive to cellular levels of it
- Increased levels of Cholesterol in a hepatocyte will lead to inhibition/destruction of HMG-CoA reductase – reducing ability for cholesterol to be produced.
- Dysregulation of HMGR leads to increase in cholesterol levels

https://www.ncbi.nlm.nih.gov/books/NBK22336/

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Conventional treatment

- Statins work by slowing down the production of cholesterol by the liver. They do this by interfering with the action of a key enzyme, HMG-CoA-Reductase.

- Side effects include:

  Muscle pain

  Muscle weakness

  Tummy upset

  Increase risk of diabetes II

  Reduction in vitamin D

STATINS?

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The gut-heart link

- Growing research into the reduction of LDL with probiotics
- A natural method harnessing the body's own mechanisms.

- Reis et al (2016) *Mechanisms responsible for the hypocholesterolaemic effect of regular consumption of probiotics. Nutritional Research Review*. 2016 Dec 20:1-14

-Thushara RM et al (2016) *Cardiovascular benefits of probiotics: a review of experimental and clinical studies.* Food and Function. 2016 Feb;7(2):632-42.

- Other relevant studies: Cho YA and Kim J. (2015), Sun J and Buys N (2015), Tomaro-Duchesneau C et al (2015), Ishimwe N et al (2015), Huang Y et al (2013), Tuohy KM et al (2014)

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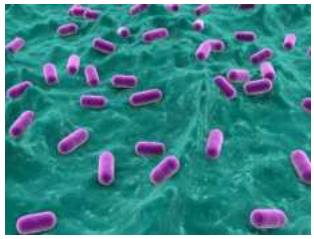
The gut-heart link

Strain specificity – a brief overview.

Not all strains in the same species, or any other species, have the same function – eg lower cholesterol

For example: *Lactobacillus rhamnosus* Rosell-11 reduces AAD, Foster et al. (2011)

Lactobacillus rhamnosus GR-1® balances the microflora in the female intimate area Reid et al. (2011)



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The gut-heart link

- **Jones L et al, (2012)** ***Cholesterol-lowering efficacy of a microencapsulated bile salt hydrolase-active Lactobacillus reuteri NCIMB 30242 yoghurt formulation in hypercholesterolaemic adults*** **British Journal of Nutrition (2012), 107, 1505–1513**

  Double blind, placebo controlled

  114 subjects – some taking the strain *L. reuteri* NCIMB 30242

  Results were an improvement in cholesterol ratio and a decrease in overall cholesterol

  American supplement - Cardioviva

- **Bosch M et al (2014)** ***Lactobacillus plantarum CECT 7527, 7528 and 7529: probiotic candidates to reduce cholesterol levels.*** **Journal of the Science of Food and Agriculture 15;94(4):803-9.**

  This In-Vitro trial showed: BSH production, adherence to cholesterol and butyrate and propionate production.

- **Fuentes et al (2013)** ***Cholesterol-lowering efficacy of Lactobacillus plantarum CECT 7527, 7528, and 7529 in hypercholesterolaemic adults.*** **British Journal of Nutrition Jan 2006 pp1-7**

Other relevant studies: Dae Hwan Kim et al (2014), Jones L et al, (2012) Jones et al (2012a), Jones et al (2012b)

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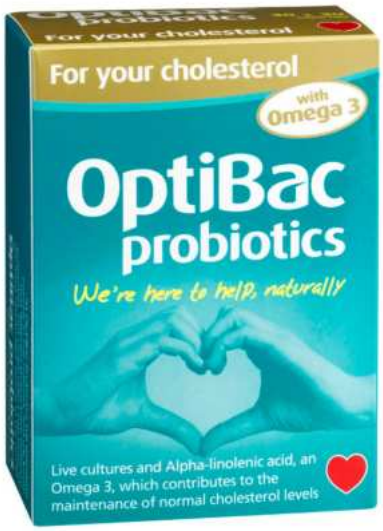
For your cholesterol



