Nutritional Pharmacy

Anna Arnoldi
Dipartimento di Endocrinologia, Fisiopatologia e Biologia Applicata, Università di Milano
& HPF-Nutraceutics SRL
anna.arnoldi@unimi.it
Greek Physician Hippocrates,
Known as father of Medicine.
(said several centuries ago)

“Let Food be Your Medicine”

The Philosophy behind is:
“Focus on Prevention”
• The term “**Nutraceutical**” was coined from “**Nutrition**” & “**Pharmaceutical**” in 1989 by Stephen DeFelice, MD, Founder and Chairman of the Foundation for Innovation in Medicine (FIM).

• It refers to the **bioactive components** that may be found in:
  • a) normal foods,
  • b) enriched foods (functional foods);
  • C) dietary supplements.
What is a Functional Food?

• A food product that is part of the usual diet, but has beneficial effects that go beyond the traditional nutritional effects.

• These beneficial effects must be demonstrated to justify two specific type of claims:
  - The enhanced function claim
  - The reduction of disease risk claim

Examples of Functional Foods

✓ yoghurts - probiotics for intestinal health
✓ foods/cereals/snacks enriched with soluble fibre, vitamins, minerals
✓ sports drinks, isotonic, energy restoring, fibre-rich
✓ cholesterol lowering spreads containing phytosterols
### EXAMPLES OF FUNCTIONAL COMPONENTS

<table>
<thead>
<tr>
<th>Class / components</th>
<th>Source</th>
<th>Potential benefit</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1. Fatty acids</strong></td>
<td>Milk &amp; Meat</td>
<td>Improve body composition, reduce cancers</td>
</tr>
<tr>
<td>CLA</td>
<td></td>
<td></td>
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<tr>
<td><strong>n-3 FA (DHA, EPA)</strong></td>
<td>Fish oils, Egyptian clover, walnut, linseed, rapeseed</td>
<td>Reduce CVD &amp; improve mental, visual function</td>
</tr>
<tr>
<td>Class / components</td>
<td>Source</td>
<td>Potential benefit</td>
</tr>
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</tr>
<tr>
<td>2. Polyphenols</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anthocyanidines</td>
<td>Fruits</td>
<td></td>
</tr>
<tr>
<td>Catechins</td>
<td>Tea, babul pods, mustard cake, rape seed, <em>Shorea robusta</em> seeds</td>
<td>Neutralize free radicals, reduce risk of cancer</td>
</tr>
<tr>
<td>Flavanones</td>
<td>Citrus</td>
<td></td>
</tr>
<tr>
<td>Flavones</td>
<td>Fruits, vegetables, soya bean</td>
<td></td>
</tr>
<tr>
<td>Proanthocyanidines</td>
<td>Cocoa, chocolate, tea, rape seed</td>
<td>Reduce CVD</td>
</tr>
<tr>
<td>3. Saponins</td>
<td>Soybeans, GNC, lucern, chick pea</td>
<td>Lower cholesterol, anti cancer</td>
</tr>
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<tr>
<td>4. Probiotics / Prebiotics / Synbiotics</td>
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<td></td>
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<tr>
<td>Lactobacillus</td>
<td>Yogurt,</td>
<td></td>
</tr>
<tr>
<td>Fructo - oligosaccharides</td>
<td>Whole grains, onions, combination of Pro &amp; Prebiotics</td>
<td>Improve GI health</td>
</tr>
<tr>
<td>5. Phytoestrogen</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Daidzein, Genistein</td>
<td>Soybean, flax, lentils, maize, berseemclover, lucerne</td>
<td>Reduce menopause symptoms, ↑ bone health</td>
</tr>
<tr>
<td>Lignans</td>
<td>Flax, rye, vegetables</td>
<td>Reduce cancer and heart diseases</td>
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</tbody>
</table>
**6. Carotenoids**

| β-Carotene | Clover, lucerne, oat & corn, carrots, vegetables, fruits | Neutralises free radicals |
| Luteine | Vegetables | Healthy vision |
| Zeaxanthin | Eggs, citrus, corn | |
| Lycopene | Tomatoes | Reduce prostate cancer |

**7. Dietary fiber**

| Insoluble fiber | Wheat bran | Reduce breast, colon cancer |
| β-Glucan | Oats | Reduce CVD |
| Whole grain | Cereal grains | |
The Health Market (U.S.A)

M. Mannion – Harnessing the healing Powers of Natural Substances: The Revolution in nutraceuticals and Medicinal Food – J. of the Mindshift Institute

**Nutraceuticals**
- **250 Billion US$**
- **Functional foods**

**Drugs**
- **150 Billion US$**

29,000 dietary supplements available in the US
1,000 new products each year

Tsourounis and Bent, *Clinical Pharmacology and Therapeutics*, 2010, 87: 147-149
Probiotic bacteria

Blockbuster
Soy protein is one of the most potent functional ingredient for the prevention of CVD.

