

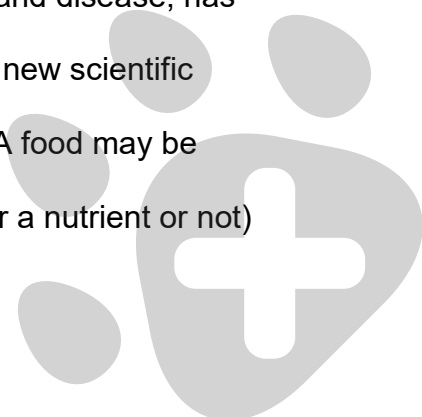
CHAPTER 1 INTRODUCTION

Synopsis

This chapter briefly examines the relationship of diet to health and defines the concept of functional foods. A dietary supplement is considered as an addition to the diet to enhance health. Foods as medicine underpins the paradigm of functional foods. The recognition of medicinal mushrooms as functional foods or as dietary supplements is fully discussed especially in the concept of Chinese holistic medicine and modern immunology.

In the developed nations of this world many causes of death or disability such as coronary heart disease, strokes, diabetes, atherosclerosis, obesity and certain forms of cancer can, in considerable part, be attributed to diet (Barasi, 1997). Poor food selection and restricted dietary intake can affect the nutritional status of an individual at any stage of life and can lead to impairment of long term health. Increasingly, scientific evidence is supporting the view that diet controls and modulates many functions of the human body and accordingly participates in the maintenance of the state of good health or homeostasis necessary to reduce the risk of many chronic diseases (Carter, 1993). Over the last few decades the science of nutrition has progressed from being largely epidemiologically based to the greater understanding of the physiological and genetic mechanisms by which diet and individual food components influence health and disease. It is indeed a paradox that nutrition is essential to support life but can also be considered as a causation of many chronic diseases.

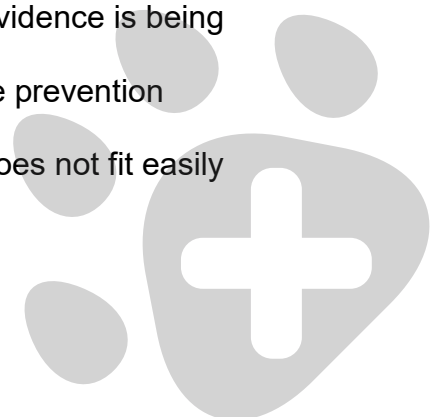
Arising from the awareness of the relationship between diet and disease, has evolved the concept of “functional foods” and the development of a new scientific discipline “functional food science” (Sadler and Saltmarsh, 1998). A food may be considered to be functional if it contains a food component (whether a nutrient or not)



which affects one or more identified functions in the body in a positive manner. Correspondingly, it can also include foods in which potentially harmful components have been removed by technological means. The US Academy of Science has defined functional foods as those that “encompass potentially healthful products” including “any modified food or food ingredient that may provide a health benefit beyond the traditional nutrients it contains” (Thomas and Earl, 1994).

Functional foods come in a plethora of name forms, e.g. dietary supplements, nutra- or nutri-ceuticals, medical foods, vita foods, pharmafoods, phytochemicals, mycochemicals, biochemopreventatives, designer foods and foods for specific health uses (Hasler, 1996; Head *et al.*, 1996). Such complex designations could well be an impediment to their rightful maturation and consumer acceptance (Zeisel, 1999). There continues to be much confusion over these names especially in the commercial world. However, the term dietary supplement (DS) is now being more widely accepted and recognised. The term DS was formally defined by the US administration in 1994 as a product intended to supplement the diet to enhance health. A DS includes *one or more* of the following dietary ingredients: a mineral, amino acid, vitamin, herb or other botanical; or it is a dietary substance used to supplement the diet by increasing the total dietary intake and is intended for ingestion in the form of a capsule, powder, softgel or gel cap and not represented as a conventional food or as a sole item of a meal or the diet (Dietary Supplement Health and Education Act, Public Law 103-417, 1994).

