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PHCOG MAG.: Invited Article
Successful Nutraceutical Products-Need for Regulatory and Marketing Strategies

Ven Subbiah
PhytoMyco Research Corporation
1800 North Greene Street
Greenville, NC 27834, U. S. A.
Correspondence: phytomyco@aol.com

Abstract: The Dietary Supplement Health and Education Act (DSHEA) passed by U. S. Congress in 1994 is accelerating the penetration of herbal products into mainstream markets. Under this Act, herbal dietary supplements are categorized as food products, and do not require approval by the FDA prior to marketing. In today's aggressive sales arena, growing and standardization for the bioactive constituents is often a source of competitive advantage. Thus one of the biggest challenges in the world of botanical extracts is the raw material and its standardization. Producers are allowed to make limited claims for structure or function as long as a significant body of historical and scientific data supports them. The regulatory environment in the United States for nutraceuticals is becoming similar to the European model, in which herbal supplements are regulated in the same manner as other OTC and prescription drugs. This will lead to demands for carefully formulated and standardized products which contain specified levels of active ingredients, and which are labelled with explicit statements of therapeutic indications and adverse effects. Consumers will pay premium prices for standardized nutraceutical products of the highest possible purity and quality. Today, the herbal/nutritional supplement market is valued over $100 billion worldwide with an annual increase of 20%. Market potential for nutraceuticals is estimated based on prevalence forecasts based on different market reports and statistical data. These products are not meant as a replacement for meals, but as an enhancement to the normal dietary intake of nutrients or as a preventative measure in reducing the risk of a particular disease. As one would expect, the production processes vary greatly both between and within product types.

Key words: Nutraceuticals, Natural products, Botanical extracts, Regulatory requirement.

1. Introduction

1a. Natural products

Natural product offer unique and novel templates on which to base further synthetic work leading to new classes of therapeutics. Historically, screening natural products for new drugs has been a lengthy process, relative to the screening of traditional preexisting chemical archives (synthetic chemical library). However, recent new reengineered strategies reduced the time for the discovery of novel chemical-leads from natural products by over 50%. These include automation of extraction, sample preparation, high intensity screening using robotics, and improved hit selection using multiparametric criteria. In the past, several pharmaceuticals, food/beverage, cosmoceutical, and nutraceutical industries have developed these natural products directly to the market or have synthesized new compounds from their base structure. However, the new technologies offer chemists a quicker way to evaluate and manipulate the active pharmacophores of these natural compounds increasing their potency as drugs, food additives, perfumes, nutraceuticals, pesticides, etc. The pharmaceutical industry has embraced these new technologies as an additional tool in their search for drug candidates from natural products. A search that continues to uncover promising compounds from the needles of yew trees as a cancer drug to marine snail venom to treat schizophrenia.

Medicinal plant research is need of the hour. The AIDS virus, the crisis of bacterial resistance to antibiotics, and other recent developments have increased the value of indigenous medicinal plant knowledge, which may hold clues for solving these deadly problems. Indigenous medicinal plant knowledge is also critical because synthetic chemical processes have proved inadequate for dealing with the rapid evolution of pathogens. Unfortunately, many opponents of medicinal plant research that involves indigenous people have chosen to ignore the fact that "western" medicine relies on plants and traditional knowledge for clues to cure our worst diseases. In addition, plant species are rapidly disappearing, and many people are not transmitting traditional medicinal knowledge to their children. In many places, the current generation represents our last chance to find ways that indigenous people can benefit from their knowledge instead of liquidating their biological resources to join a global economy in which, they are at a serious disadvantage, including not being able to afford "western" medicines. New and innovative programs of benefits sharing between indigenous people and biomedical scientists are intended to achieve this goal. Those who oppose medicinal plant research on principle (claiming that all such research is "bio-piracy") have failed to provide alternative ideas for the integration of indigenous medicinal knowledge into the global market place. But medicinal plant research includes much more than the discovery of new drugs. Recently, the field has been expanding to also include such diverse subjects as negotiation of power based on

medicinal plant knowledge and the co-evolution of humans and plants. The field also provides opportunities to study how human interaction with biological diversity is influenced by human psychology, cognition, and evolution.

Developing standardized dietary supplements using modern assay and chemical methods will culminate in the production of high-quality products that can be used reliably in clinical trials. The standardization of dietary supplements includes thorough taxonomy and the standardization of agronomic conditions, an optimal extraction protocol to obtain consistent standard extracts, qualitative and quantitative techniques for the analysis of the extract, to develop a chemical profile ("fingerprint"). Fingerprint will include the quantification of marker constituents, including the major components associated with the purported bioactivity, as well as, other major compounds of interest. This information could also be used for the clinical studies, and will be basis for future scale-up activities, which will be designed to enhance the biological activities. This type of research is a comprehensive scientific approach to botanical research, development and commercialization of safe and effective dietary supplements.

Historical use of traditional medicines by humans to combat several disease conditions is commonly termed as ethno pharmacology. Ethno pharmacology is the study of how people derive medicines from plants or other naturally occurring resources. The "discovery" that indigenous knowledge about medicinal plants holding clues for curing diseases has become one of the hot areas of scientific investigation. Furthermore, the continued use of plants by traditional healers offers a reasonable degree of certainty that the plants in question are active and safe for human use. Thus, at the time the drug development process begins, an enormous amount of critical information is available that can be employed to guide laboratory preparations of crude extracts/semi-purified compounds, to devise dosing regiments in test animals, and in certain cases, to develop formulations of drugs for pre-clinical bioassays when active principles are identified.

1b. Nutraceuticals/Dietary supplements:

Nutraceuticals are natural, bioactive chemical compounds with health promoting, disease preventing or medicinal properties. They are often referred to as phytochemicals or functional foods. Nutraceutical market data is generally collected as part of the dietary supplement (DS) industry, a diverse set of products produced by a variety of manufacturers and distributed through a variety of channels. For these reasons, characterizing the industry is difficult. The products included in this category are based on the definition of dietary supplements contained in the Dietary Supplement Health and Education Act (DSHEA) of 1994, namely:

- Vitamins- Products that are organic (carbon-containing) nutrients.
- Minerals- Products that are chemical elements in their inorganic forms.
- Herbals & Botanicals- Herbal refers to plant leaves and stems while botanical refers to these parts in addition to roots, seeds, and fruits.
- Animal Extracts- Products from animal parts (e.g., tissues and glands).
- Amino Acids- Products containing an amino group and an acidic functional group.
- Proteins- Products with the complete set of amino acids.
- Concentrates, Metabolites, Constituents- Products that are concentrated, are broken down into individual components, or are parts of other products.
- Teas- Products infused in water that contain herbals, botanicals, or other DS products.
- Other Dietary Supplements- All other products meeting the criteria of dietary supplements that cannot be classified into the categories above. Examples include bee pollen, algae, and nucleic acids.

These products are not meant as a replacement for meals, but as an enhancement to the normal dietary intake of nutrients or as a preventive measure in reducing the risk of a particular disease. Products other than vitamins and minerals are only in the initial stages of standardization by members of the industry. Thus, even a particular type may contain many heterogeneous products. As one would expect, the production processes vary greatly between and within product types.

