

SAMI LABS, BANGALORE

Leveraging science to advantage to grow nutraceuticals business

Sami Labs Ltd., a pioneering producer of standardized herbal extracts, fine chemicals and related products, is consolidating its formidable presence in this sector, by focusing on generation of intellectual property on the functionality of multifarious products extracted from nature.

By marrying modern science into age-old wisdom, including in the Indian Systems of Medicine (ISM), Sami is aiming to catapult itself into the highly valued nutraceuticals industry, especially in the developed countries, offering standardized, tested products that are backed by the rigors of clinical evaluation. **Dr. Muhammed Majeed**, Chairman and Managing Director, Sami Labs, and the guiding force behind the group, firmly believes that true value-addition can only come from moving up the value-chain and into formulated products that deliver scientifically validated performance as nutraceuticals, addressing specific preventive health maintenance needs; as cosmeceuticals in personal care products addressing specific topical/oral health maintenance needs; and as botanical drug products – either prescription or OTC.

While India, with its rich biological diversity, has focused (at varying stages of the industry's development) on exploiting this advantage, Dr. Majeed fears that the industry has for too long been trapped by the relative comfort of supplying fresh botanicals and whole dried leaves. While some companies have

climbed the evolutionary ladder and set up plants for manufacture of standardized herbal extracts and phytonutrients, it is time for the industry to take the next step and move into the supply of prepared formulations. With a strong emphasis on scientific research, thrust on new product development, quest for innovation and adherence to international standards of production, packaging, quality and assurance, Sami is all set to revolutionise the nutritional supplements industry. The company has already introduced many of its Indian herbal products in the demanding US market, by building up the credibility of these products through intensive and extensive clinical trials and the first offerings to the Indian market have only recently been made.

Sami's efforts have resulted in the generation of substantial intellectual property, which Dr. Majeed believes will hold the key to the company's sustained growth in the years to come. So far the company has received eight US patents and 15 applications are pending with the patent offices there. This has come about due a sustained campaign to develop good documentation for the safety and efficacy of products,

and the decision to conduct trials in the US-population in partnership with leading scientific institutes and hospitals.

Sabinsa Corporation, the US-based arm of the group, has so far sponsored a number of clinical studies in the country, and has already submitted an IND application for Gugulipid, and is carrying out randomised, double-blind, placebo controlled trials evaluating the safety and efficacy of the drug to treat Americans with hypercholesterolemia. Yet another 12-year trial is evaluating the utility of selenium based compounds in prevention of prostate cancer in American male population and its possibility in the treatment of Alzheimer's disease. Phase I clinical trials have also been carried out on the use of oral curcumin (diferuloylmethane) and piperine in patients with advanced malignancies. A Phase II study of green tea for treatment of patients with hormone refractory prostate cancer has also been approved, and Sabinsa will supply the tablets of decaffeinated green tea for the study. The second clinical trials are also ongoing in USA to determine the safety and efficacy of *ForsLean* (a forskolin extract) in young, mildly overweight women,

while another similar study will be launched in Japan shortly. A diabetic bar is under development in the US, Japan and India.

The company has spent four years researching the safe and proper manufacturing aspects of selenium in the form of L-selenomethionine, which according to Dr.



Dr. Muhammed Majeed
Managing Director
Sami Labs Ltd.

"It is our vision at Sami Labs Ltd. to create products that help mankind to lead a better and healthier life, by developing, manufacturing and marketing quality products based on a tradition of innovation."

"We wish to touch people's lives across the world by meeting their health needs."

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Majeed, “is the most biologically available form of human nutrition.” Today, Sami is the world’s largest producer of this substance and has been successful in manufacturing and exporting it – the first for any company in India.

Many challenges

While there is growing interest in Indian Systems of Medicines in the developed countries, the business is not without challenges. For one there are ideological differences with western medicine; in particular the emphasis on treating the patient as against the disease as part of a holistic philosophy (as opposed to the analytical approach that western medicine is tuned to). In ISM, very often, the principles are recorded in manuscripts from ancient literature, in various languages and scripts and a wide range of treatment combinations are used for specific disease conditions. In fact, some such combinations are prescribed on an individual basis.

