Functional foods

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Introduction :

- The concept of functional food backs to the middle of 1980s

- food that supplemented with a particular component that possess positive physiological influences

- This concept of functional food has been described many times

- Functional Food Science in Europe (FUFOSE) supported by International Life Science Institute (ILSI) defined functional food as " a food products can only be considered functional if together with the basic nutritional impact effect on one or more functions of the human organs thus either improving the general and physiological condition or/and decreasing the risk of the evaluation of disease.

European Consensus on "Scientific Concepts of Functional Foods" have described FF as "a food can be regarded as functional if it is satisfactorily demonstrated to affect beneficially 1 or more target Functions in the body, beyond adequate nutritional effects, in a way that is relevant to either improved stage of health and well-being and/or reduction of risk of disease"

- Possess ingredient (s) that effectively improve a number of the body functions alongside with its nutritive influence.
- They should be in the form of conventional food rather than
- tablet or capsules

- Their mission should be to decrease risks of diseases

- It should be safe and accepted by food regulation.

- It should be consumed daily as a portion of normal daily diet.

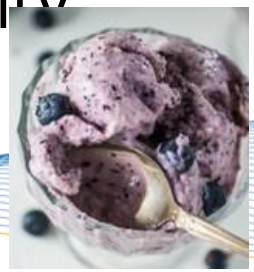
- All kinds of food from different sources can be labelled as functional
  - Functional food perhaps has more missions that discriminates them from other foods
    - Therefore, there are a numerous approaches to switch particular foods to functional

- Through replacing or removing a component that is always consumed more than recommended and could have unhealthy influence by a useful ingredients

- By increasing the amount of a natural food ingredient to become a quantity which has more benefits

  - Supplementation of a constituent that does not exist naturally in foodstuffs, but has been proved to be salutary

    - Through naturally stimulating an essential food component proportion (enhancement of the bioavailability



Many countries has developed new regulations for marketing functional foods

Then European commission started to develop new strict in relation to health claim.

In 2001 any every health-related claim was forbidden

In 2006 according to (EC) No 1924/2006 new regulation approved. Products needs substantiated source or data.

This included three categories

1- Nutrition claim(product has nutritional benefits (calorie content)

2-Health claim: any claim of having connection between any constituent and health

3-Reduction of diseases: any connection between food or constituents with reduction of diseases

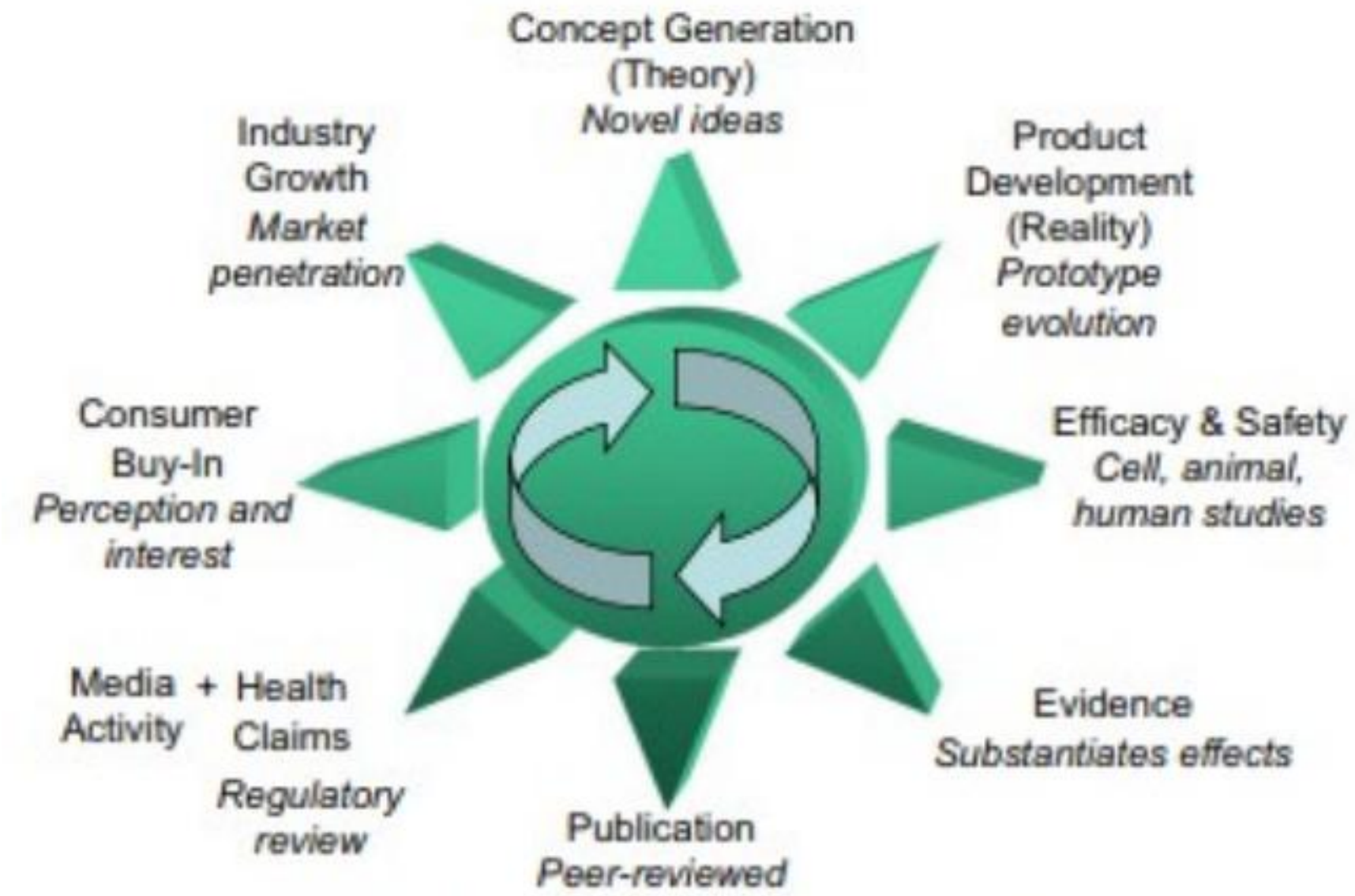


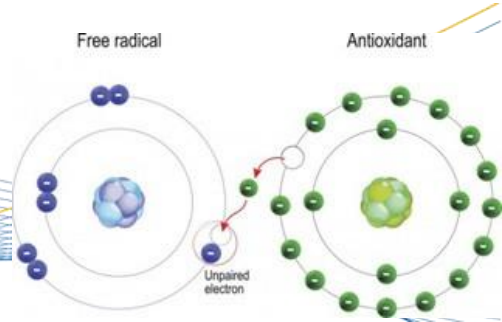
Fig. 1. Functional foods and health promotion: cycle of success.