2. Regulatory status

Stringent evaluation of the traditional medicinal product as well as herbal products by western countries, particularly the recent announcement by the Medicinal Control Agency (MCA) in United Kingdom, about the Ayurvedic and Traditional Chinese Medicines is reason for concern. MCA considers these two traditional medicines as ethnic remedies, because they lack documented quality and safety issues. In addition, the Food and Drug Administration (FDA) announced a new initiative on December 18, 2002 (Nutrition Business Journal, December 2002) to encourage the flow of high quality, science-based information about the health benefits of conventional foods and dietary supplements. The goal of FDA's Consumer Health Information for "Better Nutrition" is to facilitate the flow of information while also assuring that it is truthful, non-misleading and based on sufficient scientific evidence. FDA intends to achieve this goal through measures to encourage truthful and non-misleading claims for conventional foods and dietary supplements. In the dietary supplement area, in which FDA's statutory authority involves post-market monitoring, FDA is undertaking aggressive, comprehensive enforcement and oversight. Therefore, knowing the identity of micro compounds, and being able to analyze for them effectively, are critical aspects to achieve standardization and living up to label claim.

The climate of vigorous alternate popularity has created demand for a higher level of science, to ensure that products are safe, effective and credible. Although more people than ever before desire alternate health products, many are poorly researched, shoddily produced and ineffective. Since amounts and types of compounds in the product vary widely depending on the varieties and growing conditions, then on what are the standards based? In some cases, only the main source of bioactivity has been identified. With garlic, for example,

although it is used as a macro ingredient, the micro-compound allicin, which is a small component of garlic, is most likely responsible for the health benefit.

Even after developing product specifications and prototypes that contain standardized amounts of bioactive constituents, these compounds must be present in the required proportions after the appropriate manufacturing processes have been completed. These naturally occurring compounds are often sensitive to heat, light and other conditions such as pH and metal ions. Clearly, these sensitivities have processing implications, and must be monitored during the development process and prior to reaching the shelves. After leaving the manufacturing plant, these products, like food and pharmaceuticals, also have shelf-life issues. In order to maintain shelf life, an herbal drug product needs to maintain stable levels of bioactive compounds. This often requires extensive real-time storage stability testing, as well as, accelerated shelf life testing to determine the exact shelf life under different storage conditions.

2b. Regulatory status in the United States

For decades, FDA regulated dietary supplements as foods, in most circumstances, to ensure that they were safe and wholesome, and that their labelling was truthful and not misleading. An important facet of ensuring safety was FDA's evaluation of the safety of all new ingredients, including those used in dietary supplements, under the 1958 Food Additive Amendments to the Federal Food, Drug, and Cosmetic Act (FD&C Act). However, with passage of the Dietary Supplements Health and Education Act of 1994 (DSHEA), Congress amended the FD&C Act to include several provisions that apply only to dietary supplements and dietary ingredients of dietary supplements. As a result of these provisions, dietary ingredients used in dietary supplements are no longer subject to the pre-market safety evaluations required of other new food ingredients or for new uses of old food ingredients. They must, however, meet the requirements of other safety provisions.

Signed by President Clinton on October 25, 1994, the DSHEA acknowledges that millions of consumers believe dietary supplements may help to augment daily diets and provide health benefits. Congress's intent in enacting the DSHEA was to meet the concerns of consumers and manufacturers to help ensure that safe and appropriately labelled products remain available to those who want to use them. In the findings associated with the DSHEA, Congress stated that there may be a positive relationship between sound dietary practice and good health, and that, although further scientific research is needed, there may be a connection between dietary supplement use, reduced health-care expenses, and disease prevention.

The provisions of DSHEA are to; establish a new framework for assuring safety; outline guidelines for literature displayed where supplements are sold; provide for use of claims and nutritional support statements; require ingredient and nutrition labelling; and grant FDA the authority to establish good manufacturing practice (GMP) regulations. The law also requires formation of an executive level Commission on Dietary Supplement Labels and an Office of Dietary Supplements within the National Institutes of Health.

FDA traditionally considered dietary supplements to be composed only of essential nutrients, such as vitamins, minerals, and proteins. The Nutrition Labelling and Education Act of 1990 added "herbs, or similar nutritional substances," to the term "dietary supplement." Through the DSHEA, Congress expanded the meaning of the term "dietary supplements" beyond essential nutrients to include such substances as ginseng, garlic, fish oils, psyllium, enzymes, glandulars, and mixtures of these.
The DSHEA established a formal definition of "dietary supplement" using several criteria. A dietary supplement:

- is a product (other than tobacco) that is intended to supplement the diet that bears or contains one or more of the following dietary ingredients: a vitamin, a mineral, an herb or other botanical, an amino acid, a dietary substance for use by man to supplement the diet by increasing the total daily intake, or a concentrate, metabolite, constituent, extract, or combinations of these ingredients.
- is intended for ingestion in pill, capsule, tablet, or liquid form.
- is not represented for use as a conventional food or as the sole item of a meal or diet.
- is labelled as a "dietary supplement."
- includes products such as an approved new drug, certified antibiotic, or licensed biologic that was marketed as a dietary supplement or food before approval, certification, or license (unless the Secretary of Health and Human Services (HHS) waives this provision).

The DSHEA amends the adulteration provisions of the FD&C Act. Under DSHEA a dietary supplement is adulterated if it or one of its ingredients presents "a significant or unreasonable risk of illness or injury" when used as directed on the label, or under normal conditions of use (if there are no directions). A dietary supplement that contains a new dietary ingredient (i.e., an ingredient not marketed for dietary supplement use in the U.S. prior to October 15, 1994) may be adulterated when there is inadequate information to provide reasonable assurance that the ingredient will not present a significant or unreasonable risk of illness or injury. The Secretary of HHS may also declare that a dietary supplement or dietary ingredient poses an imminent hazard to public health or safety. However, like any other foods, it is a manufacturer's responsibility to ensure that its products are safe and properly labelled prior to marketing.

The DSHEA provides that retail outlets may make available "third-party" materials to help inform consumers about any health-related benefits of dietary supplements. These materials include articles, book chapters, scientific abstracts, or other third-party publications. These provisions stipulate that the information must not be false or misleading; cannot promote a specific supplement brand; must be displayed with other similar materials to present a balanced view; must be displayed separate from supplements; and may not have other information attached (product promotional literature, for example).

The DSHEA provides for the use of various types of statements on the label of dietary supplements, although claims may not be made about the use of a dietary supplement to diagnose, prevent, mitigate, treat, or cure a specific disease (unless approved under the new drug provisions of the FD&C Act). For example, a product may not carry the claim "cures cancer" or "treats arthritis." Appropriate health claims authorized by FDA; such as the claim linking folic acid and reduce risk of neural tube birth defects and the claim that calcium may reduce the risk of osteoporosis; may be made in supplement labelling if the product qualifies to bear the claim. Under DSHEA, firms can make statements about classical nutrient deficiency diseases, as long as these statements disclose the prevalence of the disease in the United States. In addition, manufacturers may describe the supplement's effects on "structure or function" of the body or the "well-being" achieved by consuming the dietary ingredient. To use these claims, manufacturers must have substantiation that the statements are truthful and not misleading and the product label must bear the statement "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." Unlike health claims, nutritional support statements need not be approved by FDA before manufacturers market products bearing the statements, however, the agency must be notified no later than 30 days after a product that bears the claim is first marketed.

Like other foods, dietary supplement products must bear ingredient labelling. This information must include the name and quantity of each dietary ingredient or, for proprietary blends, the total quantity of all dietary ingredients (excluding inert ingredients) in the blend. The label must also identify the product as a "dietary supplement" (e.g., "Vitamin C Dietary Supplement"). Labelling of products containing herbal and botanical ingredients must state the part of the plant from which the ingredient is derived. If a supplement is covered by specifications in an official compendium and is represented as conforming, it is misbranded if it does not conform to those specifications. Official compendia include the U.S. Pharmacopoeia, the Homeopathic Pharmacopoeia of the United States, or the National Formulary. If not covered by a compendium, a dietary supplement must be the product identified on the label and have the strength it is represented as having.