ISM formulations are usually mixtures of herbs or herbo-mineral compositions, and the ingredients act synergistically. Various categories of ingredients with diverse physical properties (for example, Ayurvedic *kashayams*, *choornams*, *gulikas*, *lehyams*, medicated oils/ghees, *kuzhamboos*, *bhasmas*, etc.) are used and laborious processing is required for obtaining optimal potency. Shelf life and storage conditions are also not adequately defined.

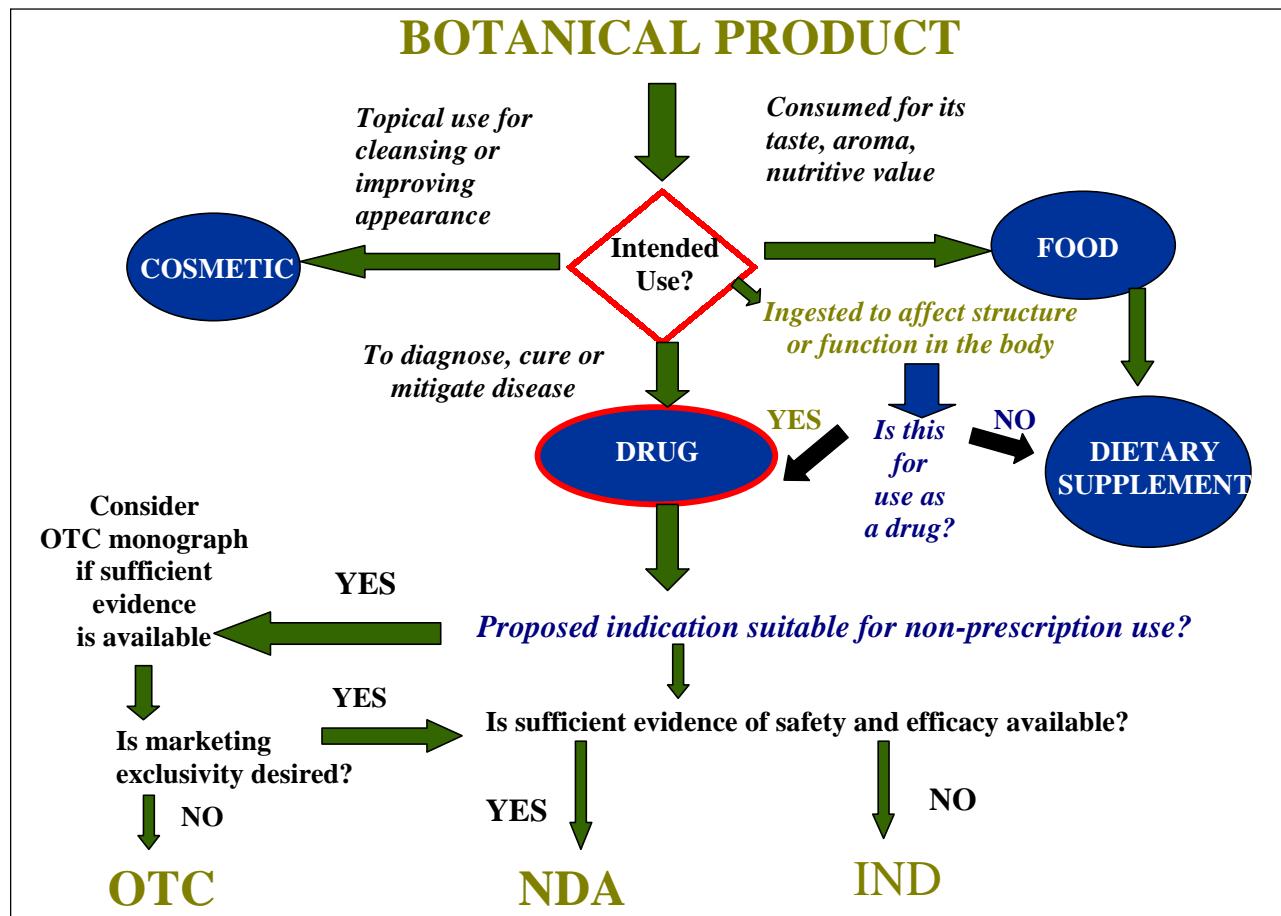
Sami will step up its endeavours to upgrading well-known traditional botanical dietary supplements to an ethical drug status through the NDA process; developing standardized manufacturing processes and analytical methods for traditional preparations; and establishing compendial standards for ingredients and formulations. At the same time the company is also in the process of constituting a product man-

