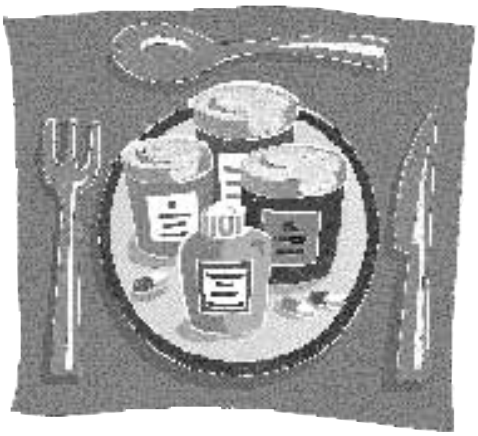
NUTRACEUTICALS

1. WHAT IS A NUTRACEUTICAL?

By Esther Bull, BSc, Lisa Rapport, BPharmS, MRPharmS, and Brian Lockwood, PhD, MRPharmS

This week we begin a short series of articles which are intended to review the scientific and medical claims relating to nutraceuticals which do not fall into the more well known categories of vitamins, amino acids and herbal remedies. This article, which introduces the series, looks at what defines a nutraceutical



Over the past few years, an increasing number of dietary supplements have become available in supermarkets and health food shops and they are also available for purchase in pharmacies.

The term "nutraceutical" is used to describe these medicinally or nutritionally functional foods. Nutraceuticals, which have also been called medical foods, designer foods, phytochemicals, functional foods and nutritional supplements, include such everyday products as "bio" yoghurts and fortified breakfast cereals, as well as vitamins, herbal remedies and even genetically modified foods and supplements. Many different terms and definitions are used in different countries, which can result in confusion.

The term "nutraceutical" was coined in 1989 by Stephen De Felice, founder and chairman of the Foundation for Innovation in Medicine, an American organization which encourages medical health research.[1–3] He defined a nutraceutical as a "food, or parts of a food, that provide medical or health benefits, including the prevention and treatment of disease".

In Canada, a functional food has been defined as being "similar in appearance to conventional foods . . . consumed as part of a usual diet" whereas a nutraceutical is "a product produced from foods but sold in pills, powders, (potions) and other medicinal forms not generally associated with food".[4]

In Britain, the Ministry of Agriculture, Fisheries and Food has developed a definition of a functional food as "a food that has a component incorporated into it to give it a specific medical or physiological benefit, other than purely nutritional benefit".[5]

Hence, both in Canada and in Britain, a functional food is essentially a food, but a nutraceutical is an isolated or concentrated form. In America, "medical foods" and "dietary supplements" are regulatory terms (see below), however "nutraceuticals", "functional foods", and other such terms are determined by consultants and marketers, based on consumer trends.[6]

Many of these new products that are being promoted to treat various disease states, find their origins in the plant kingdom. This is an obvious choice as many plants produce secondary compounds such as alkaloids to protect themselves from infection and these constituents may be useful in the treatment of human infection. There is also a long history of plant use in many cultures which can be used to identify plants with activity in the treatment of disease.[7]

FOODS OR MEDICINES?

Food labelling regulations do not allow food labels to carry health claims in many countries. This makes it hard for companies marketing nutraceuticals to advertise the benefits of their products without a medicine licence, so they may decide either not to do any research or they may research a new product thoroughly and possibly obtain a patent. Unfortunately, many companies tend towards the former option due to either expense, the problems of obtaining a patent on a natural product, or the fact that they cannot put their claims on the label without a product licence, whether verified or not.

To bring a medicine to market can take about 10 years and cost $250m whereas to market an unlicensed nutraceutical can take a fraction of this.[2] An example was the case of Cholestin, a cholesterol lowering supplement marketed by Pharmanex (Simi Valley, CA) in 1996. The product was based on an ancient Chinese remedy and proved very popular. When the pharmaceutical company Merck (Whitehouse Station, NJ) tested this successful "supplement", it found that the active ingredient was lovastatin, and the US Food and Drug Administration subsequently banned its incorporation in Cholestin. As can be seen from this example the difference between pharmaceutical and nutraceutical is sometimes difficult to define, depending only on regulatory issues.

In Britain, unlicensed herbal remedies and supplements are marketed without medical claims and as such are legally regarded as food supplements and are controlled by the Ministry of Agriculture, Fisheries and Food. In the past, as long as the products did not claim to have medicinal uses, the Medicines Control Agency (MCA), which is responsible for regulating medicinal products, has not required that the product satisfy medical legislation.[8] However, more emphasis is now being placed on the function of the marketed products as Britain moves into line with the rest of Europe.

It was recently reported that the control of herbal products is to move to the European Commission[9] and it is likely that supplements will follow a similar course. Article 1 of Directive 65/65EEC[10] defines a medicinal product as "any substance or combination of substances presented for treating, or preventing disease in human beings or animals".

The authors are from the School of Pharmacy and Pharmaceutical Sciences, University of Manchester, Oxford Road, Manchester M13 9PL. Lisa Rapport is also a practising community pharmacist. Correspondence to Dr Lockwood

It goes on: "Any substance or combination of substances which may be administered to human beings or animals with a view to making diagnosis or to restoring, correcting or modifying physiological functions in human beings or animals is likewise considered a medicinal product." This definition describes a product which has a medical function irrespective of whether these claims have been stated or not, which would include many supplements being taken for medical purposes.

British licensed medicines for human use are regulated according to the Medicines Act 1968[11] and the Medicines for Human Use (Marketing Authorisations Etc) Regulations 1994 SI 1994:3144 (the regulations)[12]. In 1995, these regulations came into effect, implementing all the controls as listed in Directive 65/65EEC. According to these regulations there are controls over variation and renewal of UK licences as well as labelling and package inserts.

