Biotechnology in Animal Production

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Introduction

Since 1953 when Watson and Crick published their work on the structure of DNA, opportunities to apply molecular biology techniques in medical, veterinary and agricultural fields have increased at a remarkable rate. The comprehensive name given to these developments has been biotechnology. Thus biotechnology is defined as the use of living organisms, cells, sub-cellular organelles, and/or parts of those structures, as well as the molecules to effect physical or chemical changes needed to generate new products for research and commercialization.

Despite such broad perspectives, biotechnology is considered to be synonymous with recombinant DNA techniques or genetic engineering. However, biotechnology in practice typically includes not only genetic engineering, but also some of the older and closely related tools such as cell culture, monoclonal antibodies, bioprocess engineering and the manipulation of reproductive processes. Thus biotechnologists manipulate, not only the genetic make-up of living organisms, but also processes or factors which pre-exist in living organisms. Hitherto the only way by which these inherent functions could be readily changed were by evolution and selective breeding. Biotechnology offers an extension to effecting change at the organism level by manipulation of cells and individual genes within an organism. It creates a new method of intervention in biological processes with the potential for bringing about changes not otherwise possible. Biotechnology is one of the frontier areas of science in the world today. This paper attempts to cover the major aspects of Animal Biotechnology and its status in India.

Major fields of biotechnology in animal production

The major fields in animal biotechnology include:

1) Manipulation of reproductive processes
2) Genetic engineering of macro-organisms
3) Genetic engineering of micro-organisms and molecules including cell-engineering (hybridoma technology) to produce desired end products such as vaccines, gene probes, monoclonal antibodies and growth promoters.

1. Manipulation of reproductive processes

a. Artificial insemination, Oestrus induction, superovulation

Manipulation of reproductive processes in domestic species started in the 1930s with artificial insemination (AI). Its use became widespread in the 1960s when AI organisations began to make routine use of frozen semen. Manipulation of female reproductive processes started with oestrus induction and synchronization, initially with steroid hormones and later with prostaglandins. Superovulation techniques with gonadotrophic hormones led to embryo transfer on an increasing scale in the 1980s when embryo freezing techniques became available. AI and embryo transfer techniques offer animal breeders a number of opportunities to enhance the rate of genetic progress in national breeding programmes.

b. Embryo sexing, embryo splitting, embryo cloning

More advanced techniques for altering reproduction in livestock have been developed in the last decade. These include oocyte removal from genetically superior cows during the dioestrous period, *in vitro* maturation and fertilisation of these oocytes, *in vitro* cultures of fertilised oocytes (zygotes) up to the blastocyst stage, sexing, splitting and cloning of embryos. Splitting and cloning of sheep and bovine embryos became possible after micromanipulation techniques were developed. As soon as these procedures can be used on an industrial level, embryo transfer could partly replace AI in dairy and beef cows. Embryo transfer could be used to produce quality breeding bulls which in turn could be utilized for AI purpose.

2. Genetic engineering of macro-organisms

Micro manipulation techniques have already been used to produce transgenic mice, sheep, pigs and cows. Gene constructs, coding for a known characteristic, can be injected into the pronucleus of a fertilised ovum. This technique enables the transfer of any gene from any source, no matter how remote the relationship between the donor and recipient is, into a population of animals. The ultimate success rate depends on whether the gene is properly expressed in the recipient and their

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offspring; i.e. whether the protein specified by the introduced gene is synthesised or not. These new technique fulfill the long-range goal of animal breeders which is to introduce particular genes into the germplasm of domestic animals. This may, together with manipulation of reproductive processes, improve disease resistance, milk production, growth, feed conversion efficiency and overall economic merit. Genetic engineering also yields new insights into basic physiological mechanisms (e.g. gene regulation), expedites the production of animals with desired production traits and will result in the creation of animals with entirely novel properties (e.g. secretion of biomedical substances in milk), completely unattainable by conventional breeding and selection techniques. However, it must be stated that considerable research is still needed as the present success rate is 0.5-1% only.

3. Genetic engineering of micro-organisms and molecules, including engineering of cells

a. Vaccines

The production of recombinant vaccines against various animal diseases that are caused by bacterial, viral or parasitic infections is a field of active research. Most vaccines used in livestock at present are still produced by conventional methods.

Importance of vaccines

Vaccine development is one of the first and most promising fields of application of biotechnology. At present, an enormous amount of research is going into this area in an effort to develop new, safer and more efficacious vaccines which give the highest protection to the animal economically.