Labels also must provide information about nutritional content. This labelling must first list dietary ingredients present in "significant amounts" for which FDA has established daily consumption recommendations, followed by dietary ingredients with no daily intake recommendations. Dietary ingredients that are not present in significant amounts need not be listed. The nutrition labelling must include the quantity per serving for each dietary ingredient (or proprietary blend) and may include the source of a dietary ingredient (for example, "calcium from calcium gluconate"). If an ingredient is listed in the nutrition labelling, it need not appear in the statement of ingredients. Nutrition information must precede ingredient statements on the product label.

Supplements may contain new dietary ingredients-those not marketed in the United States before October 15, 1994-only if those ingredients have been present in the food supply as an article used for food in a form in which the food has not been chemically altered or there is a history of use, or some other evidence of safety exists that establishes that there is a reasonable expectation of safety when the product is used according to recommended conditions of use. Supplement manufacturers must notify FDA at least 75 days before marketing products containing new dietary ingredients, providing the agency with the information on which the conclusion that a dietary supplement containing the new dietary ingredient "will reasonably be expected to be safe" was based. Any interested party, including a manufacturer of a dietary supplement, may petition FDA to issue an order prescribing the conditions of use under which a new dietary ingredient will reasonably be expected to be safe.

DSHEA grants FDA the authority to establish GMP regulations governing the preparation, packing, and holding of dietary supplements under conditions that ensure their safety. These regulations are to be modelled after current good manufacturing practice regulations in effect for the rest of the food industry. FDA intends to work with the supplement industry and other interested persons to develop GMPs and, in doing so, will seek public comment as to their scope.

Regulations on Traditional Medicine:
In the US, herbal products are considered as food, food supplement, herbal medicine or cosmetics while products with therapeutic effect are classified as medicine. Products having only the effect of regulating body functions are categorized as food supplement and not medicine.

At present, under the Federal Food, Drug and Cosmetics Act, herbal medicinal products must be registered with the FDA as medicine before they can be sold as over-the-counter (OTC) drugs in the US. To be successfully registered as an OTC drug, the medicine – whether herbal or chemical – must meet safety and efficacy standards. The FDA has in place a very stringent regulatory mechanism under which all new drugs have to undergo a series of tests and clinical studies to prove their efficacy, safety, quality and dosage standard as well as go through an approval process before they can be sold on the market. According to statistics, so far no herbal medicine has been granted approval to register as a new drug.

Given the slim chance of herbal medicinal products being registered as medicines in the US, selling such products as food supplement is the most feasible and legal way. In the US, the sale of food supplement is primarily governed by the Dietary Supplement Act, while labelling requirements are subject to the Nutrition Labelling and Education Act. According to regulations, food supplements have to meet the following criteria before they can be sold in the US market: i) they must be safe, ii) their production and storage conditions must be in compliance with the GMP standards applicable to food in the US, and iii) nutrition facts must be clearly and accurately stated on the product label. According to the labelling rules, information given on the label includes ingredients, nutrition statement, composition/function statement, and health statement. Also, it is provided that the label of food supplements

must not state, either directly or indirectly, that the product is intended to prevent any disease.

Unlike registered drugs, food supplements do not require FDA approval before they can be sold on the market. The manufacturers only have to submit to FDA the information as stipulated by the relevant rules stating that the product concerned has met the abovementioned criteria, and only then they can launch the product. However, if the product fails to meet the labelling requirements, FDA may ban its sale. Even after a product is put on sale, FDA may require the manufacturer to recall or stop the sale of the product if it is proved to cause certain hazards when used under normal conditions.

3. The Nutraceuticals/Dietary supplements Market

Viable paths to exploit natural products in the burgeoning nutraceutical market- has been demonstrated by many companies, there are multiple commercialization paths to tap the nutraceutical market. These include:

- Out license to a pharmaceutical or consumer company.
- Market and distribute ourselves.
- Co-promote with another company's non-competing products.
- Combine a marketing and distribution company's expertise with our detailing and relationship marketing expertise.
- Co-brand using another consumer company's marketing and distribution muscle.

Marketing Strategies:

- Launch products as the first and only dietary supplement with substantiated clinical safety and efficacy results.
- Gain endorsement and usage in a substantial number of targeted physicians through ethical marketing and promotion in the first three marketing years
- Obtain sufficient momentum and critical mass to expand promotion to consumers in the fourth marketing year

Consumer launch should be the subject of a different marketing plan after ethical introduction. Important considerations for a consumer launch will be profitability and retail network.

3a. Market Overview

It is difficult to assess with a reasonable degree of accuracy, the volume or value of the trade in medicinal, aromatic and dye plants simply because trade statistics do not identify all the plants individually; moreover, of those listed, statistics do not identify medicinal and other uses separately. Likewise, nutraceuticals, homeopathic drugs as well as dietary supplements include products of plant as well as animal origin, with very little scope of specifically identifying plant-based products. Moreover, products reported as medicinal plants often include gums, spices and plants where the end use includes the food industry, teas, infusions, cosmetics, and even insecticides. Finally, the situation in medicinal plants trade is rather more complicated because of the levels of secrecy maintained by traders, and the complexity and the disorganized nature of the trade structure/channel itself.

The World Health Organization estimate, suggests that over 80% of the world's population relies on traditional plant based medicine for their primary health needs. While this was initially particularly true of the less developed and the developing nations, it reflects a growing trend in the developed nations as well of late, with consumers increasingly seeking alternatives or complements to pharmaceutical drugs and modern healthcare. The increase in demand for 'natural' medicine is also strongly related to the rise of the green consumption movement. Medicinal plants have additional advantages of simplicity, effectiveness, broad spectrum of activity and emphasis on preventive rather than curative action of drugs. During the last few years there has been a massive entry into this arena by the large mainstream manufacturers, pharmaceutical and Over-The-Counter (OTC) companies with large advertising budgets and media attention, which has also contributed to rapid growth in consumer demand. Increased emphasis on safety, efficacy and quality has resulted in more research and development, a shift towards standardized products and high-quality raw materials, and as a logical consequence, improved legitimacy for botanical medicines, whose demand has been fuelled further with the acceptance of botanical medicines by national (Germany and Japan) and commercial insurance companies (USA). Furthermore, plants are also found to contain disease specific curative properties and extracts of such plants are increasingly used to manufacture effective drugs for some of the diseases. The global demand for medicinal plants therefore, is steadily increasing, both for the traditional as well as modern medicinal systems.

In many parts of the world, the personal care and cosmetics market is crowded. Companies' market shares are likely to stagnate unless they reformulate their products to address the needs of niche markets, incorporate new ingredients, and heighten the performance of products. 'Natural' or 'herbal' products fit well into such a strategy - growth in the natural personal care and cosmetics market is thus, global.

While the demand for natural dyes is showing a declining trend with the development of substitute 'organic dyes', the demand for organic colorants, including dyes and organic pigments, is forecast to increase at a healthy rate. Larger growth is expected in the natural colorants market for food, drugs and cosmetics (FD&C) where certain dyes, such as carmine and annatto, are used regularly.

According to the Nutrition Business Journal, the US nutraceutical supplement market grew by a remarkable 10% - 14% per annum throughout the 1990s. This was driven by three main factors:

- Scientific advances that established links between regular consumption of nutraceutical supplements and reduced incidence of adverse health conditions;
- Increased sponsorship in new research; and,

- Favourable media coverage raising awareness among consumers.

In addition, older consumers were beginning to seek healthier lifestyles in a healthcare environment shifting toward preventative care, there was a permissive regulatory environment (DSHEA, 1994), and there was an economic environment characterized by an expansion of new distribution channels and growing prosperity. Until late 1998, market conditions reflected those of an attractive, emerging industry with low barriers to entry.

