



Department of Biotechnology

Ministry of Science & Technology

Government of India

Pro-people Products Developed/New Initiatives taken by the Department of Biotechnology

- **Dispersible Zinc tablets**
- **Rotaviral Diarrhoea Vaccine**
- **Early Maturing Quality protein Maize hybrid**
- **Quality Planting Material of Bamboo**
- **Mycorrhiza – a Broad Spectrum Biofertilizer**
- **Biopesticides – Bollcure and Bioprahar**
- **Rural Bioresource Complexes**
- **Large Cardamom productivity improvement**
- **Patchouli- a New Aroma of Hope for Farmers**
- **An Oral, Live, Recombinant Non-residual Cholera Candidate Vaccine**

Dispersible Zinc Tablets

Introduction

More than 1.5 million children under five continue to die each year as a result of acute diarrhoea. In India alone, more than 1,50,000 deaths occur annually due to childhood diarrhoea. The use of zinc along with oral rehydration therapy (ORT) is recommended by WHO to decrease the incidence and severity of diarrhoea.

Recommendations

Provide children with 20 mg of elemental zinc supplementation per day for 10 - 14 days (10 mg per day for infants less than six months of age)

The Product

In order to ensure that these recommendations become effective, it is essential that the industry be encouraged to prepare zinc formulations which contain only zinc as active ingredient. The product should be formulated in a way so as to mask the strong metallic after taste of zinc to enhance the acceptability to children.

BIBZinC-20mg (Dispersible Zinc Sulphate Tablet, USP)

The dispersible zinc tablet, BIBZinc-20mg contains 20 mg of elemental zinc as active ingredient, sweetener and taste masker (Vanilla flavor) and is scored tablet. The product is in line with the recommendations of WHO. The product is produced with technology transfer from Nutriset (French Company) through Department of Biotechnology, Ministry of Science and Technology, Government of India. The Nutriset product has been tested in Indian population and clinical trials have evaluated the efficacy of zinc supplementation and safety.

Tablets vs. Syrups

Zinc solutions are less stable than solid dosage forms and its exact dosage intake becomes difficult to measure in practical life. Therefore, the tablets are preferable. The dispersibility makes it easy for a child to consume the product. The sweetener and taste masking further enhance the acceptability by children. Solid dosage forms have advantage over solutions as it is easy in handling, distribution and storage and relatively cheaper.

Position of Bharat Immunologicals & Biological Corporation Limited (BIBCOL)

BIBCOL a Public Sector Undertaking of DBT, is ready with tablet manufacturing facility and the company has a production capacity of 240 million tablets per annum and will soon come with commercial production. BIBCOL is aiming for standard quality product at lowly price for mass consumption.

Product Safety Issues

To date there has been no reported severe adverse reaction from any form of zinc supplementation for the treatment of diarrhoea. In trial, zinc doses have ranged from 5 to 45 mg per day and have been well tolerated in diverse settings. The human body has efficient homeostatic mechanisms that regulate the absorption and retention of zinc, which decreases the likelihood of toxic build up and adverse effects in the body.

National & International Scenario

1. In May 2004, a WHO/UNICEF joint statement on the clinical management of acute diarrhoea was issued. This statement called for the adoption of new recommendation for zinc supplementation together with a new ORS formula for the clinical management of diarrhoea.
2. Zinc sulphate included in the WHO model list of essential medicine in March 2005.
3. US Pharmacopeia has defined the quality aspects of zinc tablets.
4. In March 2007, Govt. of India has adopted the inclusion of zinc in RCH 2 / NRHM for treatment of diarrhoea. The recommendation is use of 20 mg. of zinc sulphate dispersible tablets for use in child hood diarrhoea for 14 days along with addition of ORS.

Rotaviral Diarrhoea Vaccine

Rotavirus infections are the leading cause of diarrhoea-associated mortality in developing countries. It is estimated that globally rotavirus accounts for 352,000 – 592,000 deaths annually and nearly 150,000 deaths per year in India.