There are still a large number of animal diseases for which protective vaccines are yet to be available, especially against parasitic diseases. Some antigens have been virtually impossible to incorporate into vaccines because of the difficulty in growing the micro-organisms or isolating the antigens, or because of their complexity or an inability to adapt them to a viable production method.

Research activities are now focused on subunit, recombinant DNA, synthetic peptide, anti-idiotype, deletion mutant, reassortment and vaccinia vectored vaccines. It is expected that in the next few years an increasing number of genetically engineered vaccines will be marketed.

b. Application of DNA/RNA probes

The emergence of recombinant DNA technology has given rise to diagnostic DNA/RNA probes which are based on the ability of single stranded DNA or RNA to form hybrids with a complementary labeled sequence of nucleotides on another strand of DNA/RNA. This means that DNA/RNA sequences unique to a species can be recognised by hybridising or pairing test material with DNA, labeled in a recognizable manner. Application of DNA/RNA probes in the diagnosis of infectious diseases is a recent alternative to the established isolation and determination of micro-organisms by cultural and serological methods. Expectations for this new technique are high, because probes may have advantages over the conventional bacteriological and virological methods such as a constant and well defined sensitivity and specificity which enable identification of pathogens in a relatively short time, and their direct detection in clinical specimens. Other probes and techniques are also becoming, available for the detection of genetic errors, the determination of sex of embryos, the verification of pedigrees and the monitoring of physiological changes induced by the introduction of new genetic material.

c. Monoclonal antibody technology

Parallel with developments in DNA technology are the advances in immunochemical diagnostic procedures. Serological diagnostic tests, used for many years rely on the detection of antibodies stimulated by invading organisms. The use of antibodies to detect infectious agents, proteins or pharmaceutical substances is exemplified by the expansion of monoclonal antibody technology. This involves the fusion of somatic cells to form a hybrid or hybridoma from both parents. Hybriodomas can produce antibodies (monoclonals) specific for a single antigenic determinant (epitope) which can be produced in large quantities. Monoclonal antibodies, when labeled may be used to detect substances in tissues, fluids, or cells even under field conditions.

A practical example is the bovine milk progesterone test for determining the stage of the oestrous cycle. However, many other monoclonal antibodies have been produced against a number of antigens: tumour cell markers, histocompatibility antigens, lymphocyte differentiation antigens, bloodgroup antigens, bacteria, viruses, fungi, protozoa, helminths, hormones, enzymes, nucleic acids, immunoglobulins, and receptor sites. It is expected that hybridoma technology will deliver more powerful products for both the human and veterinary medical markets in the future.

d. Growth promoters

(i) Range of hormones produced by genetic engineering

Most of the functions of the body are controlled by hormones, chemical substances produced naturally in different glands, which in minute quantities influence the performance of specialized groups of cells. Individually, they are responsible for the functions of growth, reproduction, milk secretion and the metabolism of the body in general. A number of chemical and pharmaceutical companies abroad have genetically engineered hormones or growth promotants such as human (hST), bovine (bST) and procine (pST) somatotropin, interferon, lymphokines *etc.* These are in the field testing stage and are ready to market for use in human and veterinary medicine. The use of these products may help to correct growth retardation in children, make hogs grow faster with less fat and more lean production of dairy cattle.

(ii) Biotechnology contributions to animal diets

Other growth promotants such as antibiotics and non-antibiotic tools including enzymes, yeast cultures, live bacteria and their metabolites and feed pH adjusters are being perfected for use in livestock farming. These products should offer the nutritionists, if used appropriately, great potential for improvement in their animal nutrition programmes. Addition of suitable crude enzyme preparations to diets of both pigs and poultry can lead to improvements in feed conversion efficiency and live weight gains for example.

(iii) Probiotics

Other biological tools are the probiotics which encompasses organisms and substances that contribute to intestinal microbial balance. Applications are mainly in poultry, pigs and calves. The aim is a constant infusion of friendly organisms, such as lactic acid bacteria, via the diet, to prevent colonization of the gastrointestinal tract by disease-causing organisms. It is thus based on the principle of competitive exclusion.