As a result of increasing market growth, there is a huge possible range of functional foods. These include:

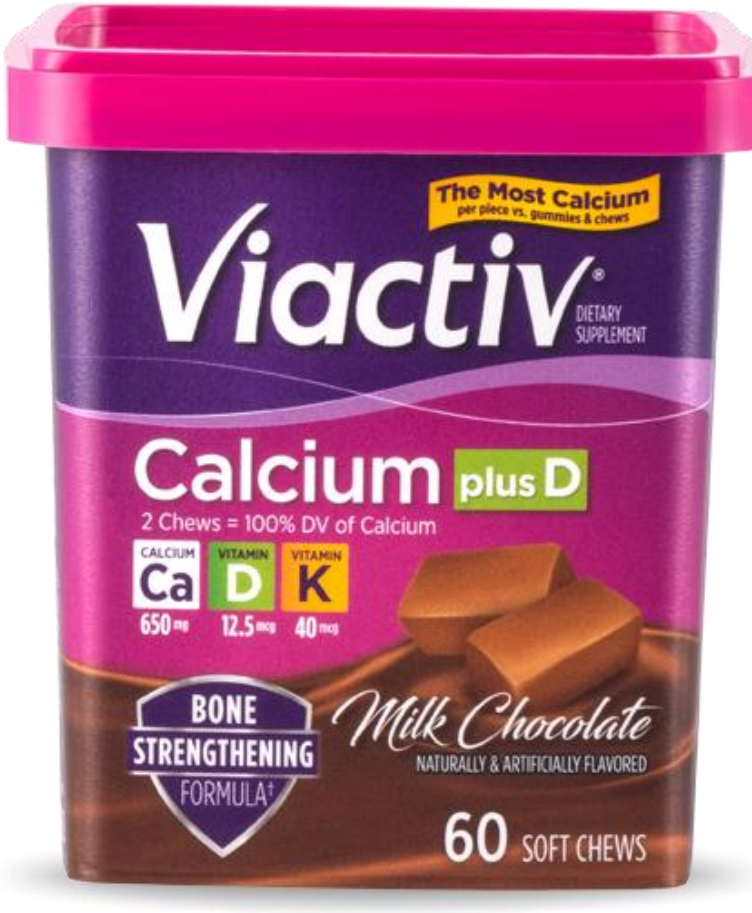
- · soft drinks such as energy and sports drinks
- · cereal and baby foods
- · baked goods
- · confectionery
- · dairy products, especially yoghurts and other fermented dairy products
- · spreads
- · meat products
- · animal feeds.

One way of categorising their mode of operation is as follows:

- vitamin and mineral fortification
- cholesterol reduction
- dietary fibre
- probiotics, prebiotics and synbiotics
- antioxidants
- phytochemicals
- herbs and botanicals.



- Examples of products fortified with vitamins and minerals include calcium fortified confectionery and fruit drinks, and calcium-enriched milk with folic acid. Folic acid, for example, is documented as a vital nutrient in early pregnancy that guards against spina bifida, while the importance of calcium has been recognised in counteracting osteoporosis.



- **Osteoporosis** among the increasing proportion of **elderly people** in developed countries, improving calcium intake has been seen as particularly significant in this sector of the functional foods market. Research has concentrated not just on ways of increasing levels of calcium intake but also in improving the efficiency of calcium absorption.

- A number of **ingredients** are associated with **inhibiting the absorption of cholesterol** which is thought to be a major factor in cardiovascular disease.
- This category includes **omega-3 fatty acids** and plant sterols. Examples of products in this area include a **margarine containing plant sterol fatty acid esters** designed to reduce cholesterol absorption, and **omega-3 enriched eggs** produced by **chickens fed a micoalgal** feed ingredient.

