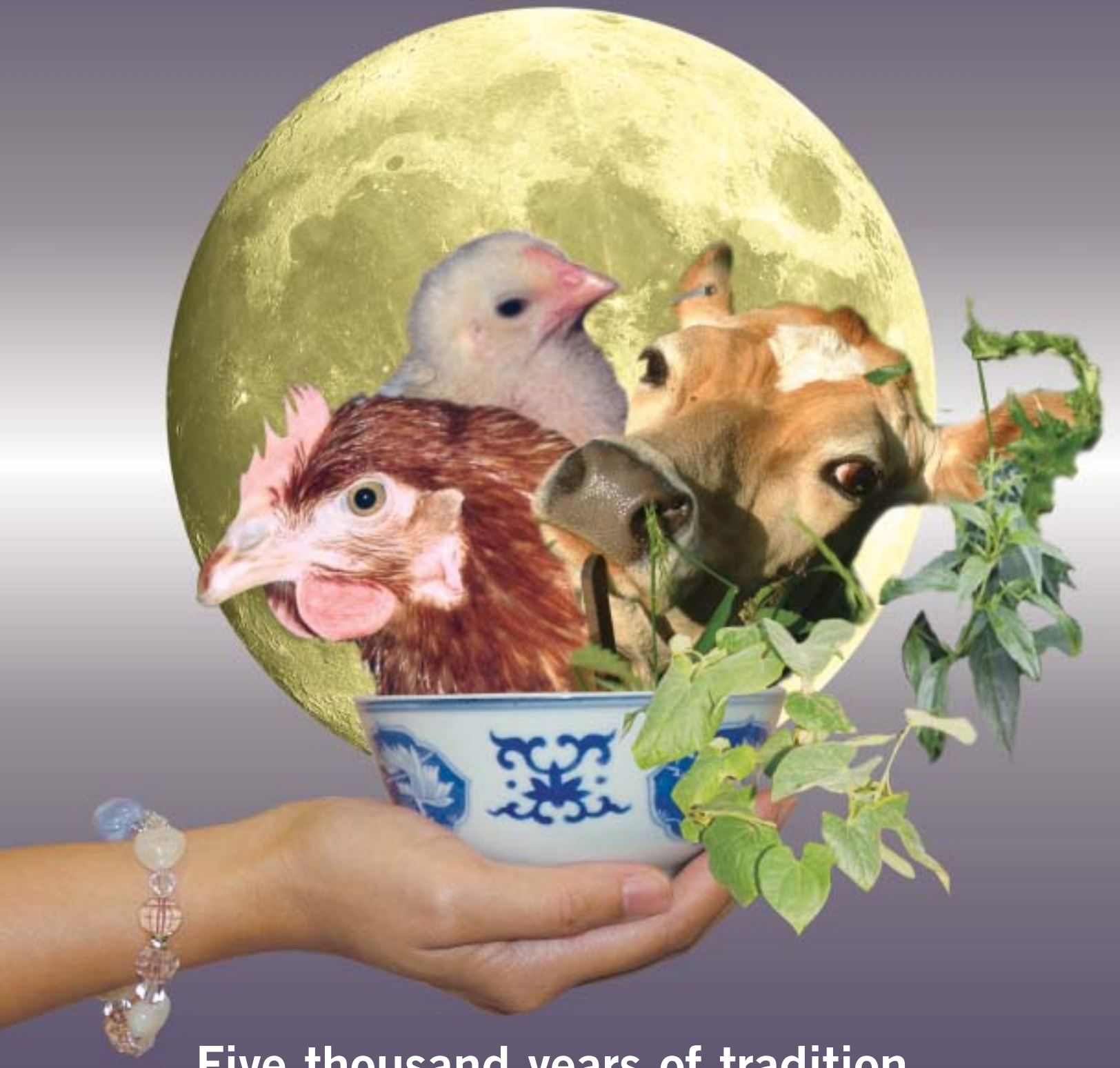
Herbal additives



Five thousand years of tradition

HUMANS AND ANIMALS WERE SATISFYING THEIR NUTRITIONAL AND MEDICINAL REQUIREMENTS FROM PLANTS LONG BEFORE THE APPEARANCE OF MODERN MEDICINE AND FEED ADDITIVES. ADAPTING THIS PRINCIPLE TO MODERN AGRICULTURE FORMS THE BASIS FOR R&D AT INDIAN HERBS' SPECIALIST CENTRE.

SARAH MELLOR **EXPLAINS HOW IT'S DONE.**

Synthetic processes for which a chemist requires enormously high degrees of heat and pressure are quietly carried out by nature in plant cells at ordinary atmospheric conditions. For example, it took chemists half a century's-worth of intensive work to synthesise alkaloids such as quinine, whereas the cinchona plant does this without difficulty every day. Many active antibiotics also occur naturally in plants, yet this is a relatively unexploited field.