agement team to handle the broader issue of adapting as many pharmaceutically useful herbs from around the world to Indian conditions, using techniques such as tissue culture to improve/better existing varieties of plant sources.

Indigenously developed SCFE facility: A first

Sami Labs has set up India’s first supercritical fluid (CO₂) extraction facility on a commercial scale on technology developed by IIT, Bombay, under the Government of India’s ‘Technology Mission’.

The technology works at pressures of more than 300 bars for selective extraction of active compounds from natural products for pharmaceutical and nutraceutical usage. The plant has been built at a cost less than half of any other imported facilities of this kind.



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Sales at Sami Labs have grown from Rs. 445 mn in 1999-00 to Rs. 710 mn in 2002-03, while the US-based Sabinsa has clocked sales growth from \$17.18 mn in 2000 to \$20.85 mn in 2002.

By 2005, when product patents will be hopefully recognized in India, as is done elsewhere in many parts of the world, Sami will have laid the founda-

tions for what Dr. Majeed hopes will be a Rs. 500 crore enterprise. It is Dr. Majeed's vision to make the group a reliable and responsible supplier, and to grow into a major research-based company of claim substantiated nutraceuticals, cosmeceuticals and drug molecules. Judging by the progress made so far, the Sami group, it seems is well on its way to achieve these goals.

Sami & Sabinsa – the success story

Sabinsa Corporation was established in 1988 and incorporated in the State of New Jersey, USA with the original mandate of importing import generic drugs into the US. The first product introduced into this discerning market was buprenorphine HCl, followed soon by Niacin. However, because of a "scandal" in the USFDA, the focus soon shifted and a new line of products was introduced into the US based on Indian herbal plants.

Gugulipid & Boswellin were early products in this category, followed by Citrin, an ayurvedic product. Concerns over the lack of control over quality of traded items, prompted a decision to set up a manufacturing and quality control centre in 1991 at Bangalore, which eventually emerged as a hub for the manufacturing operations.

The flagship of the manufacturing operations is Sami Labs, which was established in 1991 to carry out R&D, new product development based on herbal items, drugs, speciality chemicals, cosmeceuticals and development of formulations in nutraceuticals. The company is also actively involved in claim substantiation at the laboratory level and in the cultivation of selected medicinal plants using tissue culture. At the core of this activity is Dr. Majeed's conviction that intellectual property developed will prove useful when the WTO regime comes to India in 2005.

Clinical trials on products developed by the group is conducted at ClinWorld P. Ltd., while Organica Aromatics

(Bangalore) P. Ltd. is involved in the manufacturing and marketing of aroma chemicals and Anju Phytochemicals P. Ltd. manufactures and trades in herbal raw materials and products in India and overseas. The most recent addition is Johara Cosmetics, which has recently introduced a range of premium, bio-standardised cosmetic products with therapeutic value (cosmeceuticals), based on proven ingredients introduced by Sami Labs.

In the US, Sabinsa Corporation (Piscatawny, NY) is involved in market development, distribution and warehousing. A state-of-art R&D Centre (Princeton, NJ) is focused on development of processes for manufacture of new molecules, and in the last two years, has developed technologies for Q10 intermediates, methyl selenocysteine, and eflornithine (an orphan drug

for African Sleeping Sickness) by a new process that enables the drug to be produced and made available to the WHO at 1/3-1/4th of its current price.