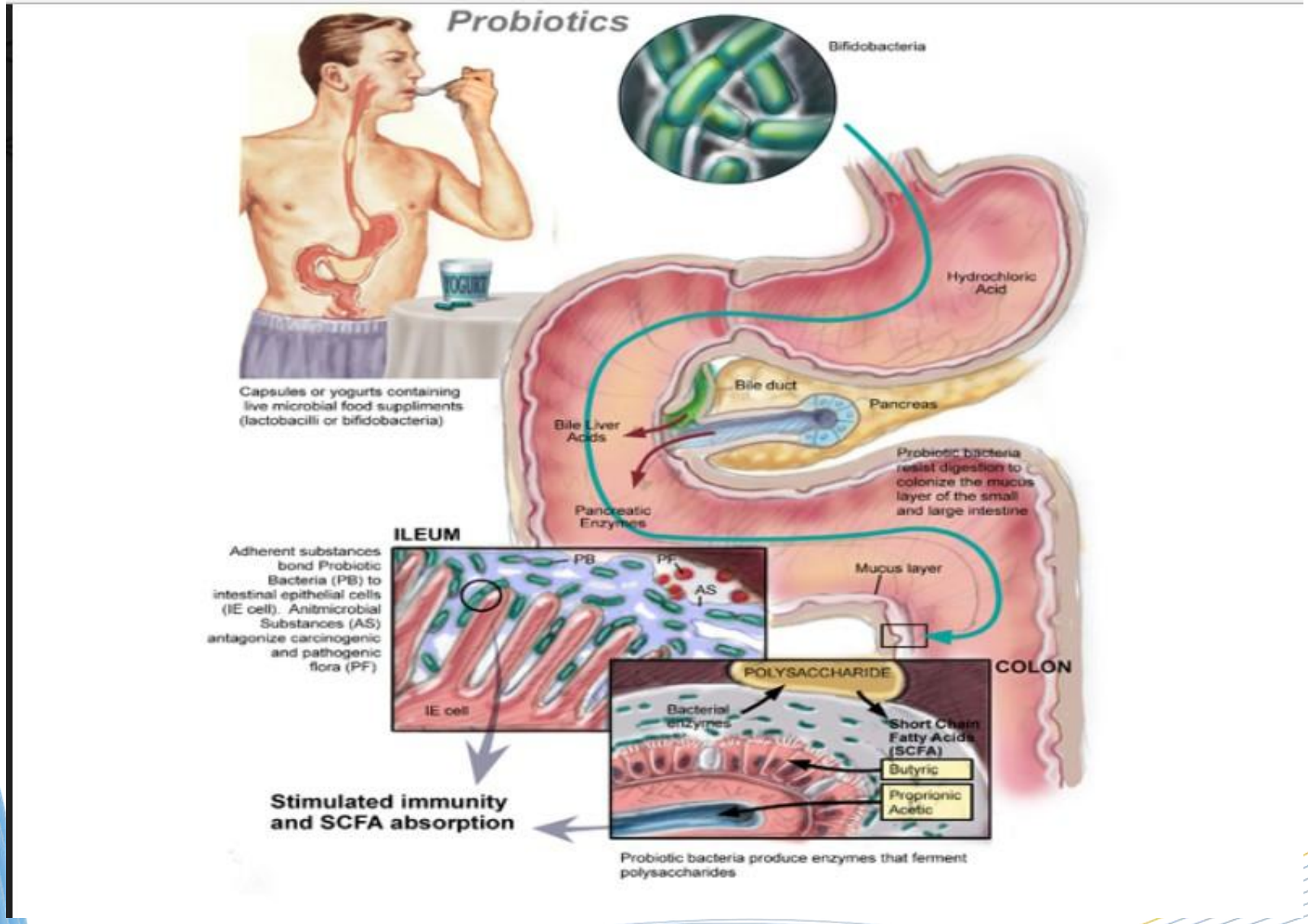
- **Dietary fibre** comprises the non-digestible structural carbohydrates of plant cell walls and associated lignan.
- **Consumption of fibre** has been linked to reduced risk of certain types of **cancer**, for example consumption of **wheat bran** which has been linked to a reduced risk of colon cancer.
- **High-fibre products** include a whole-wheat pasta with three times the fibre of regular pasta.

- A **probiotic** can be defined as a **live** microbial food supplement which beneficially affects the host by improving its intestinal microbial balance.
- **Probiotics** are thought to have a range of potential health benefits, including **cholesterol-lowering**, cancer chemo-preventative and immune-enhancing effects.

Live microbial food supplements which
beneficially affect the host animal by improving its intestinal microbial balance.

Usually strains of bacteria (lactobacilli or bifidobacteria) or yeasts (Saccharomyces)

- Human origin
- Resist upper GI tract secretions
- Adhere to human intestinal cells
- Colonize the human intestinal tract
- Production of antimicrobial substances
- Antagonize carcinogenic/ pathogenic flora
- Safe in clinical use at > 1010
- Stimulate immune system
- Fermentation


Probiotics
Bifidobacteria
Capsules or yogurts containing live microbial food suppliments (lactobacilli or bifidobacteria)
Hydrochloric Acid
Bile duct
Pancreas
Bile Liver Acids
Pancreatic Enzymes
Probiotic bacteria resist digestion to colonize the mucus layer of the small and large intestine
ILEUM
Adherent substances bond Probiotic Bacteria (PB) to intestinal epithelial cells (IE cell). Anitmicrobial Substances (AS) antagonize carcinogenic and pathogenic flora (PF)
PB
PF
AS
IE cell
Mucus layer
COLON
POLYSACCHARIDE
Bacterial enzymes
Short Chain Fatty Acids (SCFA)
Butyric
Proprionic
Acetic
Stimulated immunity and SCFA absorption
Probiotic bacteria produce enzymes that ferment polysaccharides

- **Probiotics** are viewed currently as the world's biggest functional food products.

- This sector of the functional foods market has been stimulated in recent years by the development of prebiotics, short chain oligosaccharides which enhance the growth of beneficial bacteria already in the gut, and synbiotics which combine pro- and prebiotic characteristics. The field of gut health is now an area of intense research in functional food science.

- **Cancerous** and other **mutations** can occur as a result of oxidative damage to DNA caused by free radicals generated as a damaging side-effect of aerobic metabolism. Plant and animal cells defend themselves against these effects by

  deploying so-called antioxidant compounds to trap or quench free radicals andhence arrest their damaging reactions

- **Antioxidants** thus play a role in the body's defence against **cardiovascular disease**, certain (epithelial) cancers, **visual impairments**, arthritis and asthma. Antioxidants include vitamin E, carotene, vitamin C and certain phytochemicals.
- Functional products incorporating antioxidant supplements include **sports bars containing vitamins C and E** as well as a blend of several carotenoids (alpha- and gamma-carotene and lycopene)

- Plant foods are rich in **micronutrients**, but they also contain an immense variety of biologically active, non-nutritive secondary metabolites providing colour, flavour and natural toxicity to pests and sometimes humans. These '**phytochemicals**' have been linked to reducing the risk of chronic diseases such as cancer, osteoporosis and heart disease.

- They include glucosinolates and phenolic compounds like flavonoids which are very effective antioxidants. Examples of products including phytochemicals are children's confectionery containing concentrates of vegetables such as broccoli, Brussels sprouts, cabbage and carrots.

One much-used approach is ***probiotics***Here, live microbial additions are made to appropriate food vehicles like yoghurts or other fermented milks

Including lactobacilli and/or bifidobacteria

It is proposed that probiotics exert certain advantageous properties in the gastrointestinal ecosystem

These are thought to include improved resistance to pathogens, reduced blood lipids, positive immuno-modulatory properties and better protection from chronic gut disorder.

