The particular bacteria that breaks down oil has not yet been isolated but Craig and his team from the Oregon State University hope to do so by cultivating them in a medium similar to the chemical conditions in the bowhead whale's stomach.

The university plans to apply for a patent for the whale bacteria as soon as they manage to identify the species that digests these chemicals.

According to Craig, the possibility of obtaining useful micro-organisms from animal's bodies offers tremendous scope for biological remedies to many of our environmental problems.

(Indian Express, Madras, August, 19, 1995.)

VII. FEATURES/ARTICLES

1. BIOTECHNOLOGY: NEW PRODUCTS IN HORIZON

DR. B.M. GANDHI
DIRECTOR
DEPARTMENT OF BIOTECHNOLOGY
MINISTRY OF SCIENCE AND TECHNOLOGY

Developments in the area of biotechnology during the past two decades have realised a number of products for diverse use in a variety of situation. Biotechnology has helped develop products useful in human and animal health care, agriculture and fine chemical industries.

The application of biotechnology has resulted in a number of products and processes in the area of health care specifically produced for prophylaxis, vaccine and therapy. Areas where biotechnology has already made a significant impact include pharmaceuticals, genetically engineered vaccines, growth harmones, interferon for treatment of viral diseases and cancers, antibiotics, bioactive molecules, speciality chemicals, improved drug delivery systems, immunodiagnostics, biomaterials etc. Use of monoclonal antibodies and molecular probes have helped in better understanding of molecular genetics of a number of diseases including diagnosis, prognosis and therapy of human tumors.

BIOACTIVE MOLECULES:

Several bioactive substances have been produced on a commercial scale by microbial methods by incorporating the required genes into various expression systems like **E. Coli,** yeast etc.

The DNA proteins in human therapeutic use include insulin for diabetes; human growth hormones for Dwarfism; interferons for viral diseases, cancers etc.; interleukins for various cancers; tissue plasminogen activators for thrombolysis; erythropoietin for thrombolysis and epidermal growth factor for wound healing, burns and fractures. In addition, a large number of rDNA products are in advanced stages of development which includes arterial natriuretic factor for hypertension and kidney diseases; blood factor VIII and IX for haemophilia; plasminogen activator for thrombolysis; tumour necrosis factor for antitumour and antiviral therapy; superoxide dismutase for cardiac treatment and organ transplants etc.

In addition bioactive peptides being used as vaccines are being produced for hepatitis B vaccine, malaria vaccine, herpes virus vaccine, influenza vaccine etc.

VACCINES:

Biotechnology has the potential of producing more effective vaccines, against various viral, bacterial and parasitic diseases by using new emerging technologies for vaccine development such as recombinant virus vaccines, recombinant DNA subunit vaccines etc. These vaccines have proved advantageous over conventional vaccines like attenuated or inactivated vaccines, peptide based or live vaccines.

Vaccines are already being produced for hepatitis,Herpes and other sexually transmitted diseases, influenza, mononucleosis, malaria, cholera, filariasis, leishmaniasis, schistosmiasis and trypanosomaisis and other diseases. It is expected that in coming few years vaccines would also be available for a number of parasitic diseases which are the cause of high mortality in the developing countries.

MOLECULAR PROBES:

Molecular probes have been successfully used in the diagnosis of a number of viral, bacterial and parasitic infectious diseases and plant diseases agents such as viroids, viruses and mycoplasms. Molecular probes and monoclonal antibodies have emerged as the most important tools in the new generation approaches to diagnosis, prognosis and therapy of human tumors.

DNA hybridisation, when coupled to enzyme restriction analysis, is an essential tool in the diagnosis of a constantly growing number of genetic diseases. Genetic disorders where diagostic probes have been useful are Duchenne Muscular Dystrophy, Becker Muscular Dystrophy, Hutington's Disease, Cystic Fibrosis, Fragile X-Syndrome, Haemophillia etc. Synthetic Allele-specific oligonucleotide probes are being used to detect point mútation in prenatal and carrier diagnosis of the hereditary prophyrias and anti-trypsin deficiency.

Non-radio active probes based on ribosomal RNA provide a powerful means of microbes detection which are available in abundance as cellular molecules.

Chemically synthesised oligonucleotides are finding ever increasing use in molecular biology, medicine, genetic engineering and many other areas of biological research. Synthetic oligonucleotides have been used for making of insulin, interferon and growth harmones etc.

IMMUNODIAGNOSTICS:

With an objective to develop simple, sensitive and reliable methods, kits for the diagnosis of physiological status or pathological and communicable disease conditions, are being developed for the diagnosis of viral, bacterial and parasitic diseases. In India diagnostic kits are being developed for the early detection of pregnancy; filariasis; hepatitis-B; amoebiasis; toxoplasmosis; brucellosis; tuberculosis; leprosy; typhoid fever; malaria; giardiasis; leishmaniasis; rotavirus and shigellosis. Some of these kits have already gone into commercialisation.