The United States market:

The US market for herbal products showed significant growth during the 1970s, when holistic forms of medicine gained popularity with the consumers. Products could be introduced faster in the US market as against say, Europe or Japan, since as per US laws, products were considered safe unless proven otherwise. This situation has since changed and standards have been developed in the US market as well.
Nonetheless, about 25 percent of all prescription drugs in the US today are derived from medicinal plants, and sales of herbal remedies at drugstores, supermarkets and other retail outlets have grown substantially. The market for medicinal herbs will continue to grow, albeit at a reduced pace from the boom period of the mid - to late -1990s. The current challenge facing the industry today is in attracting new consumers to herbal products, as indicators suggest the number of people consuming medicinal herbs has levelled. Medicinal plants used in OTC medicines and for which legal drug claims are made can be expected to enjoy a relatively stable market compared with others.

In general, Americans tend to take herb-based health foods for flu, allergy, muscle/joint/back pain and menopause discomforts. According to another study, since 1998, Americans have become less worried about health problems such as fatigue, stress and depression, and are instead, increasingly concerned about headaches, skin problems, pre-menstrual discomforts, stomach problems and heart disease. Meanwhile, women tend to be more concerned about the symptoms of certain women's diseases. As herb-based health food is known for its efficacy in alleviating such symptoms this, coupled with the fact that the majority of health food consumers are women, has prompted many manufacturers to develop products that are targeted at female consumers.

Obesity is a serious problem in the US, with an estimated 139 million people in the country currently categorized as overweight or obese – a figure that is projected to increase to almost 14% of the population by 2010. A substantial proportion of the population, specifically women, either go on diet to shed weight or purchase products that help keep body weight in check. Hence, low-calorie health foods and those that can help lose weight are very popular.

Popular medicinal plants and herbs in the US market include:

- Ginseng - one of the most commonly used medicinal herbs, consumed in tea, tablet and extract form. It is used to boost energy, improve stamina and resistance to stress, and is said to improve virility.
- Echinacea - a species of chrysanthemum, its primary use is to boost immunity and prevent colds and the flu, as well as symptoms such as respiratory tract infections.
- St. John's Wort - A native of Europe and derived from the yellow flower of that name, it is used in the treatment of arthritis, bruises, sprains, circulation problems and gout. In the US, it is also a popular treatment for mild depression and anxiety.
- Kava Kava - obtained from the root of a pepper plant, it has been in the news of late after its withdrawal from many European markets. Kava Kava is fairly popular in the US as a stress-reliever.
- Gingko - a native Chinese herb, it is popular in the US among the elderly as a treatment for memory loss by improving the flow of blood through the arteries. It is also said to help with depression and headaches.
- Valerian - native to Europe and Asia, it is popularly used as a sedative to treat nervous tension, muscle spasms, cramps, and related conditions, and is also said to aid digestion.

Consumer use of herbal products in the US has increased quite substantially over the years – going up from less than 5% of the population using these products in 1991, to almost 40% in 1998, and the number further increasing. The massive increase in consumer usage of medicinal plants and herbs is a factor of increased advertising, positive press publicity, and the spin off from the natural, green and organic movements within the country.

As seen above, eight products contribute to nearly 47% of total sales in the US. The prominence of aloe amongst these is largely due to the introduction of numerous Aloe vera gels and creams for cosmetic purposes and for the treatment of skin conditions and sunburn. Another significant feature is the large share of multi herb products (27%). There is a growing recognition of the concept of combination formulae compared to individual herbs. Since botanical extracts and herbs cannot be patented, manufacturers are increasingly looking for additional methods of product protection, and combination formulae are harder to copy. Botanicals are also appearing as healthy ingredients in conventional foods – Gingko crisps for example.

Unlike the EU, the most important distribution channels for herbal medicinal products and health foods in the US are stores specialized in such products (e.g. Fred Meyers and Cornucopia), which account for 47% of the sale. Direct sales companies like Amway and Herbalife follow with 27% of the share, and supermarkets and drugstores account for 18% and 8% respectively. Over the next few years however, the distribution channels are likely to undergo changes, the most significant being that more and more Americans are buying through the Internet. Statistics show that total online sales of herb-based health foods had risen sharply from $ 5 m in 1997 to $ 152 m in 2000, and it can be expected that the Internet will become an even more important distribution channel for this category in the coming years.

Vitamins and herbs/botanicals dominate the US dietary supplement market, accounting for over 65% of the share. This provides immense potential for herbal products and remedies from the South Asian region.

Market entry: New entrants to the nutraceutical industry have historically followed a traditional product life cycle.
As new herbal products or combination products designed for a particular health benefit are introduced to the market, they must communicate their story to individual consumers. Because they are "new" or act in a new way, these products are "story intensive". Consumers must be educated on the benefits and risks. This phase is best handled by multi-level marketers and niche suppliers (e.g., health food stores). Who, historically have had customers that are more health-conscious and are receptive to innovative products. These outlets also enjoy relatively high margins to cover the relatively high costs of market entry. Products may be in the "story intensive" phase for an indeterminate length of time, and some may never appeal beyond a narrow niche in the market or grow beyond this stage of development.

Market Growth. After initial acceptance by the most precocious consumers, a more mainstream following develops for the new product. At this stage, some of the more forward-thinking mass marketers may decide to market the product. In addition, raw material suppliers take note of the product's growing acceptance and increase supply, thereby lowering the raw material pricing. During the market growth stage of development, the product innovators find themselves increasingly unable to hold onto the value of their new product unless they have meaningful patent protection or a lock on the raw material supply. During this stage, products may reach up to $50 million in sales, but the number of products that attain this level of sales revenue is extremely small.

Mainstream. Very few products reach the mainstream phase (greater than $50 million in sales). Products that do reach the mainstream tend to be single herb products with simple and powerful value propositions that have received significant mass media attention. During the "mainstream" phase, the basis of competition is mainly through aggressive and resource intensive consumer marketing. Raw material suppliers and technology owners capture only a very small percentage of value unless they have a meaningful barrier to entry (a patent position or control over raw materials).

Within this context, it is important to note that, by late 1998, the nutraceutical supplements market entered a significant slowdown period, and the flow of new products and growth of existing products was slowed tremendously. According to Information Resources Inc. (IRI), herbal supplements sales in the United States fell 15 per cent to $591 million in 2000. The IRI data measured predominantly single-category herbal sales in grocery stores, pharmacies and mass merchandiser outlets such as Wal-Mart and Kmart. Unit sales fell at a slightly higher rate of 17 per cent, implying that prices maintained a modest upward trajectory. By the latter half of 2001, the drop in mass-market herbal sales had slowed, but still fell four per cent over the year ending August 2001. Several industry sources predict that the US market for nutraceutical supplements will slow from its historic double-digit growth rates to levels of 4-6% per annum for the next 2-3 years.