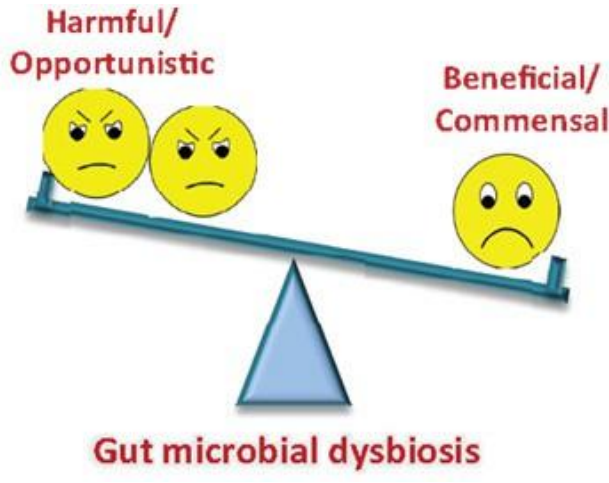
- More recently, herbs and botanicals such as ginkgo, ginseng and guarana have been linked to improved physical and mental performance. These may lead to a new generation of 'performance' functional foods including these and other components such as creatin, caffeine and tryptophane. Products in this area include beverages, chewing gum and sports bars

Colonic functional foods

- The microbiota of the human gastrointestinal tract plays a key role in nutrition and health. Through the process of fermentation, gut bacteria metabolise various substrates (principally dietary components) to form end products such as short chain fatty acids and gases

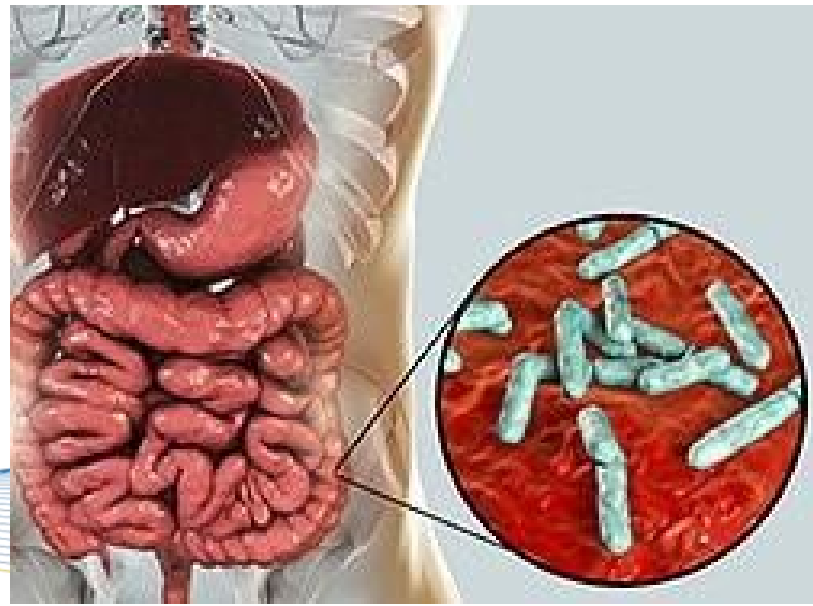
- This anaerobic metabolism is thought to contribute positively towards host daily energy requirements

Usually, the human host lives in harmony with the complex gut microbiota. However, under certain circumstances like antimicrobial intake, stress, poor diet and living conditions, the microflora balance' may be upset



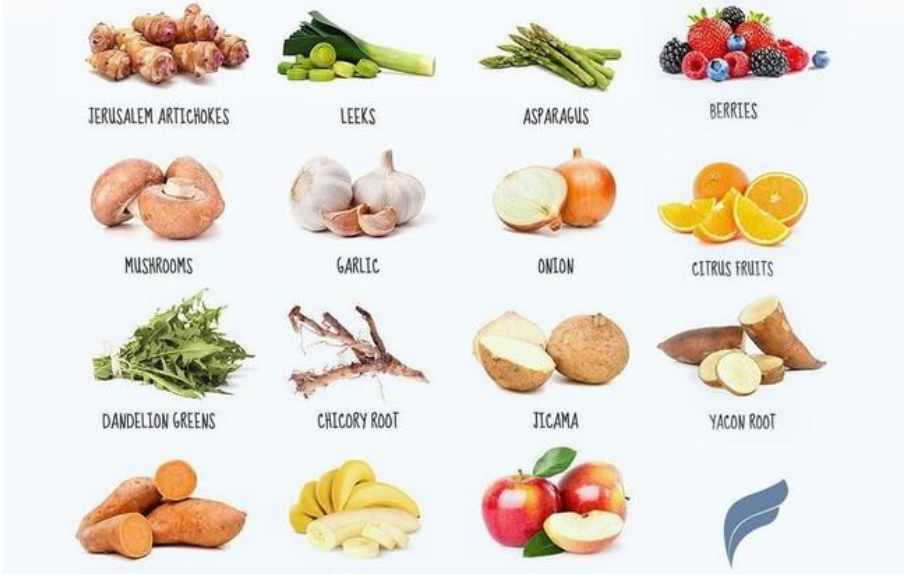
Moreover, the normal fermentative process may produce undesirable metabolites like ammonia, phenolic compounds, toxins, etc. The gut flora is also susceptible to contamination from transient pathogens, which further upset the normal community structure.

It is clear that the colonic microbiota is susceptible to manipulation through dietary mechanisms that target specific bacterial groups.3There is current interest in the use of dietary components that help to maintain, or even improve, the normal gut microflora composition and activities



Prebiotics serve a similar purpose to **probiotics** *in* that they aim to improve the gut microflora community structure.

A **prebiotic** is a non-digestible food ingredient that beneficially affects the host by selectively stimulating the growth and/or activity of one or a limited number of bacteria in the colon, that may improve the host health



A complex, resident gastrointestinal microflora is present in humans. While the transit of residual foodstuffs through the stomach and **small intestine is probably too rapid** for the microflora to exert a significant impact, this slows markedly in the colon

As such, colonic micro-organisms have ample opportunity **to degrade available substrates**, of which **around 70g/d may be** derived from the diet. These can be recognised **as 'colonic foods',** metabolism of which occurs through the anaerobic metabolic process known as fermentation