Herbal preparations have been in use in India throughout the ages to improve the health and production of animals. During the Mahabharat war, for example (1000-900 BC), the book Nakul Samhita describes how the Pandav Princes Nakul and Sahdev used to treat thousands of wounded animals every day with herbs. In 700BC, Salihotra wrote Asva-Chikitsa in Sanskrit, dealing with equine husbandry and herbal medical care. Ayurveda (2500 B.C.) gives an account of the ancient medical science of India, which includes the use of herbs.

Modern medicine was believed to be able to solve almost all the health problems of humans and animals, but this began to change, with the `green wave', characterised by an increasing demand for natural products in the form of foods, drugs and cosmetics. Mainly triggered by side effects resulting from the increasing use of chemical products, reconsideration of their use was initiated by the WHO in the 1970s.

PLANT MEDICINES

Many herbs were in use long before they were introduced to modern medicine. From the 1970s to the 1990s, 25-30% of all drugs dispensed in the USA contained compounds of plant origin and their worldwide contribution was more than 48%. Today, 15% of the basic and essential 257 drugs (WHO) are of flowering plant origin. A more recent survey found that 477 out of 868 drug molecules discovered between 1981 and 2002 belonged to natural products. In 2000 alone, seven out of twenty best-selling non-protein drugs including statins, enalaprils, augmentin etc. were derived from natural products.

Research on the use of herbs for better health and production performance of animals is also gaining importance, because antibiotic growth promoters are being restricted due to bacterial resistance and other human health issues. In this context, the progress of one pioneer in naturally-sourced feed additives, Indian Herbs, located at Saharanpur in northern India is interesting. Established in 1951, the company owes its existence to the vision of one man, Ram Lal Agrawal. Already a renowned expert on the identification and therapeutic application of medicinal herbs and fascinated by the virtues of Ayurveda, he was inspired by a thought published in a journal on practical medicine *The Practitioner* in December 1950, that *"The lore of the countrymen is built upon the experience of generations, often of centuries and the data upon which it is based have often been obtained at a price in human lives which no modern research worker would ever dream of considering. It is particularly appropriate at the present moment, when pharmaceutical companies of the world are emitting an unceasing flow of new synthetic drugs, that attention should be turned to the possible remedies that may be found among indegenous herbs of this and other countries."* Ram Lal Agrawal's innate love of animals initiated a new thought in his inquisitive mind, "if this natural form of treatment is good for humans, why can it not be applied to animals?" Thus began his dedication to research on herbs and herbal products for animals and the foundation was laid for the first herbal research & development company, Indian Herbs, in 1951. Since then, scientists at Indian Herbs have investigated what their ancestors did 5000 years ago: searched, researched, scientifically developed, pharmacologically tested and clinically evaluated the herbal products according to modern scientific methodology using the latest technology.

Son of the company's founder, Sushil Agrawala is the current managing director. He was responsible for extending his father's vision into the realm of feed additives.

Suitable for organic farming

For organic farming, the IFOAM basic standards of 1998 do not allow the use of antibiotics, coccidiostats, synthetic growth promoters, appetisers, synthetic amino acids etc. in animal feeds. Vitamins and supplements are to be used from natural origin when available. Similarly, anti-oxidants, flavours and appetite stimulants are allowed from natural sources only. Therefore, the unique herbal vitamins, amino acids and animal feed additives of natural origin, developed by Indian Herbs are also suitable for organic farming.

The Society for Control and Certification of Quality Assurance in Cologne, Germany, an authorised EEC agency has evaluated many of the company's herbal feed supplements and found them suitable for organic farming (EEC, 2092/91).

"Nature's way to animal health"

"Nature's Way to Animal Health" gives true expression to the philosophy and vision of Indian Herbs. Its founder, Ram Lal Agrawal, envisaged the use of herbal products that can be prescribed by veterinarians or can be used by farmers. A new dimension was added by his son, Sushil Agrawala, the present managing director, by developing natural vitamins, natural amino-acid sources and many herbal feed supplements to promote animal health, growth, productivity and product quality- all based on research into herbs. Indian Herbs now provides a modern research base to the ancient knowledge of Ayurveda for animal health care. The company is now also engaged in the development of herbal human medicines and dietary supplements with the objective of "bridging the gaps in modern medicine", concentrating on therapies where modern medicine does not always provide satisfactory cures.

Quality control starts at source

Quality control at Indian Herbs starts with cultivation of herbs by sowing seeds of quality in nature at the right time, location and soil condition. R&D has developed cultivation packages for remunerative farming of herbs containing an optimum quantity of the desired active constituents. The Quality Assurance (QA) laboratory maintains a specimen and comprehensive database for each plant used by Indian Herbs. Each herb is authenticated by experts, using macroscopic and microscopic examination.

HOW HERBAL R&D WORKS

Research at Indian Herbs is generally focused in the following areas:

-> Selection of herbs.

After an initial selection of herbs based on a survey of traditional and modern literature, they are subjected to pharmacological screening to determine their biological activities. The herbs exhibiting potent biological activity are further subjected to toxicological studies (LD_{50}, acute, sub-acute, chronic, teratological toxicity etc.). The herbs showing both potent biological activity with a high safety profile are selected for further research.