- Three strains of probiotics have been shown in in-vitro and clinical research as unsurpassed in their ability to reduce cholesterol
- Capsules containing 1.2 billion CFU of:
  L. plantarum CECT 7527
  L. plantarum CECT 7528
  L. plantarum CECT 7529
- Capsules containing Alpha-linolenic acid from cold-pressed virgin flaxseed oil

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Clinical trial design

Fuentes et al (2013) *Cholesterol-lowering efficacy of Lactobacillus plantarum CECT 7527, 7528, and 7529 in hypercholesterolaemic adults.* British Journal of Nutrition Jan 2006 pp1-7

Gold standard:	Double-blind, randomised, placebo-controlled clinical trial
Size:	60 patients with high cholesterol
Allocation:	30 on probiotic (1.2 billion), 30 on placebo
Measurements:	Taken at baseline, 6 weeks and 3 months
Results:	Statistically significant results were seen after 3 months

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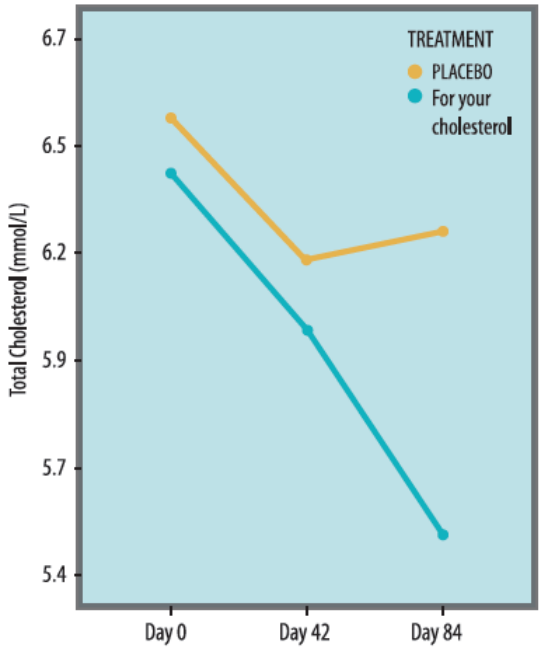
Results



- 6 week measurements were not significant
- After 3 months the probiotic group had an average decrease in TC of 0.9mmol/L (14%)
- '*Administering the L. plantarum mixture greatly reduced the atherogenic index and the cardiac risk factor. The hepatic lipid content, the triglyceride content, and total cholesterol content in the liver tissue was remarkably reduced by the administration of the L. plantarum mixture.*'

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Stratification

- The results from the group of 30 patients in the probiotic group can be divided into:

- Those with highest initial cholesterol (6.5 to 7.8 mmol/L)

- Those with medium-high initial cholesterol (5.2 to 6.4 mmol/L)

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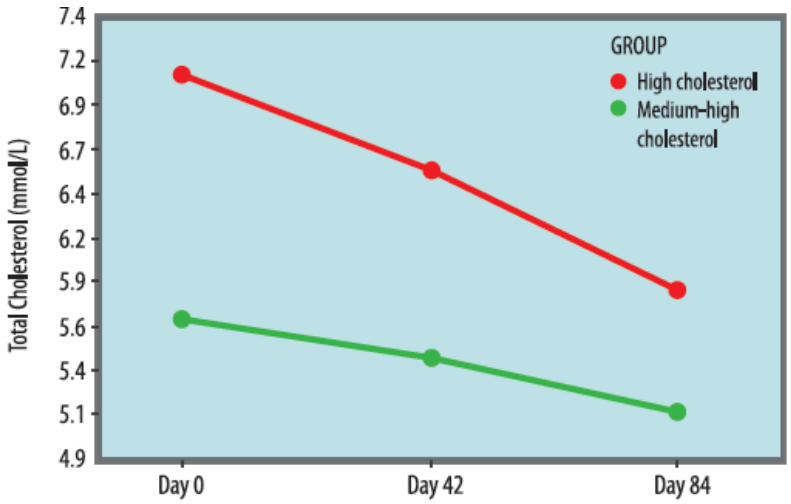
Stratification



Those who had higher initial cholesterol had a larger decrease in TC (1.2 mmol/L – 17%) than those in the medium-high group (0.5 mmol/L – 9%)