No clear consensus appears within the industry as to either the cause of or the solution to the precipitous slide in US sales of herbal products. However, several variables have been suggested as contributing to the downturn.

i) **Negative media coverage**. Media portraits of 'unregulated industry' have depressed consumer confidence by questioning the safety and quality standards of products. Following media stories that raised the possibility of St.John's wort interfering with the action of prescription drugs, sales of the popular herb nose-dived.
ii) **Glut of supply**. The boom years lured many new players into the market. This led to an inevitable glut in supply of raw materials and a heavy proliferation of new products with big claims and little clinical substantiation.
iii) **Impact of mass markets.** Mass-market dynamics were responsible for the rapid rise in demand, but also created price pressures to offer inexpensive products, with the result that quality was compromised.
iv) **Lack of public education**. Unlike health-food store users, who tend to know a little more about natural products, mass-market shoppers are more likely to hold unrealistic expectations about what herbal supplements can and cannot do. This may explain why herbs such as ephedra, which produce immediate reactions, have gained popularity among mass-market shoppers while slow-remedy herbal products have tended to fare more poorly. The industry is also to be blamed for either perpetuating unrealistic expectation about herbs or simply not managing the expectations of their newest consumers. Insiders agree the failure of retailers and manufacturers to educate mass-market consumers has contributed significantly to the problem. In addition, despite the growing body of clinical evidence supporting the benefits of many herbs, there is currently no way to acknowledge that information on product labelling.
v) **Industry inadequacies.** Aside from not educating the public sufficiently, some experts believe, the industry has failed the US consumer by not policing itself adequately and by offering products of varying quality. American companies have spent too much money on marketing, at the expense of research. Others bemoan the many trade associations in the supplements business (as many as nine of consequence) and their inability to create a unified voice to the consumer and to Washington.
vi) **Ineffective regulation**. Some in the industry have suggested the government- FDA and the Federal Trade Commission- has adequate authority to protect the public against unsafe or misbranded supplements, but has only selectively enforced the law. This fails to effectively weed out and make examples of the industry's bad apples, and results in sensational headlines that cast aspersions on the whole industry.
vii) **The economy**. The fall in herbal sales has coincided with a worldwide economic slowdown. Luxury products like herbals fall out of consumer budgets. Indeed, the entire nutrition industry expanded dramatically during the boom years of the extended bull market but has yet to weather a

general economic downturn. The issue of consumer education surfaces again here because making the supplements industry recession-proof, or at least recession-resistant requires more investment in the consumer.

3b. Sales

Industry statistics for dietary supplement products are scattered across at least eight different 4-digit Standard Industrial Classification (SIC codes) and nearly 80 different 6-digit international codes. In addition, there are a large number of trade organizations that cover varying aspects of the industry. Thus, estimates of retail sales vary widely; however, there is no question that the industry has grown rapidly. There is general agreement that dietary supplement sales in 2000 were approximately $6 billion. The distribution channels for these products include grocery stores, drugstores, and mass marketers increasing the range of products they carry and large pharmaceutical companies that are entering the market, often by buying supplement firms. As a result, the structure of the dietary supplement market is changing and will continue to change as the market matures.

Sales of Dietary Supplement (DS) Products

As reported in the F-D-C Tan Sheet (F-D-C Reports, 1997), vitamins account for 48 percent of DS product sales, minerals for 6 percent, and herbals and botanicals for 28 percent, with sports nutrition (much of which is dietary supplements), meal supplements, and specialty supplements making up the remainder. Vitamins, as the most mature supplement category, experienced growth of only about 8% from 1995 to 1996, which is slower than other DS categories. Nearly a third of sales are private label brands.

Herbal and Botanical Supplement Sales

Herbal and botanical products totalled $3 billion in sales for a 28 percent share of the DS market. Their growth rate of 20 percent from 1995 to 1996 was the highest of all DS products. However, sales volumes of specific products are relatively concentrated in a few products. Specifically, garlic, ginseng, *Ginkgo biloba*, and *Echinacea* were the best-selling herbal products in 1995 and 1996. The leading herbs in terms of sales growth in 1996, each with greater than 50 percent growth (in sales), were *Ginkgo biloba*, *Echinacea*, and saw palmetto. St. John's wort, a relative newcomer to the industry, has experienced phenomenal sales growth as well since 1996. According to one source, the American market for Ayurvedic herbs is estimated to be in the range of only $250-350 million (Source: Nutritional Outlook, May 2002) but grew by 31% in 2000 compared to a growth rate of only 1% for the overall herbal market.

Product and Brand Differentiation

Dietary supplements are by nature heterogeneous products. Even within a particular DS product type, there are many different types of products and many different forms in which the products are made available. Thus, many niche markets exist in which companies may be the only or one of a few manufacturers of a product. However, some of the products are more commodity-like and there is little differentiation among different manufacturers of the products (e.g., single vitamin products).

Products may also be differentiated based on their brand names within a particular type of product. However, according to the Nutrition Business Journal, the nutrition industry in general has few dominant brands. Some of the reasons they cite are the large number of product niches, the variety of distribution channels, the dynamics of consumer trends (changing preferences over time), and the evolution of nutrition science. In some markets, however, a few companies have established strong brand name recognition. These include, for example, Ginsana and Ginkoba in the herbal and botanical market.

3c. Market Structure

Currently, this is a fragmented market in which the majority of nutraceutical companies have annual sales of less than $100 million. In 1999, the top 20 companies captured only 50% of the market. For example, Royal Numico- the holding company of GNC, Rexall Sundown, and Enrich- is the leading player in the US market, yet is only responsible for 12% of the market. However, mergers and acquisitions have been occurring frequently and market concentration is expected to increase over time.

Part of its fragmentation is due to the varying activity levels of companies engaged in this market. Activities range from supplying raw materials to manufacturing, marketing and distributing and/or retailing. Most companies focus on one activity, while the remainder are vertically integrated. Hauser, for example, focuses on supplying botanical raw material and Leiner Health Products (a market leader) manufactures and markets private label nutraceutical supplements. NBTY, on the other hand, is vertically integrated, beginning with manufacturing and marketing and continuing through to distribution and retail.

Suppliers of raw materials are typically small and numerous. Many products, especially herbal and botanical products, can be produced in small-scale operations that are not highly capital-intensive.

The distribution channels for products are many and varied and include channels through which companies manufacture and sell their products within their own stores, manufacture products and private-label them for retail outlets, and manufacture products with a brand name label for sale in retail outlets. In addition, a large volume of sales is through direct sellers such as mail order and multilevel marketing. The raw material providers and manufacturers are distinct among the natural food, DS, and natural personal care lines, but the product lines share common distributors and retailers. In addition, foreign firms and international trade are large components of the DS industry and its distribution structure. Many products sold in the US are manufactured from imported raw ingredients or are imported as finished products. (See Attachment F)

Of the natural food stores, General Nutrition Centres (GNC) stands out with $1.2 billion in sales in 1996, or 20

percent of the $6.2 billion retail market for supplements (Nutrition Business International, October/November 1997). Large natural food store companies, such as GNC, produce their own products and may manufacture private-label products for supermarkets and drugstores as well. Other natural food stores carry both national brands and private label brands manufactured by other companies.

3di. Barriers to Entry

In the past, barriers to entry in DS product manufacturing were not particularly high, and many small firms entered the industry. However, the barriers to entry are rising and will continue to do so primarily because of the effects of consolidation and of regulation, both federal and self-imposed.

As many distributors and retailers are consolidating, it is becoming harder for small companies to gain access to customers. Mass merchandisers that carry DS products need to acquire adequate product from manufacturers to supply all their needs and, hence, prefer to deal with larger, established suppliers. Also, because other manufacturers are consolidating, they are purchasing inputs in volume and thus are able to negotiate lower raw material prices than smaller manufacturers.

In addition, regulation is making it more difficult for small firms to enter the industry. It may be more difficult for these firms to acquire the needed resources to comply with labelling regulations as well as Good Manufacturing Practices (GMPs). Larger pharmaceutical firms that are branching out into DS product lines will have little trouble complying as their existing products lines in general must conform to much stricter regulations.

Some of the regulations are imposed by the industry itself. In particular, the industry, through organizations such as the National Nutritional Foods Association (NNFA), is working toward establishing standards for DS products. The NNFA has already established a True Label program in which it tests products to ensure that they are as represented on their labels. Although these self-imposed regulations are voluntary, consumers may come to expect products that conform and may not purchase products that do not. As with federal regulations, smaller firms may not be able to garner the resources for compliance.