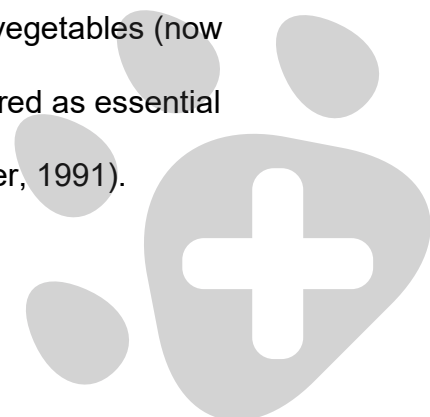
However, foods as medicine underpins the paradigm of functional foods. Functional foods cannot claim to cure diseases but, increasingly, evidence is being produced that supports the role of some functional foods in disease prevention (Steinmetz and Potter, 1991). The concept of foods as medicine does not fit easily



within the current expertise of either pharmaceutical or food companies and the full creative development of functional foods may well require new alliances between these companies with respect to regulatory issues.

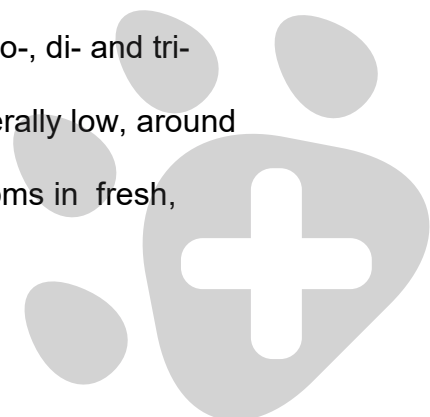
Functional food science is now considered as a part of nutritional science in which the primary objectives are to maintain good health, improve homeostasis and to create the conditions for disease risk reduction. In this way it should be seen to be quite distinct from the medical and pharmaceutical sciences where the objectives are mainly to cure or control diseases (Saris *et al.* 1998; Diplock *et al.* 1998). In many ways conventional medicine seeks to eliminate disease rather than to fortify the patient. In essence, functional food science aims: 1) to identify beneficial interactions between the presence or absence of a food component (macronutrient, micronutrient or so-called non-nutrient) and a specific function or functions in the body; 2) to understand their mechanisms so as to support hypotheses to be treated in protocols relevant for human studies. This will require multidisciplinary research programs containing the expertise of scientific partners including biochemists, nutritionists, the medical profession and process technologists.

Functional foods are set to play an increasingly important role in national efforts in developed nations to curtail medical expenditure and also to improve the dietary habits of the populace. Consumers are becoming increasingly more health conscious and discerning in the types of foodstuffs that are purchased. It is now not possible to overlook the critical role that diet, including functional foods, can play in general health and well-being. Many types of cancer can now be linked to inappropriate diets. In contrast, regular consumption of fruits and vegetables (now viewed as classical examples of functional foods) are now considered as essential ingredients in cancer prevention programmes (Steinmetz and Potter, 1991).