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Safety

- ✓ No adverse effects were reported
- ✓ Slow mechanism of action = gradual effects = reduced risk of side effects
- ✓ Negative feedback mechanism – harnessing a natural process

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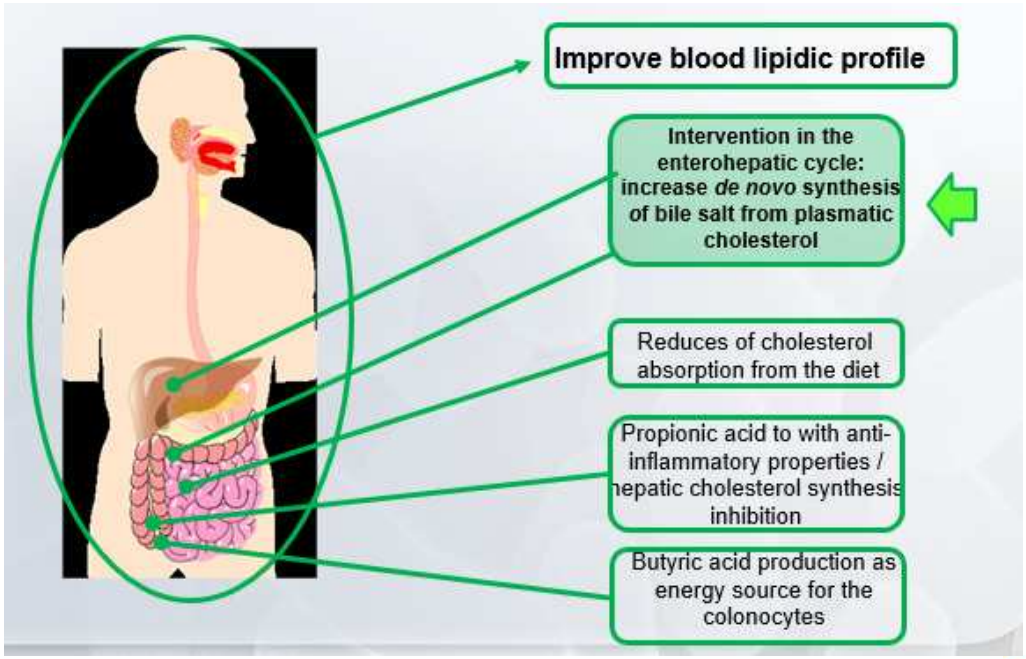
How do probiotics reduce cholesterol?



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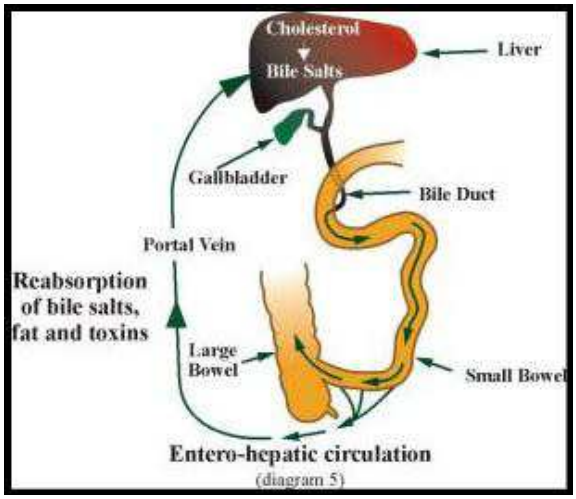
Breakdown of bile salts – Enterohepatic cycle



- Probiotics produce **bile salt hydrolase** (BSH). This breaks down bile salts to bile acid & amino acid = precipitation
- High BSH activity means **less bile is reabsorbed**.
- Therefore **cholesterol is taken from blood** for new bile synthesis in the liver

Bosch et al, (2014)

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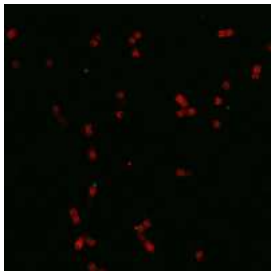
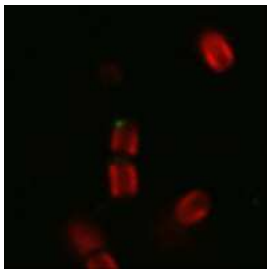
Binding to dietary cholesterol

- Cholesterol binds to the bacterial cellular surface of CECT 7528.
- The bacteria incorporates the cholesterol into it's cellular wall
- Cholesterol bound to the bacteria inhibits intestinal cholesterol micelles from forming so cannot reach the intestinal surface – leading to lower cholesterol being absorbed into blood stream.