3dii. Vertical Integration

Vertical integration refers to the extent to which firms operate at more than one level of production and marketing. In general, firms that are more vertically integrated expect to retain a higher level of profits than firms that concentrate on a single level of the industry. In the DS industry, while many firms concentrate on a single level, others, such as GNC, span nearly the entire spectrum from manufacturing to consumer sales. According to the Nutrition Business Journal, the chain of manufacturing from raw materials to finished products may span four or five companies. On the other hand, multilevel marketers and mail order companies, both of which have a large presence in the DS industry, span many of these levels.

3diii. Market Trends

As discussed in the previous Market Overview section, the traditional market drivers that once fuelled double-digit growth rates in the US nutraceutical supplements market have experienced a substantial slowdown. In the opinion of an industry analyst at Rabobank International, this slowdown is causing a paradigm shift in the fundamentals of the market.

The current evolution of the industry is being caused by changes in the four traditional drivers linked to consumer, regulatory, economic and market factors.

- **Consumer Disillusionment**. Reinforced by unfavourable publicity and an enhanced knowledge gained through better access to information, mainstream consumers are quickly becoming immune to generic marketing hype, and instead are beginning to question the effectiveness of nutraceutical supplements. They are now demanding better proof of quality and brand-specific scientific evidence that shows the safety and efficacy of products. Companies, in turn, are facing increased investment requirements in R&D, manufacturing and marketing in their efforts to appease these disillusioned consumers.

- **Regulatory Requirements**. In response to the public outcry for improved safety and quality standards, the US FDA is taking measures necessary to counter these problems. It is in the process of promulgating new rules for Good Manufacturing Practices (GMP) and establishing an Adverse Event Reporting System (AERS) pertinent to dietary supplements. Manufacturers can currently earn a seal of approval from the National Nutritional Foods Association for GMP manufacturing, or a quality stamp for labels using 3rd party auditors, to exemplify their voluntary commitment to safety and quality. These new FDA rules are expected to be more rigorous than the current system, with quality assurance requirements paralleling those designed for drug products.

- **Economic Environment**. The increased pressure caused by changing regulatory environments will be accompanied by shrinking margins; meanwhile players will continue to witness a commoditization of their product in a tightening economic environment. Previously, new consumers who matched average consumer purchasing profiles were enticed into buying by premium pricing strategies, driven by media hype and expanding distribution into mass-market channels. These distribution channels are becoming saturated which, when coupled with disillusioned consumers inundated with multiple company, private label and/or inconsistent quality products, are shifting sales away from a price-driven, brand-loyalty situation to one that is volume-driven.

- This situation is becoming more perilous because recent tightening of economic conditions has prompted consumers to become increasingly price-sensitive. Simultaneously, retailers are beginning to implement strategies that reflect the slowing economy. These include aggressive discounting, inventory reductions and product-mix

rationalizations. Furthermore, retailers increasingly expect companies to provide additional sales support to move their products- laying more promotional responsibilities onto manufacturers. Manufacturers who are unwilling or unable to provide this support can expect inventory returns at the mass- market level.

- **Market Environment**. These changes are taking place in an increasingly competitive environment where substitution is becoming a painful reality. The US market players are faced with two main problems: first, the threat of increasing private-label substitution that reduces premium shelf-space; and, second, and perhaps more importantly, a threat of substitution by food and beverage products that provide new delivery vehicles for nutrients, instead of the current drug-like forms. These food and beverage products, like meal replacement bars (designer foods) or calcium-enriched orange juice (functional food/ beverage), appeal to the general public who want to fulfil their nutritional requirements by eating and drinking rather than by popping a pill. Many large multinational food companies (e.g., Nestle, Unilever, Kellogg and Novartis) have resources to drive this substitution movement and are behind such products.

The changes in these drivers are altering the traditional structure of the industry in a number of ways. They are increasing the entry barriers and the bargaining power of customers; they are raising substitution threats; they are decreasing overall demand; and finally, they are adversely affecting growth and profitability prospects for US nutraceutical supplement manufacturers.

One commentator suggests that three well-differentiated segments will develop in the industry:

- Functional foods: improve nutritive value of food; used by healthy individuals to stay healthy;
- Medical foods: already FDA regulated; specific needs for chronic diseases; and
- Nutraceuticals: to enhance both physical and cognitive performance; slow down biological manifestations of aging; and, alleviate symptoms of chronic diseases.

All will require significant scientific and clinical substantiation to validate safety and efficacy. (Nutraceuticals World, Nov. 2001)

Another commentator suggests a convergence of pharmaceutical companies-who have research and development and manufacturing expertise, but little or no experience dealing with retail customers-with food companies-that have expertise dealing with retail customers but little or no experience with R&D and manufacturing. (Partnerships for Profit in Nutraceuticals Conference, Atlantic City, NJ, April 2002)

3div. Responses to the Changing Market Trends

Operations. All companies, regardless of size or activity, are feeling the impact of the changing industry structure. At the operating level, these changes are being translated into higher levels of expenditure in research, development, manufacturing and marketing. At the same time, sales are slowing. It is therefore becoming increasingly difficult for companies to generate sustainable growth prospects and create value for stakeholders. These changes have had a significant adverse impact on the average financial performance of the top US nutraceutical supplement manufacturers over the past two years.

Many believe that, to sustain business for the long term, suppliers of botanical raw materials and extracts will need to focus on product innovation, value-added services and partnerships with key distributors and retailers. Some suppliers are working on branding campaigns to promote quality. To cope with demand once the market improves and with growing customer concerns with raw materials quality, there are reports of efforts by suppliers to control cultivation and focus on direct sales at the expense of distributor-based sales. Some suppliers are cautiously optimistic about the future, believe the supply glut is close to being sold through, and are even reporting modest increase in activity as well as stabilizing prices of raw materials.

Another strategy will be the search for new markets. Botanicals are finding applications in area such as personal care, where herbals such as grape seed, milk thistle and willow bark (Salix alba) are finding favour because of their antioxidant properties and role in ultraviolet protection. And, while demand for St. John's wort, ginkgo (*Ginkgo biloba*), Echinacea (*Echinacea purpurea*) and other herb staples was almost nonexistent in 2001, other botanicals showed more buoyant growth. For instance, Suppliers report an improvement in demand for bilberry (*Vaccinium myrtillus*), milk thistle (*Silybum marianum*) and vinpocetin (a synthetic derivative of a compound found in the Periwinkle plant I *Vinca minorl*). Demand for herbs targeted at women, such as black cohosh (Cimirifiga racemosa), chaste tree berry (*Vitex agnus castus*) and horse chestnut (*Aescilus hippocastanum*) also remain strong. Herbs related to energy, weight loss and joint health continue to perform well, as do saw palmetto (*Serenoa repens*) and valerian (*Valaroana officinalis*).

Ironically, the downturn has led to some suppliers and growers exiting the business altogether guaranteeing that when demand does recover, supply pressure will push up prices again. But most within the industry remain optimistic despite the obvious dilemmas at hand.

3dv. Market Consolidation.

With demand slowing and expenditures on the rise, the market is destined to mature. Faced with an increasingly competitive situation, companies have a limited number of possibilities: they can seek other avenues of high growth and enhance top line growth; they can consolidate and focus on cost reductions to cushion the effects of shrinking margins; alternatively, they can use a combination of both strategies.