American FDA approves soy health claim for food labels (1999): “… 25 g/day of soy proteins may help to reduce the cardiovascular disease risk”.
History of the Soy Protein Health Claim

Milestones

- **1977**: First clinical trial (Sirtori et al, Lancet, 257)
- **1977-1995**: 38 clinical studies, 31 report complete data (total & LDL cholesterol reductions).
- **1995**: Meta-analysis (Anderson et al. NEJM, 276)
- **1999**: FDA approves soy health claim for food labels: “… 25 g/day of soy proteins may help to reduce the cardiovascular disease risk”
- **2007**: Application for the European Health Claim sent to EFSA
The US market of soy products.
Estimated Prevalence of Cardiovascular Disease in Americans by Age and Sex

Source: http://www.americanheart.org
Partial List of Lifestyle-related and other Disorders/Diseases where Nutraceuticals/Functional Foods can play a Major Role in Prevention/Management

1. Cardiovascular Diseases (CVD) and risk factors (blood lipids, b.p., etc.)
2. Type 2 Diabetes
3. Cancers (colon, prostate, breast)
4. Inflammatory conditions (arthritis, bowel, etc.)
5. Osteoporosis
6. Kidney Disorders
7. ‘Psychiatric disorders’
8. Cosmetics
Advantages of Nutraceuticals/Functional Foods in Prevention/Management

Lifestyle (diet)–related chronic diseases/disorders are major burden on health care costs (particularly with ageing population).

Dietary advice often proven to be ineffective on longer-term (e.g., blood cholesterol-lowering by dietary advice).

Offer low-cost and early control of risk factors for subsequent disease (e.g. heart disease).

Offer a ‘preventive’ model for disease prevention rather than the current ‘medical’ model.

Offer control of ‘moderately’ elevated risk factors (e.g. blood cholesterol, triglyceride, etc.), which current health-care system fails to control.
Paradigm Shift in Health Care is Needed

Current: ‘Medical Model’ (later in life)

Medical Management with or without Dietary Advice of Chronic Disorders/Diseases (no Functional Foods/Nutraceuticals)

Future: ‘Preventive Model’ (early in life)

Wide introduction and use of Functional Foods/Nutraceuticals for Prevention of Chronic Disorders/Diseases
• **FUFOSE**: Concerted action (1996-1998) Consensus on the definition of a Functional Food and types of claims to be raised.

• Process for the Assessment of Scientific Support for Claims on Foods (**PASSCLAIM**):
  a) Produce a consensus on principles for the scientific substantiation of health-related claims for food.
  b) Select common criteria for how markers should be identified, validated and used.
  c) To evaluate critically the existing schemes, which assess the scientific substantiation of claims.

Main Regulations to be considered for Nutrition Products in the EU

- General Food Regulation (EC) No 178/2002
- Novel Food Regulation (EC) No 258/97
- Food supplements Directive 2002/46/EC
- Fortification of Food Regulation 1925/2006
- Directives on Food Labelling
- Regulation on Nutrition and Health Claims (EC) No 1924/2006
Regulation (EC) No 1924/2006 on Nutrition and Health Claims for Food

- Entered into force January 19th 2007
- Applied from July 1st 2007
- Covers labelling, presentation and advertising of a food
- Only allows products with genuine health or nutritional benefits to refer to them on their labels
General Health Claims (art. 13.1)

• All Health Claims other than those referring to the reduction of disease risk and to children's development and health

• Claims can be used without an authorisation, if they are provided in the Community list

• The Community list currently under evaluation

• New additions of claims can be requested and protected (Art. 18)
Art. 13.5: Health claim applications based on newly developed scientific evidence and/or proprietary data (other than those referring to reduction of disease risk and to children's development and health).

Art. 14: Reduction of disease risk claims & claims referring to children's development and health
Application for Health Claims Authorization

- Health claims based on new scientific data must be submitted to EFSA (European Food Safety Authority) for evaluation before they can be authorised for use.

- A simplified procedure was established for the authorisation of these health claims, in order to encourage innovation.