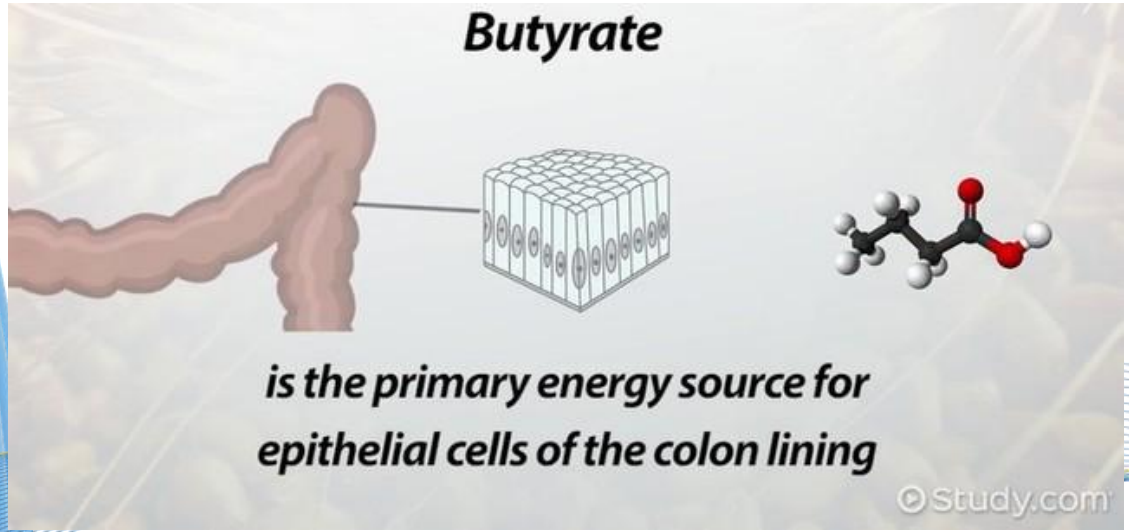
Type of substrates available for bacterial growth in the human large intestine

- Bacteria resident in the large gut depend upon a supply of fermentable substrate for their growth and activities.
- Principally, this is provided by the **diet**, (any food that resists digestion) although there is also a contribution from endogenous sources like **mucins** and **chondroitin** sulphate

- Any foodstuff that resists digestion in the upper gastrointestinal tract (stomach, small intestine) can serve as a colonic food in that it feeds the resident microbiota

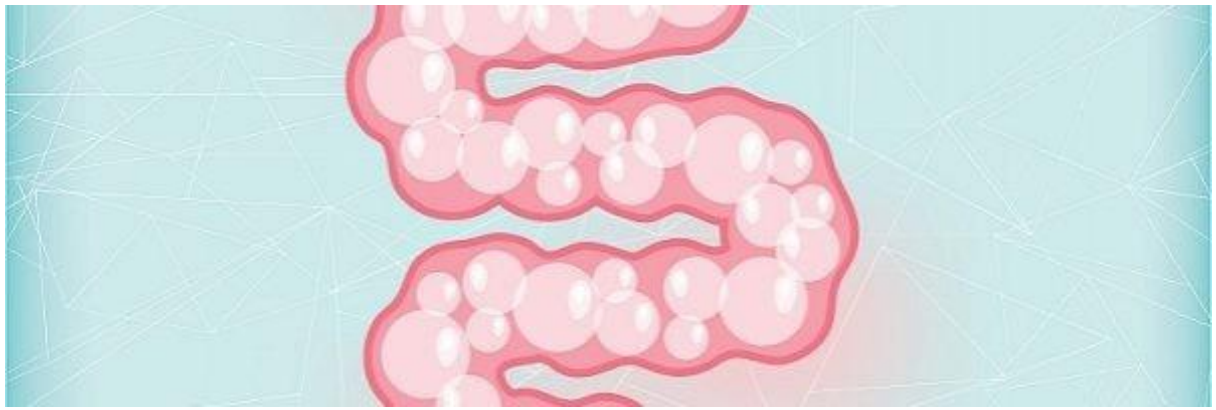
Major **SCFA** produced are acetate, propionate and butyrate. It is thought that acetate is cleared
in peripheral tissues such as muscle. Propionate is largely broken down in the liver.

whereas butyrate acts as the primary source of fuel for colonocytes. The systemic metabolism of SCFA in the liver is thought to contribute about 7–8% of host daily energy requirements which in itself confirms the significant role of gut micro-organisms in human nutritional processes



Gases are also derived by bacterial action in the large intestine. Principally,these are **hydrogen**, **carbon dioxide**, **methane** and **hydrogen sulphide**. While gas formation is usually considered to be the terminal stage of food digestion , it remains an enigmatic process through the 'balance' of H2 generation/ metabolism

A number of possible fates occur for intestinal H2 in that it may be excreted or further metabolised by gut bacteria. In the latter case, sulphate reducers (producing H2S), methanogens (expiring CH4) and acetogens(excreting acetate) may all be involved



Medically, H2 and its fate have been, at least tenuously but usually scientifically, linked with pneumatosis cystoides intestinalis, ulcerative colitis and bowel cancer

Factors affecting colonisation and growth of bacteria in the gut

Predominant end products of protein fermentation are SCFA, including branched chain forms, as well as phenolic compounds, **ammonia** and some amines

These metabolites have been associated with various clinical states such as tumourigenesis, schizophrenia, migraine

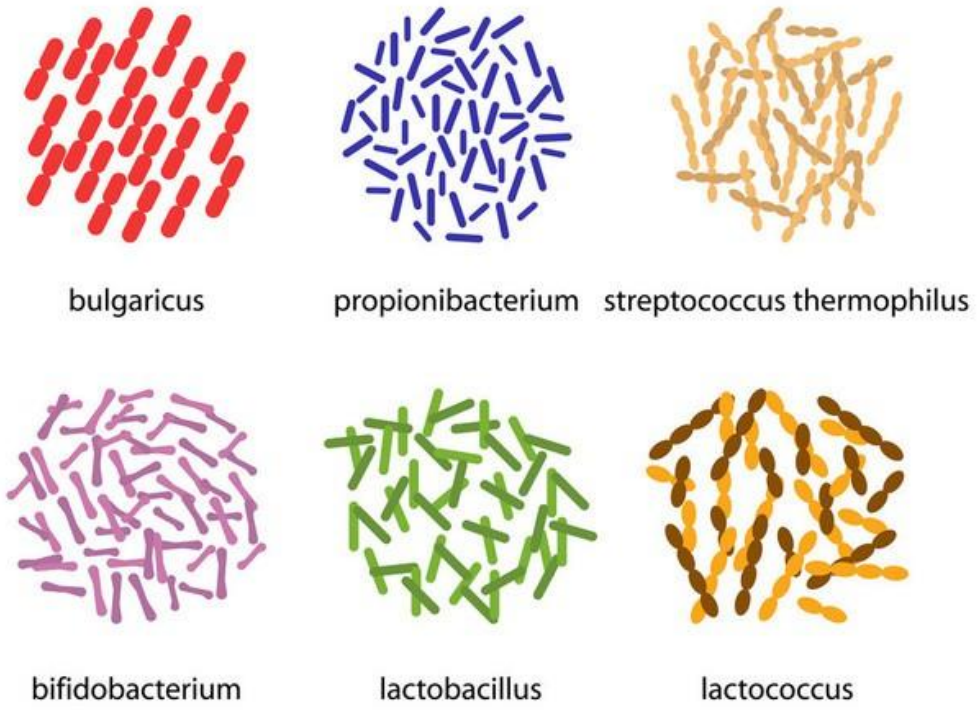
In very general terms, the metabolites of a **saccharolytic metabolism** in the gut are **benign**, whereas those that arise from proteolysis can be **detrimental**. As such, there can be positive or
negative outcomes associated with gut bacterial fermentation.