In this developing scenario, companies can make use of the following strategic options:

- Expanding national market share by merging and/or acquiring complementary companies or product lines within the US market;

- Expanding vertically or horizontally into faster growing and under-developed international markets such as Europe, Latin America and Asia;
- Licensing-in new technologies and products from universities, biotechnology and/or innovative nutraceutical companies;
- Tapping into growing Internet distribution channels; and,
- Addressing cost-efficiencies in manufacturing and/or along the supply chain

In view of this, it is expected that the market will soon become polarized, with a handful of top tier companies attaining a global critical mass and smaller companies becoming more specialized in niche markets. Larger companies will be able to weather the growing bargaining power of mass-market retailers by implementing one-stop shopping strategies. They will be capable of leveraging their size and supporting scale in R&D (both internal and external), manufacturing, and marketing activities. Meanwhile, specialist companies will retain their flexibility and speed in launching tailor-made products for targeted consumer segments; they will also grow by using price-premium strategies.

However, there is still the issue of renewing consumer confidence in the safety and efficacy of products in the US nutraceutical supplements market. Some argue that a fundamental change from a marketing-driven market to one that is knowledge-based is required to ensure the sustainable development of the US nutraceutical supplements market. However, successful marketing in a consumer goods environment often depends on a company's ability to be first-to-market. Incentives, therefore, are lacking for the necessary R&D investments needed to support safety and efficacy claims in a knowledge-based environment.

Despite disillusioned consumers, most observers believe the future for the nutraceuticals market still looks bright. This optimism is supported by two factors: the expanding number of aging Americans and their movement towards preventative health maintenance. Growth projections for the market still exceed those for traditional food and consumer goods, as well as that for the US GDP. Nevertheless the US nutraceutical supplements market remains at a crossroads and only time will tell if it will continue to mature into a polarized market, or if it will shift toward a knowledge-based market. The only certainty is that change is imminent and only companies responsive to these changes will survive.

4. What are the options available for the Growers and Small companies?

Option 1: Raw Material Supplier.
This may not be the most viable strategy for a variety of reasons. Primary market research has confirmed the glut of raw materials and raw material suppliers and the difficulty of establishing a supply relationship with distributors or manufacturers. We have spoken with distributors who verify that they have tremendous choice and bargaining power in choosing suppliers of raw materials. We also confirmed this trend with purchasers of raw materials, who are generally satisfied with the quality and availability of raw material products. Successfully identifying and negotiating a supply arrangement with a distributor or manufacturer would likely require the full-time services of a business development professional, with no guarantee that the volumes, pricing and timing of contracts would generate sufficient revenues for this to be a successful strategy. Raw materials have become a commodity and it is likely that pricing pressures will reduce margins to unattractive levels for the foreseeable future or until a shake-out occurs. This is not an optimal environment for a new supplier to enter the market. In addition, the perishable nature of the product add additional disadvantage for marketing the product.

Option 2: Direct Marketer
One option open to small companies is to market directly to the end-consumer, capturing the full value of its products. This concept involves the distribution of products directly to consumers using the Internet or direct access TV ("infomercials"). The cost of an infomercial is approximately $15,000 to $50,000 (plus a royalty of 2-3%) for the production and airing of a 2-minute segment, and approximately $150,000 for a 30-minute segment. The advantages of this option are the potential of early generation of revenues and visibility for the company. Both would help to increase the valuation of the company for future financings or acquisitions.

However, there are several potential difficulties with this approach. First, before it can proceed, the company must still fund and develop a marketable product that has the potential to attract significant consumer interest. In addition, small company would need to undertake all of the production, packaging, labelling and regulatory issues associated with the retail sale of a product. This is not an area of expertise for management of the company.

Option 3: Independently Financed Nutraceutical Venture
The concept of this option is to develop a business plan, and attempt to finance a stand-alone nutraceutical development company. There are a limited number of specialty venture capital (VC) firms, a larger number of more general life science VC firms, and potential corporate partners that might be interested in the companies nutraceuticals venture.

The difficulties here are that the risk capital markets (e.g., the venture capital community), in general, have taken a long pause in their investment activity and the lack of a defensible intellectual property position.
We believe that any of the listed options could be viable under certain circumstances; however, each of them varies in terms of its potential attractiveness and whether it is a realistic strategy under current conditions.

- The industry is becoming mature and going through a period of consolidation. While a start-up venture in raw materials supply (Option 1) might succeed on its own, the barriers to entry are increasing. Access to customers becomes more difficult as the industry consolidates; larger customers demand higher volumes and lower prices; and, the relative costs of compliance with increasing regulatory standards for labelling and GMP places smaller firms at a competitive disadvantage to large companies.

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Table. 1. In reviewing the options, it is possible to characterize them in terms of near term cash requirements, potential value and risk. This is shown in the chart below.

Strategy	Near term cost	Goal	Key factor for success	Probability of success
1) Raw Material Supplier	Less than $100k for business development efforts required to establish supply channel relationships	Material supplier to industry. Most specialty materials suppliers have sales in $1 million range	Pricing on raw materials	Low-glut of products in market
2) Direct Marketer	Approximately $500k to develop product and finance initial marketing efforts	Could become a niche player with sales of product in $5 million range	Quality of advertising and promotion	Low-Medium, depending on quality of product and efficacy of marketing
3) Independent Financing	None, other than management time to attract financing	Stand-Alone company – would have to project near term revenues in $50 million range to be attractive to venture capitalists	Management team, size of opportunity and intellectual property	Low – unfavourable financing environment and minimal intellectual property
4) Nutraceutical Partnering	$250k to develop patented technologies and perhaps $100k of business development effort to establish licensing relationships	Obtain 1-4% royalties on sales of each product – typically in $10 million range	Intellectual property	Low-High- depending on quality of intellectual property

- Direct marketing and sales (Option 2) have a similar challenge. Traditionally, sales of the top five products account for over 75% of total revenues in the nutraceuticals market. It will be extremely difficult for small companies to introduce a new product or products and achieve this level of market penetration without a major consumer product marketing campaign. This is far beyond the resources of an early stage company. Thus, Option 2 is difficult because of the required scale of marketing effort to be successful in this industry.

- Option 3 involves all of the organizational tasks of creating and operating a start-up venture, although in this case it would probably begin as a wholly owned subsidiary. Before they will provide financing, venture investors typically require a company to demonstrate: (a) a large target market; (b) great, proprietary technology; and, (3) an experienced management team. In the eyes of prospective investors, the proposed nutraceutical company would begin with access to some assets but lacking in those that are most important, namely: (a) its target market is relatively small except for a select few products with wide consumer acceptance; (b) it has no current patent protection; and (c) it has no separate, dedicated management team with successful start-up experience.

In addition to all of the operating issues, this option would also involve significant consequences from the standpoint of equity ownership. To recruit a management team, stock ownership in the company would need to be offered due to the career risks associated with joining a start-up. Investors would undoubtedly place a low initial valuation on the company until its asset base (particularly its intellectual property asset base) is better established. As a hypothetical example, in a seed funding of $500,000, if the company's current value is assumed to be $1 million, the investor(s) would receive 33% of the stock, with a management team reserve probably equal to at least another third. This would leave the company with a 33% stake. Assuming a subsequent first round financing of $2 million and a company pre-investment valuation that has doubled to $3 million, new investment would receive 40% of the company stock and all prior stockholders would be diluted to 60% of their previous holdings.

As the industry matures and consolidates, it is likely to place increasing emphasis on science and clinical results. Expertise in these areas is strength of small companies and one of the most important assets to leverage for value going forward. However, the absence of a patent position can jeopardize this advantage. It will be extremely important for the Company to identify and aggressively protect any intellectual property that currently exists or arises in the course of its research and development programs. The fundamental structure of the natural product market is being altered by a number of factors, including changing consumer demands and economic pressures, coupled with tightening regulatory requirements and competitive market conditions.