- The World Health Organisation and the Global Initiative for Vaccines and Immunization – have made the accelerated development and introduction of rotavirus vaccine a priority.
- The DBT is supporting the rotaviral diarrhoea vaccine development project since nineties under Indo-US Vaccine Action Programme (VAP).
- *Partner Institutions / Industry*
 - All India Institute of Medical Sciences New Delhi
 - Centre for Disease Control and Prevention, Atlanta
 - Indian Institute of Sciences, Bangalore
 - Stanford University, USA.
 - Society for Applied Studies, New Delhi
 - M/s Bharat Biotech International Limited, Hyderabad
 - National Institute of Immunology, New Delhi
- Two candidate vaccines 116E and 1321 have been developed.

cGMP Production

- A live attenuated rotavirus vaccine (116E) manufactured by M/s Bharat Biotech International Limited, Hyderabad under GMP conditions.
- The first rotaviral diarrhoea vaccine (116E) specific to India completed phase-II human clinical trial in India. The vaccine induced immune response was reported in ~90% of recipients of 116E vaccine candidate in phase-II clinical trial. No serious adverse events have been reported in the trial.
- The Phase-III trials are being planned.

Early Maturing Quality Protein Maize Hybrid

Maize is one of the major sources of calorie and protein. However, it is deficient in essential amino acids viz., lysine and tryptophan. Quality protein maize (QPM) with *opaque-2* gene along with associated modifiers contains twice as much lysine and tryptophan, essential amino acids and 30% less leucine than the normal maize. The reduced level of zein further improves the nutritional quality of the QPM. In India, absence of commercial QPM hybrids in the market is singularly responsible for the poor spread of this nutritionally balanced maize. Although, there are few hybrids available but all of them are late maturing; thus, they do not fit in the cropping sequence of the hills where short duration hybrids are required. Hence, DBT undertook a project through Vivekanand Parvatiya Krishi Anusandhan Sansthan(VPKAS), Almora to convert the existing early maturing inbreds to QPM inbreds for developing early maturing QPM hybrids.

Vivek Hybrid 9 is one of the best maize hybrids developed by VPKAS and was released for commercial cultivation in many states. Under the project, the conversion was undertaken for the parents of Vivek Hybrid 9 viz., CM 212 and CM 145 into QPM versions using 'Molecular Marker Assisted Selection'. The QPM version these inbreds showed 9-12% superiority in grain yield over the normal inbred versions. The reconstituted QPM hybrid (Vivek QPM 9) yielded at par with Vivek Maize Hybrid 9 in the Himalayan states (58 q/ha) as well as in Peninsular India (54 q/ha) under the **All India Coordinated Maize Improvement Project** during 2005 and 2007. Based on its performance, the hybrid has recently been released for commercial cultivation in the Himalayan states as well as Peninsular India. The new hybrid, Vivek QPM 9 possesses all the good quality of Vivek Hybrid 9 with added advantages of 30% higher lysine and 44% more tryptophan. Better quality of protein in QPM is expected to help in reducing protein malnutrition among rural masses.



Vivek Maize Hybrid 9
and Vivek QPM 9

Vivek Hybrid-9

QPM version of
Vivek Hybrid-9

Quality Planting Material of Bamboo

Recognizing the potential of Bamboo and its contributions to the economic trade of our country, a National Mission on Bamboo Technology and Trade Development was launched by the Planning Commission. To meet the envisaged targets of production, it is essential to increase the area of plantation through production and plantation of quality planting material.

- Tissue culture offers enormous potential in producing large quantities of the desired material in a short time frame. However, it is essential that enough care is taken in selection of the initial material, production of the plants, nursery development and field plantation.
- The Department of Biotechnology is coordinating a Programme on “Large Scale Production and demonstration of Quality Planting Material of Bamboo”. Under this programme 9 species are being produced and demonstrated on large scale- *Dendrocalamus strictus*, *Dendrocalamus asper*, *Bambusa bambos*, *Pseudoxytanthera stocksii*, *Bambusa Balcooa*, *Bambusa nutans*, *Bambusa tulda*, *Dendrocalamus hamiltonii* and *Gauda angustifolia*. Under the network programme 11 states (Andhra Pradesh/Karnataka, Tamil Nadu, Gujarat, Himachal Pradesh, Uttaranchal, Kerala, Rajasthan, Haryana, Goa and Madhya Pradesh) have been covered and all the 7 states of North East. So far nearly 821 ha has been covered with tissue culture planting material of the identified 9 species.
- This is the first plantation of tissue culture plants on such a large scale. The tissue culture industry has also shown keen interest to multiply the material. For this the technologies developed at R&D Institutes have been transferred to the industry. In addition, research groups are also working on perfecting the protocols for other species of importance.
- A special initiative was taken by the department for formulation of operational guidelines for producing quality planting material, standards for production of quality planting material through tissue culture have been developed, which include virus indexing and quality certification with specific reference to genetic fidelity.