- The first records of ingestion of live bacteria by humans are over hundred years ago. However, at the beginning of this century probiotics were first put onto a scientific basis by the work of Metchnikoff at the Pasteur Institute in Paris.

Metchnikoff hypothesised that the normal gut microflora could exert adverse effects on the host and that consumption of 'soured milks' reversed this effect.

Metchnikoff refined the treatment by using pure cultures of what is now called *Lactobacillus delbrueckii subsp. bulgaricus which, with Streptococcus salivarius subsp.thermophilus, is used to ferment milk in the production of traditional yoghurt*

- A formal probiotic definition is a live microbial feed supple which beneficially a the host animal by improving its intestinal microbial balance



Over the years, many speciesof micro-organisms have been used. They consist not only of lactic acid bacteria (lactobacilli, streptococci, enterococci, lactococci, bifidobacteria) but also *Bacillus spp. and fungi such as Saccharomyces spp. and Aspergillus spp.*

Main positive effects associated with probiotics include

- cholesterol and/or triglyceride reduction, Anti-tumour properties.
- protection against gastroenteritis,
- improved lactose tolerance
- stimulation of the immune system through non pathogenic means

- Prebiotics allow the **selective growth** of certain indigenous gut bacteria. Thus, the prebiotic approach involves administration of a non-viable food component and considers that many potentially health-promoting micro-organisms such as **bifidobacteria** and **lactobacilli** are already resident in the human colon

- Neither be hydrolysed nor absorbed in the upper part of the gastrointestinal tract;
- Have a selective fermentation such that the composition of the large intestinal microbiota is altered towards a healthier composition

- **fructose-containing oligosaccharides** (FOSs) banana, onions, legumes, Jerusalem artichoke……
- Galacto-oligosaccharides (GOSs) are another class of prebiotics that are manufactured and marketed in Europe as well as Japan. dairy products Legumes, Cashews and pistachios, soya milk or soya drink and Oat milk.
- Xylo-oligosaccharides (XOSs) are also used as prebiotics in Japan. Sources: bamboo shoots, fruits, vegetables, milk, and honey

- A synbiotic is a marriage of the concepts of probiotics and prebiotics. A synbiotic consists of a live microbial food additive together with a prebiotic oligosaccharide. They can deliver the benefits of probiotics and prebiotics.

Coronary heart disease and functional food

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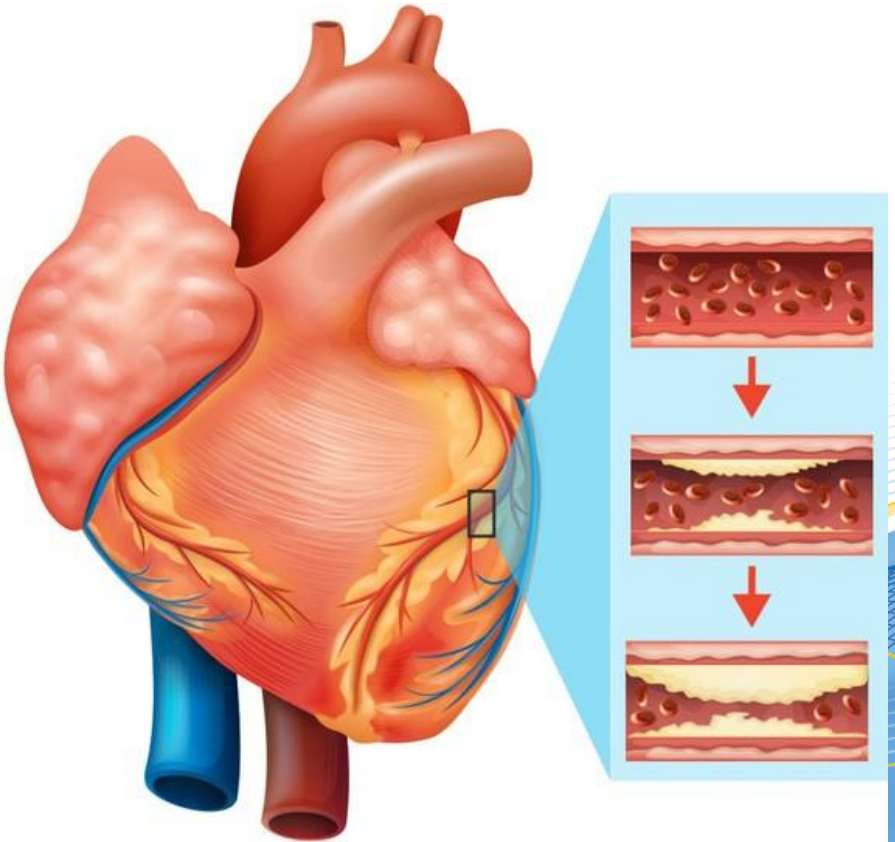


Coronary heart disease

- Coronary heart disease (CHD) is one of the major causes of death in adults in the Western world.
- CHD is a condition in which the main coronary arteries supplying the heart
- are no longer able to supply sufficient blood and oxygen to the heart muscle
- (myocardium).