- If the EFSA opinion on the claim is positive, the commission takes a decision on whether to authorise or not the claim after simple consultation of Member States.
EFSA’s scientific criteria for substantiation of claims

• Regulation (EC) No 1924/2006 - health claims substantiated by:
  - generally accepted scientific evidence
  - taking into account the totality of the available scientific data, and by weighing the evidence

• EFSA’s scientific criteria for evaluation
  - similar for Art 13.1 (Terms of Reference from EC) and Art 13.5/14 - similar to FDA (2009), Codex Alimentarius (2009)

• Whether the evidence is sufficient to represent generally accepted scientific evidence to substantiate the claim is a scientific judgement of NDA Panel

• Opinion - nature & quality of evidence
Main issues addressed by NDA Panel

The extent to which:

1. the food/constituent is defined and characterised
2. the claimed effect is defined and is a beneficial physiological effect
3. a cause and effect relationship is established between the consumption of the food/constituent and the claimed effect (for the target group under the proposed conditions of use)

- scientific substantiation requires a favourable outcome to all three questions
<table>
<thead>
<tr>
<th>Claim type</th>
<th>Received</th>
<th>Withdraw</th>
<th>Adopted</th>
<th>In progress</th>
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</thead>
<tbody>
<tr>
<td>Children (art. 14)</td>
<td>219</td>
<td>32</td>
<td>48</td>
<td>2</td>
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<tr>
<td>Disease risk reduction (art. 14)</td>
<td>48</td>
<td>7</td>
<td>15</td>
<td>7</td>
</tr>
<tr>
<td>New science / proprietary (art. 13.5)</td>
<td>36</td>
<td>8</td>
<td>22</td>
<td>5</td>
</tr>
<tr>
<td>Total applications</td>
<td>303</td>
<td>47</td>
<td>85</td>
<td>19</td>
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<tr>
<td>Art. 13 list claims</td>
<td>4637</td>
<td>298</td>
<td>1080</td>
<td>3259</td>
</tr>
<tr>
<td>Food/constituent</td>
<td>Health relationship</td>
<td></td>
<td></td>
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<tr>
<td>Vitamins, minerals</td>
<td>Cardiovascular, brain, gut, immune, bone, dental, antioxidant, metabolism</td>
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<td>Protein, carbohydrate</td>
<td>Muscle, bone, energy,</td>
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<tr>
<td>Fatty acids</td>
<td>Brain, cardiovascular, vision</td>
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<tr>
<td>Fibre(s)</td>
<td>Gut, cardiovascular</td>
<td></td>
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<tr>
<td>Other substances - phytosterols/stanols, meal replacements, tomato extract</td>
<td>Cardiovascular, dental, weight management</td>
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</table>
Novel Versus Functional Foods

- **Novel Foods:** safety
- **Functional Foods:** efficacy
- **Novel Functional Foods:** efficacy & safety
Standing Committee for Food Commission informs applicant of decision.

M/S writes to applicant.

Objections resolved by QMV.

European Commission

Initial assessment completed

Summary report to other M/S

Initial assessment to other M/S

Comments / objections

Authorisation Procedure

Standing Committee for Food

Scientific Committee for Food

Commission informs applicant of decision if objections resolved by QMV.

Dossier

M/S where product will be first marketed

Day 0

Day 90

Day 0

Day 60

Free to market product

EU Novel Foods Process

Y

N
Safety Assessment of Novel/Functional Foods

• How is the ingredient made?
• Is there a history of safe consumption from food?
• Will higher levels of intake be necessary to influence health and well-being?
• Are there any structural alerts for toxicity?
• Is it absorbed into the body following ingestion and how is it then handled?
• What studies are necessary to identify the hazard?
• What is the range of likely intakes of the functional food ingredient and how will it be used?
• What is the safe level of intake?
• Are there vulnerable groups within the population?
Plant Sterol-esters
Esterification of Plant Sterols to Fatty Acids

Sterol

Fatty Acid

Sterol Ester
Overview of Cholesterol Lowering Trials with Plant Sterols

plant sterols (g/d)

% change

-16
-12
-10
-8
-4
0
0.5 1 1.5 2 2.5 3 3.5

total cholesterol
LDL cholesterol
Needs for Education on Nutraceuticals

• The fact that many applications for health claims got negative opinions from EFSA shows that dossiers were not properly prepared (in a few cases the list of references contained a citation from the Bible or Wikipedia).

• It is responsibility of the Faculties of Pharmacy to prepare specialists able to perform all the analytical, biological and clinical experimentation to strongly substantiate the applications.

• MD’s in Food Science and Technology do not have the necessary competencies.
Experience of the University of Milan

We have proposed a specific 2nd Level Degree Course, not yet accepted by the Government due to economic restrictions.

Required competencies: chemistry, biochemistry, advanced analytical chemistry, food chemistry and technology, pathophysiology, pharmacology, clinical pharmacology