Sabinsa Utah (Payson, UT) is involved in marketing, distribution, warehousing and part manufacturing; while America's Finest Inc. (AFI), manufactures and markets a range of nutraceuticals. The more recently set-up, Sabinsa Japan Corporation is focused on marketing into this finicky market.

The efforts of the group have been recognized by the Government of India and the Spices Board (Kerala):

- In 1994, it received a National Award for Quality Products (Basic Drugs) from Ministry of Industry, Government of India;
- In 1994-95, the Spices Board, Ministry of Commerce, Govt. of India, recognised the efforts of the company in developing the markets for a new product, Garcinia, with a National Award. Again, in 1999-00, the Board recognized the group as the 'Topmost exporter of value added spices from India'; the 'Topmost exporter of newly developed value added spice products', and for 'Outstanding Performance in the export of spices and spice products.'



Sami Labs' SCFE Unit in the outskirts of Bangalore

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A view of the R&D lab at Bangalore

- In 1995-96, it received a 'Certificate of Merit' for outstanding export performance for spice products, fine chemicals, extracts and oleoresins, and vegetable extracts from the Ministry of Commerce;
- In 2002, it received the 'National Award for R & D Efforts in the Industry' in the category of 'Chemicals & Allied Industries' from Department of Scientific & Industrial Research (DSIR), New Delhi.

Formulations Division enters Indian market

Sami Labs has recently launched a new formulations division at Peenya (near Bangalore), to cater to the needs of the emerging Indian markets. The division, in partnership with American

Formulary Inc, USA, has already rolled out a significant portfolio of nutritional products aimed at providing therapeutic, prevention and adjunctive support towards cardiac ailments, diabetes, BPH, hepatic dysfunction, post menopausal symptoms, etc.

The products are being marketed under the 'Care' brand name and although they have been launched more than a year ago, Ms. **Neerja Shetty**, CEO, Formulations Business, believes that the business has now achieved a critical mass in terms of the range of products and the size of business.

The products will initially be marketed in seven states – Madhya Pradesh, Chattisgarh, Maharashtra, Andhra



HepatoCare™



Co.Q.Care™

Pradesh, Karnataka, Tamil Nadu and Kerala – as a prelude to a nationwide launch. "While the general awareness of nutritional products in India is low, we believe that they could account for as much as 8-10% of the pharmaceuticals market," Ms. Shetty told *Chemical Weekly*, during the course of a telephonic interview.

By April next, five more new nutraceuticals would be added to the range of products, along with a foray into herbal cosmeceuticals, Ms Shetty said.

Nutraceuticals & Functional Foods: A Primer

Nutraceuticals are products isolated or purified from plants or other foods that are sold in dosage form not associated with food, in order to provide a physiological benefit and/or protection against chronic disease.

Nutraceuticals are frequently referred to as 'dietary supplements' or 'nutritional supplements', i.e., products that: "Contain 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."

As such, nutraceuticals occupy a middle ground between drugs on the one hand, and so-called functional foods on the other. It is true that nutraceutical sales overlap or cannibalize sales to the drug and functional

foods segments. An estimated 10% of all nutraceutical sales (principally herbals) replace sales of therapeutic drugs as consumers attempt to self-medicate themselves. Similarly, an estimated 5% of all nutraceutical sales (principally fitness/sports supplements) take the place of functional foods such as sports drinks. However, while they may overlap the drug and whole foods markets in certain segments, nutraceuticals are a distinct market in themselves.

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Nutraceuticals are essentially prophylactic or preventive, in contrast to drugs, which are active chemical substances used to treat an illness or symptoms of an illness. They represent a different approach to medicine, one based on nutrition and the health or wellness of the whole body, rather than treating the symptoms or effects of disease. While nutraceuticals may compete with or cannibalize the sales of certain types of drugs (particularly over-the-counter drugs), they form a distinct market.