4. Animal Biotechnology in India

In India, the setting up of a separate Department of Biotechnology (DBT), under the Ministry of Science and Technology in 1986 gave a new impetus to the development of the field of modern biology and biotechnology. In more than a decade of its existence, the department has promoted and accelerated the pace of development of biotechnology in the country. Through several R&D projects, demonstrations and creation of infrastructural facilities a clear visible impact of this field could be seen. The DBT has made significant achievements in the growth and application of biotechnology in the broad areas of agriculture, health care, animal sciences, environment, and industry.

a. Current research programmes in animal biotechnology

Department of Biotechnology (DBT) funded project are as follows:

1. Standardization of embryo transfer technology in cattle, buffalo, goats and camel.
2. Crossbred Sahiwal bull produced through Open Nucleus Breeding programme are being used in National Artificial Insemination programme.
3. Standardized Transgenic technology and 18 lines of transgenic mice were produced which are available for researchers.
4. DBT supported leather technology mission for biotechnology oriented programmes and 24 carcass utilization centre were developed for improving leather quality.

b. Technologies/Products

Technologies transferred to the Industry:

Technology transferred	Industry to whom transferred	Status of the technology
i) Process know-how manual for infectious Bovine Rhinotracheitis (IBR) Vaccine, developed by the BAIF Foundation Pune	Hoechst Roussel India Ltd. (HRV)	Vaccine is available in the market
ii) Reconstituted collagen sheet (RCS) developed by CLRI, Chennai.	Eucare Pharmaceutical Pvt. Ltd., Chennai	Reconstituted collagen sheet is available in the market.
iii) Diagnostic test for peste des petis ruminants virus, by TANUVAS Chennai.	Indian immunolocials, Hyderabad.	Technology has been transferred.
iv) Recombinant protective antigen (rPA) against Anthrax developed by JNU, New Delhi	Panacea Biotech Limited, B-1 Extension/ A - 27, Mohan Co - operative Indl. Estate, Mathura Road, New Delhi -110 044.	Pre-clinical trials are on.

c. New initiatives for the 10th Five Year plan

The thrust areas identified :

1. Animal feed enrichment including utilization of agro byproducts; ligno-cellulose degradation through enhancement of white-rot fungi activity for ligno-cellulose degradation. Genes for ligninase to be transferred appropriate fungal strains for improving the activity. Production system are proposed to be scaled up.
2. Molecular characterisation and upgradation of indigenous animals breeds to receive attention. DBT has proposed to launch genetic improvement programmes in some breeds and also conserve them through ex-vitro approaches.
3. Development of improved vaccines and diagnostics for major diseases and also new and emerging ones. Zoonotic diseases also to receive special attention. The strategies employed is to be based on conventional and recombinant routes.
4. A major multicentric initiative has been initiated on buffalo genome. This would involve construction of a linkage map, micro satellite markers especially for traits of economic importance. Besides mapping specific regions of the genome, breed characterization is also to be attempted.
5. Efforts are to be made towards the development of transgenics in large farm animals for expression of new genes and production of novel proteins. This would be based on the success already achieved in generating a number of transgenic mice lines and the expertise developed.
6. Ovum pick up technique and enhancement of various embryo technologies has been initiated by DBT multiplication of elite animals. Efforts are on to evolve appropriate methods for somatic cloning of large animals.

Though DBT is the major player in the field of Biotechnology in India various laboratories of ICAR, CSIR, Veterinary and Agricultural Universities have also developed a number of similar useful technologies in Animal Biotechnology.

5. Opportunities for banking sector

1. Of late State Governments are showing keen interest in Biotechnology, some have already set up Biotech parks also. Banks can finance units which are viable and bankable in such biotech parks.
2. Embryo transfer labs for production elite male animals can be financed. Already, Embryo transfer technology unit for production of good quality Rams for semen production has already been financed under cofinance in Andhra Pradesh.

NABARD and Biotechnology

1. NABARD may refinance biotech units at attractive concessional terms in the areas of rate of interest, soft loan assistance for establishment & growth of Biotech units.
2. NABARD may give special thrust to applied research in Biotechnology with R&D fund assistance. For this, NABARD can play a proactive role by identifying institutes for sponsoring projects.
3. NABARD may also support the workshop/ seminar related to Biotechnology that are farmer oriented, especially which explore the lab to land transfer of technology through user industry, selected agriculture universities/research institutes.
4. Explore the possibility of developing bankable models for biotech products. Biotech schemes could be made eligible for venture capital assistance under GoI schemes. NABARD may also create a Venture capital fund for R&D and assistance to biotech.

Assistance for setting up or modernization of high tech vaccine production or diagnostic kit production units could be considered under RIDF assistance. Setting up of modern disease diagnostic labs could also be covered under RIDF assistance.