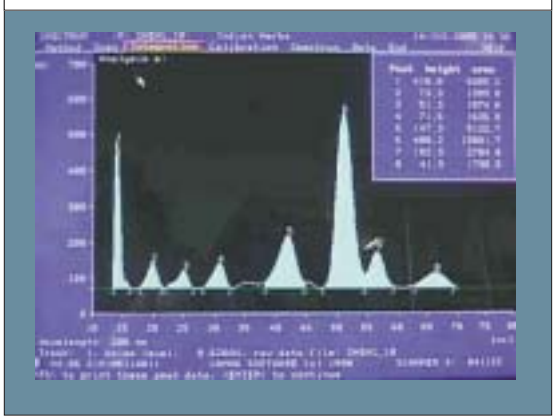
-> Dose determination.

Keeping in mind the dose range of herbs in the traditional literature, the optimum therapeutic dose is established from a dose-response curve generated by classical pharmacological techniques and further confirmed in clinical trials. In the case of extracts, the dose is calculated on the basis of the extractive value of the particular extract.

-> Identification and quantification of active substances.

The bioactive principles of herbs are identified by a bioactivity guided fractionation assay. The herb is successively extracted with solvents of increasing polarity and the different solvent extractives are subjected to biological screening. After further fractionation to separate the individual chemical constituents using chromatoraphic and molecular sieving, the isolated individual chemical constituents are subjected to biological screening to identify the biomarker(s) of each herb. The structure of the biomarker is established by studying the physical and chemical properties and using NMR, IR, mass spectroscopy, UV-spectrometry etc. By quantifying each of the biomarker fractions by chromatography, a chemical fingerprint is obtained for each fraction (*Figure 1*). The Rf value of each chromatoband generated for each active principle is compared with the standard reference chromatogram, to quantify and standardise the active principles in each herb, forming the basis for standardisation of herbs and herbal formulations. The biomarker(s) in the individual herbs or their extracts are then quantified, and a specification limit assigned, taking into account the results of locational and seasonal variation studies.

FIGURE 1 – HPTLC FINGERPRINT OF A HERBAL FORMULATION



-> Product formulation.

The selected bioactive and safe herbs or extracts are formulated into a suitable dosage form such as powders, liquids, tablets, capsules, ointments etc. and are subjected to clinical trials to validate their efficacy and safety. Generally where a single herb can not fully serve the purpose, synergistically active herbs are selected for development of a formulation. For example, to develop a product for better production performance of animals, by improving the utilisation and metabolism of nutrients, suitable herbs were identified which improve appetite, digestion and metabolism of nutrients, liver function and paracrine (digestive enzyme) secretion etc.

OUTSTANDING ACHIEVEMENTS

The government of India granted recognition and formal certification to the company's R&D Centre in 1986 and it is also accredited for research on indigenous systems of medicine. GMP certification (Govt. of India) and ISO 9001:2000 certification (DNV, The Netherlands) for research, manufacturing and customer care outline the quality management systems and international standards followed at Indian Herbs. Indian Herbs is the only company from the herbal animal health care sector in the Top 50 biotechnology led enterprises of India (BioSpectrum, September, 2003).

A dynamic team of scientists which include botanists, chemists, pharmacists, microbiologists, pharmacologists and veterinarians is engaged in continuous research in the R&D centre's various departments, such as pharmacognosy, pharmacology, phytochemistry, microbiology, formulation development, quality control, literature survey, the animal house and veterinary services; all well equipped with state-of-the-art analytical equipment. Extensive research studies have been conducted on Indian Herbs products at veterinary universities, farms and feed mills etc. in the UK, Italy, Austria, Spain, Denmark, Bulgaria, the Czech Republic, Taiwan, Korea, Malaysia, Bangladesh, Nigeria, South Africa etc. besides India. So far, more than 150 scientists have been awarded Post-graduate and Doctrate degrees for outstanding research on Indian Herbs products and over 600 research papers have been published in scientific journals.

Curcuma longa | Eucalyptus spp. | Adhatoda vasica | Withania somnifera | Tinospora cordifolia | Andrographis paniculata | Boerhaavia diffusa

TABLE 1 – THE MAIN ACTIVE CONSTITUENTS, PHARMACOLOGICAL ACTIONS AND FEATURES OF SOME COMMONLY USED HERBS

Name of herb	Main active constituent	Pharmacological action(s)	Features
Curcuma longa	Curcumin	Anti-microbial, anti-inflammatory	Controls inflammation and infections
Eucalyptus spp.	1,8-cineole	Anti-microbial	Controls respiratory infections
Adhatoda vasica	Vasicine	Anti-tussive, Expectorant, Mucolytic	Relieves coughs and congestion
Withania somnifera	Withanolides	Antistress, adaptogen	Overcomes stress and improves production performance under stress conditions
Tinospora cordifolia	Tinosporine	Immune modulator	Improves immune competence to fight against infections
Andrographis paniculata	Andrographolide	Hepatoprotective, Choleretic	Optimises liver function
Boerhaavia diffusa	Boerhavinone	Diuretic, Hypouricaemic	Flushes kidney and helps excretion of excess uric acid