A five-year study of side effects of traditional remedies and food supplements was carried out between 1991 and 1995 in the medical toxicology unit at Guy's hospital, London.[13] The authors concluded that the overall risk factor with these products was low and that they were generally considered to be safe. However, because many health care professionals considered these products as little more than placebo, side effects that were occurring were often not traced back to the supplements being used. Many of these products are self-prescribed which may lead to inappropriate use, overdose, or interactions with other medicines. This highlights why the safety of these supplements must be ensured as many consumers are unaware of the difference between licensed and unlicensed products, and the differences between food legislation and medicines legislation. There are many inaccurate claims made for many supplements available, as well as much variation in the actual products, depending on storage, manufacturing process, or even batches of the same material. It is vital that these discrepancies be resolved, possibly with the creation of a third type of regulatory category for supplements.[13]

In America, a new product may be eligible for regulatory status as a food, a dietary supplement, or as a medical food.[14] The US Congress passed the Dietary Supplement Health and Education Act (DSHEA) in 1994. This set up a new regulatory body for dietary supplements under the FDA. Unlike foods, dietary supplements are allowed to use "nutritional support statements". These may offer nutritional support in nutrient-deficiency disease, or state a description of the intended role, mechanism of action or effect on general health as a result of taking the product. For those dietary supplements for which such a statement is used the label must also state: "This statement has not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure or prevent any disease."

In effect, because legally they are in a class by themselves, dietary supplements in the US can be marketed without the FDA being satisfied that they are safe. This makes it relatively easy for a manufacturer to market a product without investing the time and money required for its safety.

Of all three categories (food, dietary supplement or medical food), medical foods have the least formal regulatory controls. The US Congress in 1990 defined a medical food as "a food which is formulated to be consumed or administered enterally under the supervision of a physician and which is intended for the specific dietary management of a disease or condition for which distinctive nutritional requirements, based on recognized scientific principles, are established by medical evaluation".

These products are usually promoted through health care professionals, including pharmacists, and in the UK this would make them prescription only or pharmacy medicines.

IMPLICATIONS FOR PHARMACY

Speculation on who the winners of the nutraceutical venture will be is becoming a popular topic in papers discussing the pharmaceutical industry. Because new medicines are harder to find and more expensive and risky to develop than ever before, many companies, for example, Du Pont, Abbott Laboratories and Warner Lambert, which have produced conventional pharmaceuticals in the past are now merging to survive, or are turning to nutraceuticals.[2] This offers them a chance of a very large market. Datamonitor, a website that follows market trends, estimates the nutraceutical market at $17bn, and Dr Felice himself, speaking at a conference in 1998, put the figure at $250bn in America alone.[3] Although these estimates vary widely, the nutraceuticals market is undoubtably very large and growing. As companies increase in size, more jobs may be created for industrial pharmacists, but the real impact of nutraceuticals on pharmacy will be in the community.

It has been suggested that a move from dietary supplements, sold in health food shops and most pharmacies, to nutraceuticals aimed at the prescription market could occur. This would not necessarily be in manufacturers' best interest, as it would limit the size of the market. However, many indications under research are for serious disease states which do not require self-medication. At present, consumers may try dietary supplements for many indications believing them to be safer than synthetic substances, and this presumption of safety is erroneous.

In either case, whether prescribed by a doctor or self-selected, the logical place for the supply of these supplements is the pharmacy where pharmacists are able to offer professional advice. The challenge is therefore to be up to date with research developments so that both conventional practitioners as well as members of the public are able to receive accurate information.

Future articles in this short series will be reviewing the scientific and medical claims relating to nutraceuticals which do not fall into the better known and well-researched categories such as vitamins, amino acids and herbal remedies. Most products reviewed are naturally occurring biochemicals which are effectively being used to supplement endogenous levels of these constituents that occur naturally in human metabolism, whether single component products such as glucosamine, or more complex products such as proanthocyanidin.

REFERENCES

1. Jack DB. Keep taking the tomatoes — the exciting world of nutraceuticals. Mol Med Today 1995:118-21.
2. Brower B. Nutraceuticals: Poised for a healthy slice of the market. Nat Biotechnol 1998;16:728-33.
3. Mannion M. Nutraceutical revolution continues at Foundation for Innovation in Medicine Conference. Am J Nat Med 1998;5:30-3.
4. Mazza G. Functional foods. Pennsylvania, US: Technomic Publishing Company Inc, 1998.
5. Cockbill CA. Food law and functional foods. Br Food J 1994; 96:3-4.
6. Aarts TA. How long will the "Medical Food" window of opportunity remain open? J Nutr Function Med Foods 1998, 1:45-57.
7. Senior K. Pharmaceuticals from plants: promise and progress. Mol Med Today 1996:60-4.
8. Newall CA, Anderson LA, Phillipson JD. Herbal medicines: a guide for health care professionals. London: Pharmaceutical Press, 1996.
9. Herbal medicines controls move to Europe. Pharm J 1999; 263:775.
10. Council Directive 65/65/EEC. Off J EC 1965;22:369.
11. The Medicines Act 1968. London: HM Stationery Office,1968.
12. The Medicines for Human Use (Marketing Authorisations Etc) Regulations. Statutory Instrument 1994:3144.
13. Shaw D, Leon C, Kolev S, Murray V. Traditional remedies and food supplements. A five-year toxicological study. Drug Safety 1997;17:342-56.
14. Bidlack WR, Omaye ST, Meskin MS, Jahner D. Phytochemicals. Pennsylvania, US: Technomic Publishing Company Inc, 1998.