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Herbal therapeutics: Scope and Perspectives

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Currently, a resurgence of interest in herbal medicines has resulted from the preference of many consumers for products of natural origin in developed countries too along with developing countries. The potential benefits of herbal medicines could lie in their high acceptance by patients, efficacy, relative safety, and relatively low cost. Patients worldwide seem to have adopted herbal medicines in a major way. The current and future market estimates bear testimony to the increasing interest in herbal products. Given below are few market facts.

Global market scenario

Global nutraceuticals' market, comprising of two principal segments – Dietary Supplements and Functional Foods as measured by sales was projected to reach US$ 199,672 million by 2010 as against an estimated US$ 133,661 million for 2004 (Nutraceuticals Global Business Report, 2004)

Sales for this segment in US are expected to witness continued growth and reach US$65,628 million by 2010, registering a compounded annual growth rate of 6.82% during 2000-2010. Following US, Europe and Japan are the next largest markets for' nutraceuticals.

Herbals, account for largest share in the worldwide dietary supplements market, with sales estimated at US$17,125 million for 2004. USA is the largest herbals market with sales estimated at US$4,815 million for 2004, and is projected to retain its dominance in herbals markets through 2010.

Market for Herbal dietary supplements in US is projected to reach US$23,122 million by 2010 registering a CAGR of 4.84% during 2000-2010 (Nutraceuticals Global Business Report 2004),

Indian market scenario

Market comprising of Ayurvedic, Unani, Siddha & Homoeopathic medicine is around US $ 1.5 billion Rs 7000 Crore of which the approximate share of Ayurvedic formulations is 84%, Homeopathy 14%, Unani 2% and Siddha less than 1%.

Motivation for use of herbal medicine

Factors driving the growth of herbal medicine market are:

1. Increase in consumer interest in herbals
2. Increased awareness about the health
3. Rising herbal care costs
4. Ageing population

Ernst *et al* (2002) have summarized the positive and negative motivations for use of herbal medicines as below:

Positive Motivations	Negative Motivations
Perceived effectiveness Perceived safety Philosophical congruence: Zeitgeist; emphasis on holism; embracing all things natural Control over treatment Accessibility Affluence	Rejection of science and technology Rejection of the establishment Desperation Dissatisfaction with (some aspects of) pharmacology: ineffective for certain conditions, serious adverse effects

Some of the success stories from plant sources:

Natural products have played a dominant role in the field of development of drugs. Newman *et al* have analyzed the origin of new drugs between 1981-2002 and have come to a conclusion that almost 60% of the new drugs have their origin from natural products. This paper has quoted a commentary by Danishefsky, which is reproduced below as such:

"Thus, the decision on the part of several pharma companies to get out of the natural products business is gross foolishness. There are major teachings in these natural products that we would do well to consider. They may be reflecting eons of wisdom and refinement. The much maligned natural products collections, did, after all, bring us to statin, -lactam, aminoglycoside, and macrolide blockbuster drugs. In fact, one of the most promising approaches in diversity chemistry is to produce diversity-chemistry-derived collections that benefit from or partake of the 'wisdom' of natural products".

Artemisinin for resistant Malaria recommended by WHO, Tamifulu for Bird flu which is prepared from Shikimic acid, a plant derived raw material, besides several anti cancer drugs like Paclitaxel from *Taxus baccata* and Topotecan from *Mappia foetida* are few of the success stories.

Recent major R&D initiatives on Herbal medicines

1. New Millennium Indian Technology Leadership Initiative (NMITLI)

This shceme of the Council of Scientific and Industrial Research (CSIR) has the following objective:

"To catalyze innovation centered scientific and technological developments as a vehicle to attain for Indian industry a global leadership position, in selected niche areas in a true 'Team India' spirit, by synergizing the best competencies of publicly funded R&D institutions, academia and private industry".

In this unique initiative, CSIR is having the projects to develop herbal products backed with standardization, safety and efficacy data in the following therapeutic areas.