Quality Planting Material of Bamboo

The technologies perfected under this programme would be useful for large scale adoption in different agroclimatic zones of the country.

- The germplasm which is being collected from different parts of the country is being conserved and characterized using molecular marker at two centers, TERI, New Delhi and IHBT, Palampur. This would provide useful information with reference to traits of specific interest



**Tissue Culture raised
Bamboo Plants**



Mycorrhiza - a New Generation Broad Spectrum Biofertilizer

This biofertilizer organism is a broad-spectrum non-specific organism which colonizes 85% of land plants. This biofertilizer has a broad ecological adaptability. It offers up to 50% of reduction in Phosphate fertilizer application and also provides better uptake of nutrients like phosphorus and many immobile trace elements like Zn, Co, Mn, Fe, Cu, Mo etc and hence provide better nutrition to plants. It offers tolerance to a range of soil stresses like heavy metal toxicity, salinity, drought and high soil temperatures and also provide high resistance to various soil and root -borne pathogens. Its helps in improving soil health productivity.



Application of Mycorrhiza Biofertilizer - a field demonstration

The DBT-TERI mass production technology for Mycorrhiza already transferred to following the industries:

Cadilla Pharmaceuticals Ltd.	--	500 tonnes per year
Majestic Agronomics (P) Ltd.	--	1000 tonnes
Neesa Agritech Pvt. Ltd. Ahmedabad	--	500 tonnes
Cosme Pharma Lab. Ltd. Goa	--	750 tonnes
KCP Sugar and Industries Corp. Ltd AP	--	750 tonnes
		<hr/>
		3500 tonnes

Biopesticides

(i) Bollcure - a new Botanical Pesticide

The Department of Biotechnology through The Energy and Resources Institute (TERI), New Delhi has developed plant extract based biopesticide formulation '**Bollcure**' extracted from eucalyptus plants. The formulation is effective against cotton bollworm (*Helicoverpa armigera*). It effects the growth of the bollworm larva resulting in reduction of larval weight. The larva does not reach the crucial late instar, which, actually is responsible for the crop damage. Thus, the formulation restricts the population to early instar, resulting in ultimate death of the larva in early instar itself, thereby, preventing the crop damage.

Salient features of the formulation are

- Effective against *Helicoverpa armigera*
- Significant reduction in larval weight (88%)
- Mild antifeedancy
- Suitable for both organic and IPM crop practices
- Suitable for conventional as well as Bt cotton
- Cost benefit ratio for cotton 1:4.15
- Cost benefit ratio for chickpea 1:17.1
- Environment friendly
- Multi-locational trials conducted at four ICAR centers for Bollcure against cotton and chickpea have proved it to be an effective biopesticide.
- Toxicity tests proved it safe for mammals with LD50 > 2000/5000 mg/kg.



Effect of Bollcure on growth of *Helicoverpa armigera* larva

Bollcure - A User Friendly Formulation with High Shelf life.

- Type of Formulation: Liquid Emulsifiable Concentrate (EC)
- Mode of Application: Spray
- Dose: 1L/Acre
- Frequency of Application: 2-3 sprays required each after 7-10 day interval
- Shelf Life: 1 Year
- Eco-friendly

Present status and time frame for commercialization of technology

Technology for the production of Bollcure has been transferred to Sri Biotech Laboratories India Pvt. Ltd., Hyderabad and Pasura Biotech Pvt. Ltd., Hyderabad.