Lye HS (2010), Araki YI (1996), Bosch et al (2014)





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Producing propionic acid

- These strains produce a particularly large amount of propionic acid – especially CECT 7529

Short chain fatty acid

↓

Absorbed into blood stream

↓

Perceived as a signal by the liver

↓

Less cholesterol produced

- Propionic acid is also anti-inflammatory

  Pereira DI and Gibson GR (2002), Orlicz-Szczesna G and Gabka M (1999), Hanssonn GK et al (1989), Bosch et al (2014)

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Producing Butyric acid

- Butyrate is a key nutrient for metabolic activity and growth of colonocytes
- Now thought to be a regulator of intestinal fat absorption and circulating lipoprotein concentrations

Valérie Marcil, et al (2003), Alvaro A et al (2008)

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Anti-inflammatory

1. Probiotics increase anti-inflammatory cytokines e.g. IL-10

2. Probiotics decrease pro-inflammatory cytokines e.g. IL-6

3. Short chain fatty acids are known to be anti-inflammatory (Vieira EL et al, 2012)

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3257741/
http://ndnr.com/autoimmuneallergy-medicine/anti-inflammatory-probiotics immunomodulation-in-the-gut-and-beyond/

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What other options are there for reducing Cholesterol on the market

- Statins
- Artichoke
- CoQ10
- Fish oil
- Insoluble fibre
- Lecithin
- Niacin
- Plant sterols
- Red yeast rice
- Soluble fibre

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How do these compare to AB-Life strains

How does 'For your cholesterol' compare?

	For your cholesterol	Statins	Artichoke	CoQ10	Fish oil	Insoluble fibre	Lecithin	Niacin	Plant sterols & stanols	Red yeast rice	Soluble fibre
Daily effective dose used in clinical trials	1.2 billion probiotics	5 - 80mg	1 - 1.5g	30 - 200mg	>2g EPA & DHA	>3g	1 - 54g	>1.5g (Risk of flushing at this dose)	1.5 - 2.4g	1.2 - 2.4 g containing ≥10mg monacolin K	>3g
Dosage commonly provided	1.2 billion probiotics & 300mg ALA	5 - 80mg	250 - 600mg	30 - 200mg	>100mg - 2g	>3g	1.4 - 15g	100 - 500mg	As above in foods, 400 - 800mg in supplement	600mg (often not standardised for monacolin K)	>3g
Deconjugates bile salts	✓										
Binds to bile salts						✓					
Increases bile production			✓								
Reduces absorption of dietary cholesterol	✓					✓	✓		✓		
Reduces cholesterol production in liver	✓	✓	✓					✓		✓	✓
Down regulation of genes for cholesterol production	✓										
Improves ratio of 'good' to 'bad' fats consumed	✓				✓						
Reduces inflammation	✓				✓			✓			
Reduces triglycerides					✓			✓			
Reduces statin side effects				✓							

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Vascular health protocol

- Specific probiotic strains to lower cholesterol and reduce inflammation

- Include as an important part of your protocol to:

  - ✓ Reduce excess LDL cholesterol
  - ✓ Reduce inflammation
  - ✓ Increase antioxidants
  - ✓ Support healthy immune function

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Conclusion

- There is more to probiotics than gut health
- Heart and vascular health is complex, involving many factors, of which cholesterol is an important one
- Specific strains are *clinically trialled* and *shown to reduce* cholesterol
- *New and exciting* concept in natural medicine

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Thank you for listening

joanna@wrenlabs.com

For a full trade guide please email Christina

christina.georgallou@wrenlabs.com

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