Historically, there has been some tendency to group nutraceuticals together with functional foods. Today, however, the tendency is to treat nutraceuticals and functional foods as separate markets. While certain nutraceuticals (e.g., broccoli extract) are whole-food extracts, nutraceuticals and functional foods are essentially different types of products. Functional foods may contain nutraceuticals, but they are complete foods similar in form to other, conventional foods, with which they compete in the marketplace. Nutraceuticals are isolated and consumed in medicinal form.

The Global Market for Nutraceuticals

Worldwide demand for nutraceutical chemicals will increase 6.2% annually through 2006 to \$8.6 billion, supplying a \$155 billion nutritional products industry. Herbal and non-herbal extracts will provide the strongest growth opportunities as constraints on healthcare availability and pharmaceutical expenditures in most economies promote the widening use of alternative medicines.

Ginkgo biloba for enhanced cognitive properties, ginseng for energy boosting and saw palmetto for benign prostatic hyperplasia will generate the fastest sales gains among herbal extracts. Glucosamine (in combination with chondroitin) will lead demand growth in non-herbal extracts based on proven benefits in arthritis manage-

ment. Nutraceuticals are also subject to a different regulatory regime than functional foods in many countries and are distributed through distinct channels. As described above, the U.S. Dietary Supplement and Health Education Act of 1994 contains an explicit definition of dietary supplements, but there is no equivalent legal definition of functional foods in the United States.

In the US, functional foods are treated the same as conventional foods from a regulatory standpoint. This does not mean that functional foods are not regulated, but they are regulated within a different framework than dietary supplements.

Nutraceuticals are distributed through variety of specialized channels, including drug stores, health food outlets, and the Internet, as well as grocery stores and supermarkets. Functional foods by and large are distributed through the same channels as conventional foods. Indeed, functional foods manufacturers can be regarded as an alternative distribution channel for nutraceuticals.

In general, the world market for herbal and non-herbal extracts will derive most upward momentum from new applications in high value-added combination products sold in the US and other prosperous economies.

Nutrients, food additives also robust

Nutrients and functional food additives will generate above average growth in world demand, spurred by new product introductions, broadening end-use applications, greater pricing flexibility and an increasing number of health conscious consumers, especially in the developed countries. Soy and fibre compounds for liquid meal substitutes, energy-boosting shakes, sports beverages and fortified foods will realize the fastest sales gains among nutri-

ents based on trends toward healthier dietary practices.

Spurred by widespread evidence of health benefits, lycopene, polyunsaturated fatty acids, probiotics and tocotrienols will account for the strongest growth opportunities among functional food additives.

Slow growth in vitamins & minerals

Minerals and vitamins will generate comparatively slow growth in worldwide nutraceutical applications due to fierce pricing competition, the overall lack of proprietary compounds and mature product applications. Vitamins A and E will fare the best among bulk vitamins due to increasing evidence of health advantages and expanding end-user preferences for value-added natural formulations. Calcium and potassium will see the fastest sales gains among minerals based on proven preventive benefits in geriatric and women's health care.

Herbal extracts and functional food additives to lead gains

Herbal extracts will continue to fare well in the global marketplace based on the increasing use of alternative medicine to offset health-care shortages in virtually all countries. Compounds indicated for cholesterol and blood pressure reduction (garlic), enhanced physical and mental stimulation (gingko biloba and ginseng), immune system stimulation (Echinacea and golden-seal), depression (St. John's Wort) and benign prostate problems (saw palmetto) will continue to generate the largest share of demand, spurred by evolving morbidity patterns — especially in developed countries.

New product introductions and stepped-up efforts by food and beverage makers to introduce higher value-added goods, with greater pricing flexibility, will create a rapidly growing world market for functional-food additives, especially ingredients offering

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preventive medicine benefits. Less favourably, stricter government regulations in many countries will moderate demand for herbal extracts and functional-food additives by limiting end-use applications for compounds lacking clinical proof of effectiveness.