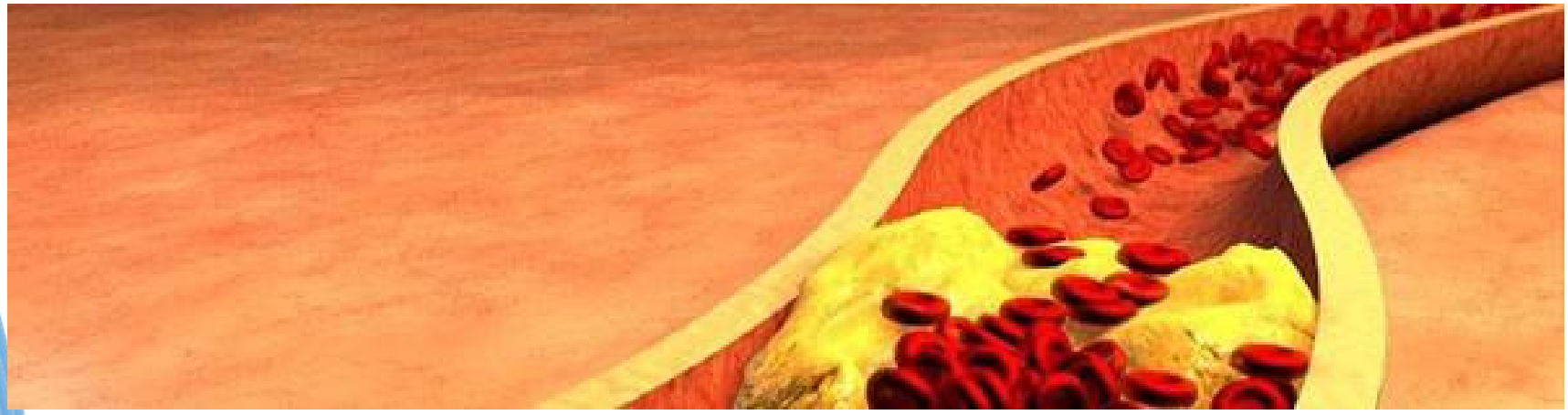
The main cause of the reduced flow is an accumulation of plaques, mainly in the intima of arteries, a disease known as atherosclerosis.

- This is a slow but progressive disease which usually begins in childhood, but does not usually manifest itself until later life

- Depending on the rate of the narrowing of the arteries and its ultimate severity, four syndromes may occur during the progression of CHD. These include angina pectoris, unstable angina pectoris, myocardial infarction and sudden death.

- A number of risk factors known to predispose an individual to CHD have been categorised into:
- **those that are not modifiable**, such as age, sex, race and family history
- **those that are modifiable**, such as hyperlipidaemia (high levels of lipids (fat) in the blood), hypertension (high blood pressure), obesity, cigarette smoking and lack of exercise

- A recently recognised risk factor for CHD is an elevated level of triacylglycerol (TAG; major fat in the blood) in both the fasted and fed (postprandial) state



- Individuals with CHD and those with a high risk of developing the condition are treated in a number of ways to help lower their LDL cholesterol and TAG concentrations while elevating their HDL cholesterol
- Many studies have confirmed that modifying diet is one of the ways if treatment.
- This is implemented by reducing the percentage of dietary energy derived from fat to approximately 30%, with a reduction of saturated fatty acids to 10% of the dietary energy derived from fat

- The effect of the ingestion of different fatty acids on plasma cholesterol levels is varied and is summarised in Table 5.5. Substitution of SFAs by MUFAs or *n-6 PUFAs significantly reduces LDL cholesterol levels although n-6 PUFA* are more effective in this respect.

Table 5.5 Effects of fatty acids on plasma lipoprotein concentrations

Fatty acid	*Total cholesterol*	*LDL cholesterol*	*HDL cholesterol*	*Triacylglycerol*
Saturated FA	Increase	Increase	Neutral	Neutral
n-6 PUFA	Decrease	Decrease	Decrease	NA
n-3 PUFA	Unchanged	Unchanged*	Increase	Decrease
Trans FA	Increase	Increase	Decrease	NA
MUFA	Decrease	Decrease	Neutral	Neutral
Cholesterol	Increase	Increase	NA	NA

Notes:
FA – fatty acid. PUFA – polyunsaturated fatty acid. MUFA – monounsaturated fatty acid. NA – not available. * May increase in hyperlipidaemics.

- There has been doubt as to whether MUFAs are effective in cholesterol-lowering or whether the observed decrease in plasma cholesterol was simply due to a replacement of SFAs. Some studies have suggested that the effect of oleic acid (cis 18:1) (the major MUFA in the diet) and linoleic acid (18:2) (major *n-6 PUFA in the diet)* *on LDL cholesterol are* similar, and that the greater effect of linoleic acid on total cholesterol is through reduction of HDL cholesterol.

- In addition to this, it has been reported that PUFAs incorporated into lipoproteins can increase their susceptibility to oxidation if there is insufficient antioxidant protection. Despite the beneficial lowering of LDL cholesterol associated with increased dietary PUFA, it has been proposed that the decreased levels of beneficial HDL cholesterol and greater susceptibility of lipoproteins containing *n-6 PUFA to oxidation, result in* pro-atherogenic effects of diets in which *n-6 PUFA provide greater than 10%* energy.

- Substitution of saturates by oleic acid would avoid this and therefore MUFAs have theoretical advantages over PUFAs. It has long been recognised that, in Mediterranean populations, there is a significantly lower risk of CHD. Their diet traditionally contains high amounts of olive oil in addition to fruit and vegetables compared to the UK diet. It has been speculated that a higher intake of MUFAs could contribute to the lower rate of CHD within this population.

- However, it could also be due to the higher antioxidants found in the fruit, vegetables and within virgin olive oil itself, in addition to other dietary and lifestyle factors. Research into the reasons for this link between th Mediterranean lifestyle and CHD risk is necessary to explain this observation fully.
- As regards CHD, *trans fatty acids appear to act similarly to SFA in their* effects on blood cholesterol except that *trans FA decreased HDL whereas SFA* have little effect on HDL

- Diets where about 60% of food energy is derived from carbohydrate are associated with lower HDL levels and higher TAG levels, and despite lower LDL levels have been suggested to be associated with a higher risk of CHD.
- However, a smaller increase in dietary carbohydrate levels to accommodate a reduction in dietary fat to 30% of energy has been reported to result in a small rise in TAG levels and no fall in HDL levels, resulting in an overall positive benefit in CHD risk