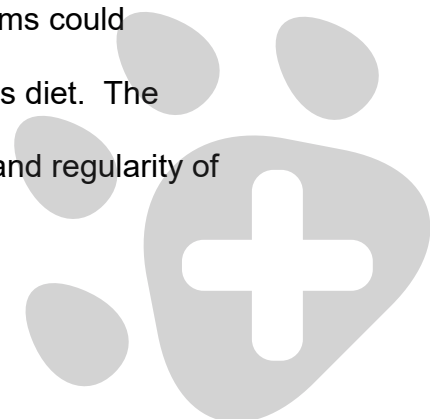
Medicinal mushrooms

Mushrooms have long been valued as highly tasty and nutritional foods by many societies throughout the world (Chang and Miles, 1989). Early civilisations, by trial and error built up a practical knowledge of those suitable to eat and those to be avoided, e.g. poisonous or even psychotropic. In many parts of the world, especially Europe, wild mushrooms are regularly collected and used directly as a main source of food or added to soups, stews and teas. Mushrooms are considered to be a good source of digestible proteins with protein content above most vegetables and somewhat less than most meats and milk. Protein content can vary from 10-40% on a dry weight basis. Mushrooms contain all the essential amino acids, but can be limiting in the sulphur-containing amino acids, cystine and methionine (Chang, 1991; Breene, 1990). Fresh mushrooms contain 3-21% carbohydrates and 3-35% fibre on a dry weight basis. Thus, a considerable proportion of the carbohydrate of mushrooms consists of dietary fibre which cannot easily be digested by humans and which function essentially as dietary fibre; in this way the calorific value of most mushrooms is low. Mushrooms probably contain every mineral present in their growth substrate including substantial quantities of phosphorous and potassium, lesser amounts of calcium and iron. Mushrooms appear to be an excellent source of vitamins especially thiamine (B₁), riboflavin (B₂), niacin, biotin and ascorbic acid (VitC). Vitamins A and D are relatively uncommon although several species contain detectable amounts of β -carotene and ergosterol which converts to active vitamin D when exposed to ultraviolet irradiation. While crude fat in mushrooms contains all the main classes of lipid compounds including free fatty acids, mono-, di- and tri-glycerides, sterols, sterol esters and phospholipids, levels are generally low, around 2-8% of dry weight (Breene, 1990). Without doubt, edible mushrooms in fresh,



cooked or processed forms are a nutritionally sound, tasteful food source for most people and can be a significant dietary component for vegetarians (Breene, 1990). In China, the term Yakuzen is generally used for medicinal food dishes of mushrooms.

However, in the Orient several thousand years ago, there was the recognition that many edible and certain non-edible mushrooms could have valuable health benefits (Bensky and Gamble, 1993; Hobbs, 1995). The edible mushrooms which demonstrate medicinal or functional properties include species of *Lentinus* (*Lentinula*), *Auricularia*, *Hericium*, *Grifola*, *Flammulina*, *Pleurotus* and *Tremella* while others are known only for their medicinal properties, e.g. *Ganoderma* and *Trametes* (*Coriolus*) – these are definitely non-edible due to their coarse and hard texture or bitter taste. The historical evolution of usage of these essentially scarce, forest-obtained medicinal mushrooms would most certainly not have been as whole mushrooms but as hot water extracts, concentrates, liquors or powders and used in health tonics, tinctures, teas, soups and herbal formulae. Nowadays, almost all of the important medicinal mushrooms have been subjected to large-scale artificial cultivation, thus removing the historical scarcity factor. This also ensures accuracy of identification and increased reliability and consistency of medicinal products. Also many of the edible species of medicinal mushrooms are gaining worldwide popularity because of their unique flavours, textures and amenability to culinary inclusion. Indeed, most people in the West who enjoy the unique organoleptic features of the Shiitake mushroom (*Lentinus edodes*) are singularly unaware of its possible health benefits. Regular consumption of whole medicinal, edible mushrooms could introduce a functional or medicinal contribution within the individual's diet. The extent of the health beneficial effect will be dependent on the level and regularity of



consumption and the relevance of whole fresh medicinal mushrooms and concentrates will be discussed in later chapters.

When used for a therapeutic intention the medicinal mushrooms are normally consumed as powdered concentrates or extracts in hot water, and the extract concentrated and used as a drink or freeze-dried or spray-dried to form granular powders which allow easier handling, transportation and consumption (Mizuno *et al.* 1995). As such, these liquid concentrates or dried, powdered mushrooms contained in capsules can be considered as *dietary supplements* or *mushroom nutraceuticals* with potential health benefits (Chang and Buswell, 1996). Mushroom nutraceuticals are usually crude mixtures and should not be confused with pharmaceuticals which are almost invariably a defined chemical preparation, the specifications for which are listed in pharmacopoeia. Regular intake of these concentrates is believed to enhance the immune responses of the human body, thereby increasing resistance to disease and in some cases causing regression of the disease state (Jong *et al.* 1991).