Developing regions to grow the fastest

Through 2006, Asia/Pacific, Latin America and Africa/Mideast will provide the fastest growth opportunities for nutraceutical chemicals, reflecting rising consumer income levels, increasing investment in both bulk and end-use product industries, and expanding per capita consumption of nutritional and herbal products. China will see the most impressive gains in nutraceutical consumption and production levels based on rising economic prosperity.

China has already evolved into one of the leading worldwide exporters of bulk vitamins and herbal extracts. Brazil, India, Pakistan, and Taiwan are among other developing countries expected to achieve a significant penetration into the nutraceuticals field.

The US, Japan and major West European countries will remain the largest global producers and consumers of nutraceutical chemicals due to high consumer income levels, widespread preferences for specialty nutritional and herbal products, and trends promoting preventive medicine and self-treatment.

The European Markets for Herbal Extracts: Germany leads the way

The European market for herbal medicine has been estimated to be worth \$5.6 billion; it continues to grow, offering opportunities for investment and high returns on capital. The German market is the largest with 10% of pharmaceutical sales being natural remedies. The French market is the second largest, with both countries experiencing positive attitudes towards herbal medicine by the medical profession,

government and pharmacies. In Germany, a large proportion of herbs are sold on prescription.

Sales through health food stores are predominant compared to other outlets like supermarkets and drug discount stores, although in the more developed markets of France and Germany, most herbal sales are through pharmacies. New legislation in France actually restricts the sale of licensed herbal products to pharmacies. Generally though, European countries allow herbal remedies to be sold only in places that provide some kind of advisory service to consumers.

Some countries like Germany and France have created a system of monographs that establish a plant's safety and efficacy. Manufacturers only have to provide proof of a product's quality. Products containing herbs not covered by existing monographs require clinical and toxicological support as vigorous as drug approval in the USA. Interestingly, the UK is not producing any monographs and the British herbal market has been restricted by negative attitudes of the medical profession, government and pharmacies. Their

herbal sales equal 2% of the UK's total pharmaceutical market.

The US markets for herbal extracts – a late entrant

The US market for herbal products is a relatively new market whose growth started in the 1960's with its roots in the alternative movement. Since then the industry has evolved from a fringe business to becoming a significant market sector, with the size of the business in excess of \$6 bn. Today, herbal products are used by nearly one-third of all Americans, which constitute a nearly 1 bn market for raw herbal and botanical products.

The business is regulated by the Dietary Supplement Health & Education Act (DSHEA), which was passed in 1994, resulting in significant changes in the FDA's regulatory authority over dietary supplements. In March 2003, the FDA proposed cGMP in manufacturing, packing, or holding dietary ingredients and dietary supplements and in subsequent discussion with industry, it has come to the view that dietary supplements are 'drug-like' and pharmacologically active, therefore drug GMP guidelines would apply.

The US Markets for Herbal Extracts

(\$ Million)

Product	1998	1999	2000	CARG 96-'00	CARG 01-'03
Ginkgo Biloba	294	287	290	-1%	-4%
St. John's Wort	303	232	235	-12%	-9%
Echinacea	207	208	211	1%	1%
Ginseng	213	185	187	-6%	-4%
Garlic	195	174	176	-5%	-4%
Saw Palmetto	104	113	114	5%	3%
Kava Kava	43	68	69	27%	-1%
Valerian	41	56	57	18%	8%
Aloe	46	52	53	7%	4%
Soy	NA	19	41	115%	50%
Cranberry	41	48	49	9%	5%
Goldenseal	57	42	43	-13%	-8%
Multi Herb Combos	1,800	1740	1,761	-1%	5%
Others*	636	866	866	17%	12%
Total	\$3,980	\$6,089	\$6,152	2%	4%

Others include green tea, yohimbe, milk thistle, black cohosh

Source: Nutrition Business Journal, Health Business Partners Consulting