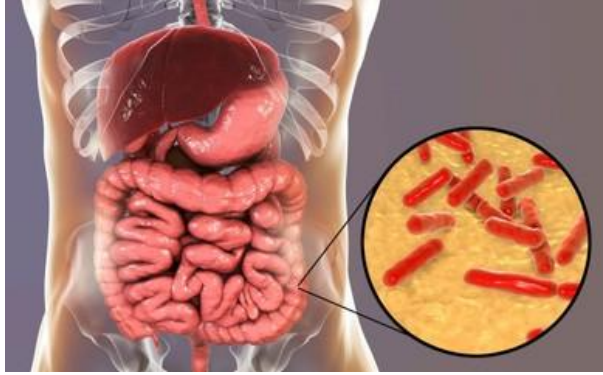
- There is a large body of evidence supporting a protective effect of the antioxidant vitamins E and C. There are, however, inconsistencies in the amount of these antioxidants associated with reduced risk of CHD.
- No specific recommendations on the levels of antioxidant intake have been given but a diet rich in vegetable and fruit and containing nuts and seeds is recommended.
- The beneficial effects of sugar beet and olive oil on CHD risk could in part be attributed to antioxidants such as flavonoids and polyphenols contained within these foods

- Sodium intake appears to be an important determinant of blood pressure in the population as a whole, at least in part by influencing the rise in blood pressure with age.
- A diet lower in common salt and higher in potassium would be expected to result in lower blood pressure and a smaller rise in blood pressure with age.

- Salt is the predominant source of sodium in the diet with manufactured foods contributing to 65–85% of the total salt ingested. Blood pressure is an important risk factor for the development of CHD and strokes.
- It has been recommended that the population should reduce its salt intake by 3 g/ day by reducing salt at the table and also the consumption of processed foods. Moreover, higher potassium levels within the diet are believed to reduce the blood pressure and foods such as fruit and vegetables, which contain this mineral, should be taken in higher amounts.

- Although there is a debate on the benefits of alcohol consumption particularly red wine, there is evidence that high consumption of alcohol is related to increased mortality, especially from CHD.

- For over 20 years it has been suspected that caffeine or coffee consumption may contribute to the development of CHD, but the evidence remains unclear.
- The Scandinavian practice of boiling coffee during its preparation appears to generate a hypercholesterolaemic fraction. Significant levels of these compounds have also been found in cafeteria coffee which have been found to increase plasma LDL cholesterol levels



- There are many studies suggesting that consuming fermented milk could reduce risks of CHD. Possible mechanisms include
  1- Deconjugation of bile acid and prevent re-absorption.
  2- There is also some *in vitro evidence to support the hypothesis that certain* bacteria can assimilate (take up) cholesterol. This might suggested as a possible explanation for hypocholesterolaemic effects of probiotics.
  3- The mechanism of cholesterol binding to bacterial cell walls has also been suggested as a possible explanation for hypocholesterolaemic effects of probiotics

- Several studies that have investigated the effects of prebiotics on fasting plasma lipids have generated inconsistent findings (Table 5.8). In studies with individuals with raised blood lipids, three studies showed significant decreases in fasting total and LDL cholesterol, with no significant changes in TAGlevels

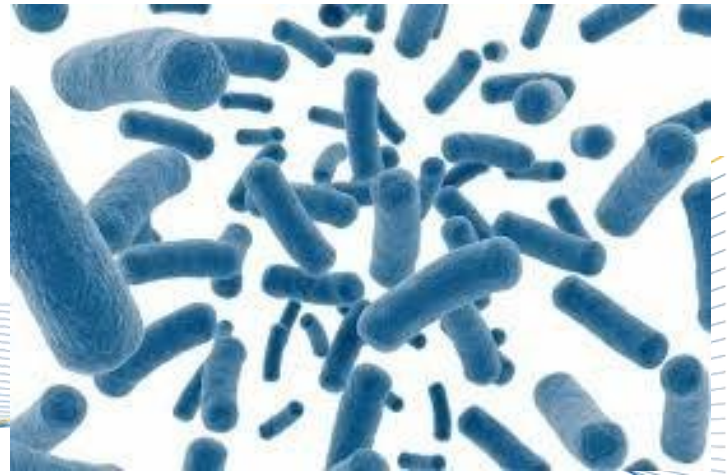


Table 5.8 Summary of human studies to examine the effects of fructan supplementation on blood lipids

Author	*Subjects*	*Fructan*	*Dose*	*Study design*	*Duration*	*Vehicle*	*Significant changes observed in*	
							blood lipids	*glucose*
Yashashati *et al.*[83]	8M and 10F NIDDM	OFS	8 g	DB, parallel	2 wks	Packed coffee drink Canned coffee jelly	↓ TC ↓ LDL-C	↓ glucose
Hidaka *et al.*[84]	37 (M & F) hyperlipidaemic	OFS	8 g	DB, parallel	5 wks	Confectionery	↓ TC	NS
Canzi *et al.*[87]	12 M normolipidaemic	Inulin	9 g	Sequential	4 wks	Breakfast cereal	↓ TAG ↓ TC	N/A
Luo *et al.*[89]	12 M normolipidaemic	OFS	20 g	DB cross-over	4 wks	100 g biscuits	NS	NS
Pedersen *et al.*[90]	66 F normolipidaemic	Inulin	14 g	DB cross-over	4 wks	40 g margarine	NS	N/A
Causey *et al.*[88]	9 M normolipidaemic	Inulin	20 g	DB cross-over	3 wks	Low fat ice-cream	↓ TAG	NS
Davidson *et al.*[85]	21 M and F hyperlipidaemia	Inulin	18 g	DB cross-over	6 wks	Chocolate bar/paste or coffee sweetener	↓ LDL-C ↓ TC	N/A
Alles *et al.*[86]	9 M and 11 F Type II diabetes	OFS	15 g	SB cross-over	3 wks	Supplement not specified	NS	NS
Jackson *et al.*[91]	54 M and F normolipidaemic	Inulin	10 g	DB, parallel	8 wks	Powder added to food and drinks	TAG	↓ insulin

Notes:
M, male; F, female; DB, double blind; N/A, not measured; NS, not significant; SB, single blind; TC, total cholesterol; LDL-C; LDL cholesterol; OFS, oligofructose; TAG, triacylglycerol.

- Proposed mechanism include
- 1- cholesterol synthesis inhibition by short chain fatty acids produced from prebiotic fermentation.
- Synbiotic can also help reducing risks of CHD.