(ii) Bioprahar

- "Bioprahar", a microbe-based biopesticidal formulation has been developed by ICGEB, New Delhi. The formulation is effective in controlling diamond-back moth in cabbage and cauliflower; white woolly aphids in sugarcane; mealy bugs in grapes, citrus and mango; and white ants in teak plantations.
- After several unsuccessful attempts, an effective formulation comprising the bacterium, surfactants and adjuvant was arrived at. Its shelf life is over a year with no drop in the potency or efficacy of the formulation. The product has been commercialized in India.

Advantages of Bioprahar

- Highly effective against diamond back moth, mealy bug and woolly aphids, red mites of brinjal & okra.
- Ideally suited for integrated pest management programs on cotton, okra, tomato, tobacco, castor etc.
- No chemical residues in fruits, vegetables, grains, feeds and fodder. It prevents soil, water and air pollution.
- Eco friendly and safe to use.



A bottle of Bioprahar

Rural Bioresource Complexes

A Rural Bioresource Complex (RBC) is a cluster of villages in which economically viable and ecologically compatible technologies would be provided to the rural people, so that the development of the entire cluster is holistic and sustainable.

The basic objective of RBC is economic empowerment of the target group through income generation and better employment opportunities along with entrepreneurship development, social benefits and environmental sustainability.

DBT has established five Rural Bioresource Complexes at University of Agricultural Sciences (UAS), Bangalore; Marathwada Agricultural University (MAU), Parbhani; CCS Haryana Agricultural University (CCSHAU), Hisar; and G.B. Pant University of Agriculture and Technology (GBPUA&T), Pantnagar and Orissa University Agriculture and Technology (OUAT), Bhubaneswar.

The objectives of each RBC are being accomplished by disseminating and demonstrating a few identified, highly focused technological interventions at the farmer's field. The major interventions include production of value added products from plants, cultivation of medicinal plants, dairy farming, biofuel plantations, pomegranate cultivation, sericulture, seed production, nursery, poultry and dairy farming etc. The marketing linkages for the produce have been arranged by the respective State Agricultural University (SAU).



Ragi-Seed Production



Vermicompost

Rural Bioresource Complexes



Shoot rearing and Mounting of Silkworms

The summary of achievements till date is as follows

	UAS, Bangalore	CCSHAU, Hisar	OUAT, Bhubaneswar	MAU, Parbhani	GBPUA&T, Pant Nagar
Number of interventions	20	4	16	6	4
Number of beneficiaries families	8340	3764	1058	1419	2828
Training programmes conducted	344	295	34	25	47
Number of direct beneficiaries families	8340	1813	1058	1618	2828
Number of indirect beneficiaries families	14562	8606	2360	4644	3226

Large Cardamom Productivity Improvement

Large cardamom (*Amomum subulatum*) is presently cultivated in Sikkim and Darjeeling district of West Bengal with the total production of 6154 tonnes with an average productivity of 246 kg/ha. The agroclimatic conditions prevailing in other north-eastern states i.e. Arunachal Pradesh, Nagaland, Mizoram, Meghalaya, Manipur are also suitable for cultivation of large cardamom. However, the current productivity is very low.

- With a view to enhance the productivity, the Department of Biotechnology, jointly with the Spices Board (Ministry of Commerce), has implemented a demonstration project on the performance of high-yielding varieties of test tube-raised large cardamom in farmers' field over an area of 55 ha in Sikkim and Darjeeling district of West Bengal. Over 250 farmers have benefited through this joint project directly and indirectly.
- Tissue cultured plantlets started giving satisfactory yield earlier than open pollinated seedlings. Three-year yield data recorded for elite clones of test tube cardamom in the seventh year after field planting ranged from 520 to 856 kg/ha compared to 68 to 115 kg/ha for seed-raised plants of similar age.
- SBLC-47A (Varlangey) is found to be generally superior in yield (yield: 624.43 to 643.26 kg/ha) compared to other selections and showed better yield performance in North, East and West Sikkim. Maximum yield of 609.52 kg/ha was recorded in SBLC-5 (Sawney) in South Sikkim.
- A comprehensive package of practices has been developed for cultivation of high yielding tissue culture-raised large cardamom plantlets. Different elite clones adapted to the high, medium and low altitude situations of the large cardamom growing tract have been identified.
- The project has established superiority of the plantlets over open-pollinated seedlings in terms of yield.