1. Diabetes
2. Osteoarthritis
3. Rasayana – products to prevent degenerative disorders

2. Golden Triangle Partnership programme

In the year 2005, Council of Scientific and Industrial Research (CSIR), Indian Council of Medical Research (ICMR), and Dept. of AYUSH, Ministry of Health & Family Welfare, Govt. of India, joined hands for a novel national endeavour to develop evidence based herbal products in the following therapeutic areas with an allocation of Rs.120 crores for a period of 5 years.

1. Sleep disorder
2. Joint disorders
3. Cardio Vascular Disorders
4. Irritable Bowel Syndrome
5. Memory disorder
6. Malaria/Filaria/Lieshmaniasis
7. Diabetes
8. Fertility & Infertility
9. Bronchial asthma
10. Menopausal Syndrome
11. Vision disorders
12. Rasayana (Rejuvenators/immunomodulators)

3. Indian Council of Medical Research (ICMR)

ICMR has taken up several projects both by extending financial support and on its own in various therapeutic areas. Examples of some such directly taken up projects are:

1. Kshar sutra for Fistula-in-ano,
2. Clinical Trials on Guggul lipid
3. Clinical Trials on Vijaysar for diabetes.

4. CSIR Labs

Several CSIR labs are involved in conducting state of the art research on herbal medicines. Notable among them are Central Drug Research Institute, Lucknow, with success story like guggul lipid, Central Institute of Medicinal and Aromatic Plants (CIMAP), Lucknow, National Botanical Research Institute, Lucknow and Regional Research Laboratory, Jammu with success story like Boswellia serrata for Osteoarthritis.

5. Department of Biotechnology

DBT has funded several projects to conduct studies on research on herbals. The out come of these projects in form of products will be visible only after few years.

6. Department of Science and Technology

DST has set aside a corpus of Rs.150 crores for funding the pharmaceutical industries through private/public partnership projects. Under this scheme, research projects of several herbal manufacturing companies have been funded through this project. One of such projects was on sourcing of fermentation on *Asav arishta.* At the end of the project, one single strain could be availed from *Woodfordia fruticosa* flower as a source of fermentation material.

7. TIFAC

TIFAC has funded several research projects on herbal medicines in India. They are also helping the small entrepreneurs to sell their products to the buyers.

8. Dept of AYUSH, Ministry of Health & Family Welfare, Govt. of India

AYUSH is a nodal agency for all the coordinating works such as education, research and health care through Indian Systems of Medicine, Ayurveda, Homeopathy, Naturopathy, Siddha and Yoga. This dept funds several extramural projects besides having a research council called Central Council for Research in Ayurveda and Siddha, dedicated to research in Ayurveda, through its several labs.

In order to lay down standards on medicinal plants, Dept of AYUSH have prepared and published 7 volumes of Ayurvedic Pharmacopoeia of India on medicinal plants till date.

<u>Status of research on Herbal medicines in India</u>

Despite having very rich systems of medicines like Ayurveda, India as a country could not put the desired level of contemporary science behind its products. As a result, we had to face criticism at several international fora like Lord Walton's committee in UK, which refused to give full recognition to Ayurveda as system of medicine. However, it agreed to accept some of the single herbal products, where sufficient scientific data was available.

The status of research on Indian medicine can be gauged through the Clinical Trials conducted on its herbal/Ayurvedic products. Given below is the self explanatory broad analysis of 68 studies evaluated by the authors.

Number of Clinical Trials reviewed : 68		
S. No.	Trial Design	No of trials
1	Double blind placebo-controlled	7
2	Double blind comparative	3
3	Open comparative placebo-controlled	3
4	Single blind placebo-controlled	5
5	Open non-comparative	1
6	Randomized open	28
7	Open add-on	1
8	Flexi-dose open	1
9	Double blind cross-over	1
10	Open add-on comparative	1
11	Open comparative	13
12	Single blind reference controlled	4

Some of the single herbs studied for various indications are mentioned below:

Single drug studied for various indications		
S. No.	Disease entity	DrugName
1	Rheumatoid Arthritis	Raasna
2	Non-Insulin dependent Diabetes mellitus	Vijaysaar
3	Gastric ulceration	Yashtimadhu
4	Non-ulcer dyspepsia	Aamalaki
5	Stress	Ashwagandha
6	Bronchial Asthma	Pushkarmula
7	Urolithiasis	Varuna
8	Liver disorders	Katuka
9	Osteo-arthritis	Shallaki
10	Immunomodulation	Guduchi
12	Cognitive functions	Brahmi
13	Women cycle regulator	Ashoka
14	Cancer	Rohitaka
15	Malaria	Chirayata
16	Kala-azar	Shakhotak
17	Hypolipidemia	Guggulu
18	Ischaemic Heart Disease	Arjuna
19	Fistula-in-ano (Kshar Sutra)	Haridra + Snuhi

Yet it is a matter of pity that despite such a rich traditional information and experience available, we as a country have failed to come out with even a single herbal mega brand to the world.

Scientific susceptibility

Szapary *et al* (2003) in an article published in JAMA questioned the efficacy of guggulipid as lipid lowering product proved through several CTs conducted in India by the reputed agencies/institutions like Indian Council of Medical Research and All India Institute of Medical Science, New Delhi. Saper *et al* (2003) published an article in JAMA, highlighting the presence of heavy metals in 14 of the 70 Ayurvedic products tested by him from Boston market in US. This one single article provided an excuse to Canada and UK to ban these products. This shows the susceptibility of our Ayurvedic products/regulatory systems to the negative data generated abroad on the products showing positive results in India, besides the low level of consumer awareness in India.

Issues to be addressed to circumvent the situation are:

- Standardization
- Improving the quality of herbal medicine
- Generating all data to find out the mode of action
- Conducting internationally acceptable randomized controlled Clinical Trials

Future directions

Possible way forward to make us leaders in Herbals on the global arena is through state of the art contemporary research without any shortcuts. Some of the major recommendations for it are as below:

1. System biology approach

This appears to be the perfect way of validating the holistic approach of Ayurvedic products. This approach involves bioassay guided fractionation and then preparing their combinations to prove not only the efficacy of herbal medicine but also the mechanism of action.

2. Chemical marker to bioactive markers

For the purpose of standardization, we have to move from one to more than one chemical marker in the herbal products and in the next stage from pure chemical marker to biologically active marker. Biological activity guided fractionation with molecular target based screening is one way to achieve it.

3. Randomized controlled Clinical Trials

Randomized controlled Clinical Trials are the need of the hour. Extra care need to be taken while designing the protocols for Clinical Trials on herbal products. Basic Ayurvedic principles of treatment need due consideration during the process.

4. Quality improvement

Leadership through quality has to be our slogan if we have to become leader in herbal medicines in the world. Strict monitoring of implementation of GMP and some of the other existing laws are the need of the hour. Licensing conditions need to be more stringent as recommended by Dr. Mashelkar's committee also.

5. Herbal INDs

Indian industries should start filing herbal INDs with Drug Controller General of India backed with full scientific data. This will boost the confidence of conventional doctors on herbal medicines for at least medical unmet needs.

6. Botanical drugs for developed markets

Indian industry should gear up to file at least single digit applications with US FDA for botanical drugs. This will require moderate investments and high level of standardization, organic cultivation, quality maintenance, besides conducting safety and efficacy studies. But even if one or two good products click in US market, the financial rewards may add up to more than the total AYUSH products sales in the country in a year. However, this may take 5-7 years time, therefore it needs patience.

7. Forming consortium of industries

The investments in research in future are going to be drivers of growth globally. Keeping in view the size of the companies involved in herbal/Ayurvedic medicines, it may be difficult for them to provide the required financial inputs individually. Therefore, there is an urgent need for industry to come together to form a consortium and build a world class R&D centre to cater to the needs of all of them in their chosen therapeutic areas.

Conclusion

India has the potential for becoming a global leader in the field of herbal medicines. However, concerted national efforts are required in this direction without any shortcuts and emotional attachment. This is one of the areas, which if harnessed, nourished and cherished properly has the potential of becoming bigger than the IT industry. We need to be optimistic and to take all the desired steps to achieve it.

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