MONOCLONAL ANTIBODIES:

Monoclonal antibodies specific for almost all antigens can be generated today with wide applications. These antibodies are being widely used as Drug Targetting Agents. The high specificity of antibodies for antigens has long attracted the interest of scientists in the field of immunodiagnostics and protein purification. The rapidly increasing availability of monoclonal antibodies has stimulated their use in the immunoaffinity chromatography of therapeutic proteins.

Catalytic monoclonal antibodies with unlimited range of recognition site structure, provide potentially an enormous repertoire of new catalytic agent, and is becoming an important biotechnological tool. They have wide applications, especially where non suitable enzymes or chemicals catalysts are currently in use. Some of its potential applications are in the synthesis of organic fine chemicals, as biosensors and in protein engineering applications.

Another exciting application of fusoma technology has been the generation of bivalent mAbs with specificity for the T-cell receptor complex and tumor antigens. These reagents are able to activate and direct cytotoxic T-lymphocytes to their targets with consequent efficient cytolysis. This approach has proved useful in in-vitro killing of tumor cells and a valuable adjunct therapy in cancer treatment.

LYMPHOKINES:

Lymphokines are capable of directing the function of other cells in the area where nonself invasion is occurring. These lymphokines include: (i) gamma interferon (IFN), which causes mononuclear phagocytes to have enhanced killing function; (ii) Interleukin 2, which acts as a growth factor for T lymphocytes, causing increased cellular proliferation; (iii) B-cell Growth Factor (BCGF), which causes B lymphocytes clones to proliferate predominantly by killer T lymphocytes and can cause tumor target cell death. All these substances play an important role.

DRUG DELIVERY SYSTEM:

New Technologies for delivering drugs, are addressed to the need of maximising the time the drug's active ingredients are present. With the exception of monoclonal antibodies, most of the new delivery vehicles are synthetic and one used transderamally. Some new drug delivery systems include bioerodable non-toxic synthetic polymers trandermal application of medicaments, nitroglycerine for treating angina and scopalamine for combating motion sickness; microsponges made by using synthetic polymer spheres of 5 to 300 microns.

Liposomes: Liposomes are used for delivery of drug by oral route, ocular application and injection. Liposomes are synthetic as well as natural. Liposome intercalcated drug formulations using amphotericin-B (for treatment of fungal infections), doxirubicin hydrochoride (anti-tumor anti-cancer drug), rifampicin (for treating tuberculosis) etc.

Nasal Spray: Nasal memberane permeation technology works by coating the drug molecules with an adjuvant that allows it to permeate the mucus membrane. The technology is convenient and hormonal drugs can be delivered in a pulsatile manner similar to the way the body does it.

BIOCOSMETIC INDUSTRY:

There are over 1600 different chemical entities used in the production of cosmetics. A number of areas of application for biotechnologically produced components are in pigments, fragrances, pharmacological skin products, water retention agents and hair care products. Biotechnology has reduced the production cost of expensive components of cosmetics and at the same time the products are more acceptable than biological products.

BIOMATERIALS AND BIOMEDICAL DEVICES:

Cellular and Tissue Engineering is important in the development of biomaterials and in reconstructive surgery. An important current approach to the fabrication of biomedical materials and devices includes molecular, enzymatic, genetic and organellar engineering. Already a number of biomaterials and therapeutic devices have been developed. A few important items include neural prostheses and devices for brain vascular and cardiovascular materials, blood cells and plasma substitutes, bone graft substitutes, tissue/biomaterial interface, controlled drug delivery etc. In addition, noval material and techniques being used include bone as a biomaterial, orthopedic material and prostheses and new dental materials. Artificial organs are produced and implantable electric devices are being developed.

R & D EFFORTS FOR FUTURE PRODUCTS:

Major interest of industries in developed countries for the year 2000 include a number of products and devices. Under fine chemicals, interest lies in the new antibiotics, vaccines, immunogenic products, clinical diagnostic tests, enzymes and marine organisms for production of new compounds. Under basic chemicals,

interest lies in plastics from microorganisms, transformation of waste into useful resources, pulp from wood resources, bulk chemical synthesis using enzymes, chemical synthesis using artificial enzymes etc. Under energy and food resources, major interest would be alcohol fermentation, bioreactors for food production, new hybrid plants resistant to diseases and environmental stress, and yeast and microorganism battery. Under environmental protection, recovery of crude oil and biological immobilisation of Carbon dioxide are the areas of interest.

In addition, biocomputer, biochip, biosensors, biodegradable plastics, biomaterials, robotics molecular machines,synthetic organ and blood are the other areas of interest.

CONCLUSION:

Thus it may be seen that advancements in the fields of biotechnology will have far reaching results during the coming times in improving the general condition of health in developing countries through viable products in the form of vaccines, bioactive substances, diagnostic kits, drug carrier, quality food biomaterials and biomedical devices.