Large Cardamom Productivity Improvement

- The project has generated demand in the region for high yielding TC plantlets of large cardamom. Two farmers cultivating TC large cardamom plantlets were awarded for high productivity by Spices Board during 2005 and 2006.
- Spices Board has currently taken up area expansion of large cardamom in Sikkim as well as other north-eastern states. To meet rising demand, test tube-raised plants of SBLC-5 (Sawney) variety are being supplied to farmers in the region.



**Tissue Culture raised
plant of SBLC 42 at the stage of
fruit formation**



**Cardamom capsules
produced by test tube-raised
SBLC 47 A plant**



Patchouli- a New Aroma of Hope for Farmers

Patchouli (*Pogostemon cablin*), an herbaceous plant is a source of essential oils used as a base in perfumery industry due to its fixative property and cannot be substituted by synthetic chemicals. Global demand for patchouli oil is 1500 tons per annum and Indonesia is the world's leading producer today. India imports up to 150 tons per annum, as the current production in the country is only around 10 tones. This offers great scope for cultivation of patchouli as an import substitute besides providing opportunities for export.

India has a wide range of agroclimatic conditions of which the soil and climate along the coast and North Eastern regions is similar to that prevailing in Indonesia and hence there is a huge potential for India to produce and market this oil.

With a view to popularize the crop among farming community, the Department of Biotechnology jointly with Kelkar's Scientific Research Centre, Mumbai has implemented a demonstration project on multi-locational trials of patchouli cultivation in farmers' fields on 32 acres covering 128 farmers using tissue culture-raised plantlets as well as rooted cuttings of an elite variety.

Agro-techniques have been standardized for cultivation of patchouli in Gujarat, Konkan and Karnataka regions. The biomass obtained from the demonstration plots has been analyzed for oil yield and profile. The oil composition obtained from different experimental trials was found to be similar to that produced by parent plant.

Keva Biotech Pvt. Ltd. Mumbai has provided buy-back arrangements to the dried biomass produced by the farmers covered in the project.

The project has demonstrated that tissue culture-derived elite variety of patchouli can be cultivated in wide range of agroclimatic conditions. However, best growth and oil yields were obtained in coastal areas with laterite soil and good humidity. The plant has

Patchouli- a New Aroma of Hope for Farmers

attracted attention of farmers all around the country including the tribal regions of Assam, Mizoram, Madhya Pradesh and Himachal Pradesh.

Due to the coordinated effort of DBT and its partner institutions (Kelkar's Scientific Research Centre, Mumbai; University of Agricultural Sciences, Dharwad; National Research Centre on Medicinal and Aromatic Plants, Anand; Central Plantation Crops Research Institute, Dharwad; Konkan Krishi Vidyapeeth, Dapoli), industry and the farmers, an efficient model of supply chain has been established which is beneficial both to the farmers and the industry. This model can be expanded to cover the entire country.

Today, more than 1000 farmers cultivate this crop in their fields and have successfully sold the dried biomass to the industry for oil extraction with estimated net earnings of Rs. 30,000/- to 40,000/- per acre.



An Oral, Live, Recombinant Non-residual Cholera Candidate Vaccine

Cholera, caused by *Vibrio cholerae* O1 and O139, is an important cause of morbidity and mortality in the developing countries where sanitation and hygiene are poor. The discovery of Oral Rehydration Therapy has brought down the mortality from cholera but has no impact on its incidence. Vaccination against cholera is an attractive prevention strategy. In the early 1970s, WHO recommended discontinuation of the parenteral vaccine due to lack of efficacy. Several cholera vaccines since then have been developed but most of these produce residual diarrhoea. Therefore, DBT initiated efforts, which culminated in the development of an oral recombinant Cholera Candidate Vaccine.

Initial trials at SAS, Kolkata, SGPGIMS, Lucknow & CMC, Vellore have shown encouraging results. A Phase III trial site for covering a population of about one lakh has been prepared.

A Vaccine formulation of the Candidate Cholera Vaccine has been prepared under GMP conditions at M/s Shantha Biotechnics Pvt. Ltd., Hyderabad. Regulatory toxicology followed by Human trials would soon begin. It is expected that the Vaccine may be approved for human use in 2011.