These mushroom dietary supplements are used extensively in traditional Chinese medicine in various combinations, often with other herbal products, to treat many medical conditions. A limited number of highly purified polysaccharide compounds derived from certain medicinal mushrooms are now being used, particularly in Japan, as pharmaceutical grade products and are discussed in later chapters.

Immune system modulation has long been a feature of Chinese holistic medicine and is referred to as Fu Zheng therapy. Fu Zheng can be considered as the Oriental equivalent of Western immunotherapy. Compounds derived from certain medicinal mushrooms are used extensively in the Orient to increase disease

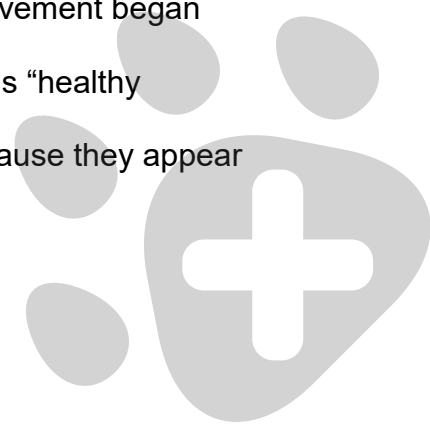


resistance and to normalise body functions. Such extracts are used to treat deficient principles or qi or ch'i, the 'vital' or life energy, blood and yin (fluid) and yang functionality (especially the kidney).

Cancer and its treatment by conventional therapies as chemotherapy and radiotherapy are known to have adverse effects on the human immune system. Cancer immunology has become a rapidly growing field in basic cancer research. Ways are now being sought to promote host antitumour immune cell activity and to overcome the ability of the cancer cell to evade immune surveillance (Curt, 1998; Cassileth, 2000). Immunostimulating agents would possibly be useful adjuncts to conventional treatments of cancer if they do not interfere with the ability of the conventional treatment to kill tumour cells. These approaches, like chemo- and radiotherapy, are designed to cause the destruction of tumour cells but to be much more tumour-specific than present treatments and, consequently, less harmful to normal cells.

As will be shown in later Chapters, one of the most noticeable features of extracts derived from many medicinal mushrooms is their ability to function as immunomodulators. As such, the physiological constitution of host defence mechanisms are improved by the intake of these mushroom compounds which restore homeostasis and enhance resistance to disease. A central premise in Oriental medicine is to regulate homeostasis of the whole body and to return the diseased individual to the normal state.

It is interesting to note that several of the medicinal mushrooms and their concentrates are becoming particularly popular in the US – the movement began with a drive towards “healthy food” in the 60s-70s; now it is towards “healthy medicine”. People are interested in the medicinal mushrooms because they appear



to have been used with considerable effect for hundreds of years in the Orient while many modern widely used pharmaceuticals while offering undoubted health benefits can also in some cases have serious side-effects. Furthermore, it is now increasingly being recognised that diet is intimately associated with optimal health and the tenet of Hippocrates c 400 B.C. "*Let food be your medicine and medicine be your food*" is fast becoming a truism for many people.

Over the last 2-3 decades scientific and medical studies have been carried out in Japan, China, Korea and more recently US which have increasingly demonstrated the potent and unique health enhancing properties of compounds extracted from a range of medicinal mushrooms. Explanations of how such compounds function in animal and human systems are now regularly appearing in peer-reviewed scientific and medical journals.

This review will aim to give a detailed analysis of the history and present state of knowledge of these organisms, methods of cultivation, range of organisms, methods of extraction, and detailed examination of medical implications with special emphasis on immuno-stimulation and cancer treatment. The review will also examine international regulations related to the use of such compounds (dietary supplements) with particular emphasis on safety. While the review will concentrate largely on their applications in the treatment of cancer, a brief overview of the wide range of other medical uses will also be included.



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