(The views expressed in the above article are those of the author in his personal capacity and do not reflect the policies of the Department of Biotechnology, New Delhi.)

2. HAIRY ROOTS - A POTENTIAL ALTERNATE SOURCE OF SECONDARY METABOLITES OF SOME ENDANGERED MEDICINAL PLANTS DEVELOPED BY CIMAP.

DR. SUSHIL KUMAR,
DIRECTOR, CIMAP,
LUCKNOW.

The scientists of the Genetic Resources and Biotechnology Division of the Central Institute of Medicinal and Aromatic Plants (CIMAP), Lucknow, have successfully developed the technology of **in vitro** secondary metabolite production through genetically transformed hairy root cultures, of certain endangered alpine zone medicinal plants.

Roots are the site of synthesis and/or storage of some of the phytochemicals of interest in a number of medicinal plants that usually occur only in the alpine areas of Himalayas.Indiscriminate exploitation of such alpine plant species is causing an alarming depletion of biodiversity in their populations endangering their survival.

There was an acute need for sustained use of the endangered plants so that they do not become extinct, while meeting the growing demand for their materials for formulations on them. Biotechnology based current development will provide an alternate source of the raw material for making drugs for which until now uprooted plants from nature were the only raw material.

The natural genetic engineering ability of the soil dwelling, gram-negative bacterium - **Agrobacterium rhizogenes** has now permitted development of organ cultures using which secondary metabolite produced **in vitro. A. rhizogenes** infects the wound sites of a wide range of plant species and the importance of this bacterium for plant genetic engineering is its natural ability to transfer a segment of DNA (transferred DNA - or T-DNA) of its root inducing plasmid (Ri - plasmid) into the plant cells. This T-DNA upon transfer gets integrated and expressed in the nuclear genome of the plant cells and causes the typical syndrome, known as hairy root disease, which is characterized by sprouting of numerous highly branched, auxin autotropic adventitious roots at the infection sites. The hairy roots can be excised and cultured in simple hormone free media where they exhibit genetic stability and high rates of growth, and production of secondary metabolites.

Atropa acuminata and **Valeriana wallichii** are two of the medicinally important alpine zone plants which are presently under the endangered plant list. The roots of **A. acuminata** plants are the source of tropane alkaloids (atropine and scopolamine) and those of **V. wallichii** that of valepotriates. **A. rhizogenes** mediated hairy roots have been induced in both the plants and the hairy roots in both cases have been successfully multiplied in liquid. In the hairy root cultures. that have been derived the secondary metabolite production levels are higher than in the non-transformed control roots. The scientists of CIMAP have also been successful in reducing the cost of **in vitro** culture of the hairy roots by using a cheaper alternative carbohydrate source without affecting the yield of biomass and secondary metabolites. The hairy root stocks are now to be cultivated on larger scales for testing their commercial potential.

VIII. BIOTECH CALENDAR

1. **5-9 November 1995**

The International Congress on High Pressure Bioscience and **Biotechnology,** Kyoto, Japan. (Dr R. Hayashi, Department of Agriculture, Kyoto University Kitashirakawa, Sakyo-Ku, Kyoto 606-01, Japan.
Tel: + 81 75 753 6112
Fax: + 81 75 753 6128)

2. **7-10 November 1995**

The Ist Annual Conference of the Society for Biomolecular Screening, Philadelphia, PA. USA (Dr. C. Giordano, Executive Director, The Society for Biomolecular Screening Inc, 36 Tamarack Avenue, Suite 348, Danbury, CT 06811 USA
Tel: + 1 203 743 1336
Fax: + 1 203 748 7557)

3. **26-29 November 1995**

Immobilized Cells: Basics and Applications, Noordwijkerhout, The Netherlands (Dr. R.H. Wijffels, Wageningen Agricultural University, Food and Bioprocess Engineering Group, PO Box 8129, 6700 EV Wageningen, The Netherlands,
Fax: + 31 8370 82337)

4. **3-7 December 1995**

Pectins and Pectinases, Wageningen, The Netherlands. (Dr. M.A. Kusters van Someren, Molecular Genetics of Industrial Mocroorganisms, Wageningen Agricultural Univerisity, Dreijenlaan 2, 6703 HA Wageningen, The Netherlands.
Tel: +31 8370 84620
Fax: +31 8370 84011)

5. **6-7 December 1995.**

Characterization of Biopharmaceutical Products, Basel, Switzerland. (Programme Division, Technomic Publishing AG, MissionsstraBe 44, CH-4055 Basel, Switzerland.
Tel: +41 61 381 52 26
Fax: +41 61 381 52 59)

6. **10-14 December 1995**

Symposium Beijerinck Centennial: Microbial Physiology and Gene Regulation: Emerging **Principles and Applications,** The Hague, The Netherlands, (Congress Office ASD, PO Box 40, 2600 AA Delft, The Netherlands.
Tel: +31 15 120234
Fax: +31 15 120250)