Table 2. Representative Examples of Botanical Extract Suppliers

Company	Location	Website (www.com)
Arya Aushadhi Pharma	Thane, India	Aryaaushadhi
Ayurveda Holistic Center	Bayville, NY, USA	Ayurvedahc
Ayurveda.com	Sydney, Australia	Ayurveda.com.au
Ayurvedic Institute	Albuquerque, NM, USA	Ayurveda
Battle Chemical	San Clemente, CA, USA	Battlechem
Cevan Nutritionals	Boulder, CO, USA	Cevan
Circle of Health	Eugene, OR, USA	Ayurveda-herbs
Doctor Phyto	Clearwater, FL, USA	Doctorphyto
Goodwin Pharma	Andhra Pradesh, India	
Handa Fine Chemicals	Nottingham, England	Handafc.demon.co.uk
Herbie's Herbs	Toronto, Canada	Herbies-herbs
Indfrag Limited	Bangalore, India	Indfrag
Laila Impex	Uttar Pradesh, India	Lailagroup
Modern Natural Products	Mumbai, India	Modern-natural
Nat. Inst. of Ayurvedic Med.	Brewster, NY, USA	//naiam.com
Nutriscience Innovations	Fairfield, CT, USA	Nutriscienceusa
OM International	Mumbai, India	Omherbals
Ozone Ayurvedics	New Delhi, India	
Pacific Phyto Products	Tamilnadu, India	Pacificphyto
Pennsylvania Food Prdct	Newtown, PA, USA	Pennfoodproducts
Surya Trading Co.	Lyons, CO, USA	Suryatrading
Vidhi Impex	Mumbai, India	Vidhiimpex

The current evolution of the industry is being caused by changes in the four traditional drivers linked to consumer, regulatory, economic and market factors.

5. Conclusions

The fundamental structure of the market is being altered by a number of factors, including changing consumer demands and economic pressures, coupled with tightening regulatory requirements and competitive market conditions. These change drivers are increasing the barriers to entry, but at the same time companies are facing a drop in demand and a growth in both substitution threats and customer bargaining positions. Players, finding growth and profitability prospects diminishing in this maturing market, are seeking alternative strategic options. A main alternative is to consolidate, while the primary challenge is to rejuvenate consumer demand.
It is critical to convey this consumer-based approach and marketing vision:

- To serve the customers by providing evidence-based nutraceutical products for the treatment and management of chronic diseases.
- To serve the customers by providing evidence-based natural products those have been demonstrated to be safe and effective utilizing stringent scientific standards.
- To serve—the customers by ethically promoting evidence-based use of natural products by utilizing internationally recognized scientists, thought leaders, community-based physicians and pharmacists.
- To lead the medical and nutraceutical communities by demonstrating an unprecedented level of commitment to the ethical development of evidence-based natural products.

Although alternative paths to the nutraceutical marketplace exist, a number of critical competitive advantages clearly steer companies toward participating with a partner to launch and support its product under the brand. These advantages include:

- Products with proven safety and efficacy.
- Promotion of the company's vision (Brand)-a unique business model.
- Controlling the message.
- Full revenue returns.
- Huge unmet needs in the marketplace.
- The convergence of two growing markets (chronic diseases and dietary supplements).
- Reachable physician populations.
- Great potential for relationship marketing.
- Internationally recognized thought leaders.
- Supply and manufacturing partnerships are established.
- Zero-based opportunity.

There are several critical success factors for novel nutraceutical product's ethical launch: Endorsement from physicians and healthcare professionals and ethical marketing to physicians and healthcare professionals is definitely a new opportunity for evidence-based products. Close to 40% of consumers said that they used vitamins or minerals because a health care practitioner had recommended them and physician recommendations for a particular brand are followed almost 90% of the time. Close to 60% of supplement users wish their primary care physicians could tell them more about dietary supplements and 35-40% said they would increase usage if they knew more about the products they take. All these data strongly suggest the enormous opportunity to build sales based on gaining the endorsement of healthcare professionals.

The major stumbling blocks in preventing physicians playing a bigger role in the nutritional healthcare are:

- Insufficient training in nutritional medicine therefore physicians are hesitant to give nutritional advice. Only 40% of medical schools require any nutritional curriculum and this number is decreasing.
- Physicians are trained to understand scientific data that are researched and presented in a familiar context. Most dietary supplements (except vitamins and minerals) do not provide the research data to back up their claims and are not promoted through the ethical detailing channel, the way business is conducted in the physician's world.

Product strategies:
With the above understanding, three product strategies are important to the success of a medical dietary supplements.

- Key opinion leaders support and advocacy
- Medical nutrition education to physicians and healthcare professionals
- Training physicians on giving nutritional advice and recommendations
- A well-balanced marketing campaign that presents the clinical value of products yet differentiates it from prescription medications, therefore unleashing its sales potential as a non-prescriptive consumer product. The goal is to establish a new concept in chronic disease management and break away from the prescription drug evaluation stereotype.

Reachable Physician Audience:
For these strategies to be successful for its first products, targeted physician audience must be easily identified and reached.

Patient Acceptance and Compliance:
According to the findings from a focus group study on adult sufferers from diabetes, the preferences and considerations on using medical remedies are:

- Prefer alternate medicine
- Recommendation from doctors or from reliable sources
- Information about the product
- Prefer capsules, but single-dose liquid formulation is acceptable
- Expectations on results
- Eager and willing to try new ways to alleviate their disease
- Want information before they try
- More willing to try if recommended by a health professional.

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List of Journals related to Pharmacognosy

- Current science
  http://www.ias.ac.in/currsci/index.html
- Chemistry of Natural Compounds
  http://www.wkap.nl/journalhome.htm/0009-3130
- Fitoterapia
  http://www.indena.it/fitotrp.htm
- European Journal of Herbal Medicine (NIMH)
  http://guest.btinternet.com/~nimh/frameacc.html
- History of Traditional Indian Medicine
  http://www.mic.ki.se/India.html
- Indian Drugs
  http://www.idma.org
- Indian Journal of Experimental Biology
  http://www.niscair.res.in
- Indian journal of Pharmacology
  http://www.ijp-online.com
- Journal of Agricultural and Food Chemistry
  http://www.pubs.acs.org/journals/jafcau/
- Journal of Asian Natural Products Research
  http://www.gbhap.com/journals/419/419-top.htm
- Journal of Ethnopharmacology
  http://www.elsevier.com/locate/jethpharm
- Journal of Herbal Pharmacotherapy
  http://www.haworthpressinc.com/store/Default.asp
- Journal of Natural Products
  http://pubs.acs.org/journals/jnprdf/index.html
- Journal of Natural Remedies
  http://www.jnronline.com
- Journal of Pharmacy and Pharmacology
  http://jpp.pharmpress.com/content/html/
- Medicinal and Plant Abstracts
  http://www.niscom.res.in/
- Natural Products Report
  http://www.rsc.org/is/journals/current/npr/nprpub.htm
- Natural Product Letters
  http://www.gbhap-us.com/journals/724/724-top.htm
- Planta Medica
  http://www.thieme.com/chemistry/aec.htm
- Plant Science (Elsevier)
  http://www.elsevier.com/inca/publications/store/5/0/6/0/3/0/
- Pharmaceutical Biology
  http://www.swets.nl/sps/journals/pb.html
- Phytochemistry
  http://www.elsevier.nl/inca/publications/store/2/7/3/index.htt
- Phytochemical Analysis (Wiley)
  http://www.interscience.wiley.com/jpages/0958-0344/info.html
- Phytomedicine
  http://www.urbanfischer.de/journals/phytomed/phytmed.htm
- Phytotherapy Research
  http://www.interscience.wiley.com/jpages/0951-418X/