J. Vet. Malaysia (1989) 1(1) : 1–9

ANIMAL BIOTECHNOLOGY – THE MALAYSIAN PERSPECTIVES

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SUMMARY: Until a few years ago, the application of biotechnology in animal agriculture was very limited but recent advances in biotechnology have demonstrated its potential uses in animal health and production. Most of these activities are very much at the preliminary stages of development. In Malaysia, there are at least three major areas of research on the role of biotechnology in animal health and production. These are genetics and reproduction, nutrition and animal health. Modern biotechnology research is concerned with some of the most complex and elegant techniques which are yet to be applied in biological science. It is essential that expertise in these new technologies be developed before long term and expensive research projects in animal biotechnology are undertaken locally. The impact of biotechnology on the livestock industry is far reaching. Its practical applications in animal agriculture and veterinary medicine are enormous. The application of this technology in Malaysia can lead to useful products and processes.

Key words: biotechnology, animal health, animal production, Malaysia

INTRODUCTION

Cattle, buffalo, goats, poultry and swine play a significant role in the farming system in Malaysia. Economically, the livestock industry can be divided into the ruminant subsector which can hardly meet the country's requirement for milk and meat and the non-ruminant subsector which has reached a stage of self-sufficiency with a capacity for further expansion. In recent years, the livestock industry in Malaysia has undergone rapid changes, besides playing an important role in eradicating poverty by increasing employment opportunities. Livestock production constitutes about six percent of the total agriculture output with an annual turnover of about 1.5 billion Malaysian ringgit.

The poultry and swine subsector has advanced rapidly in recent years. The rapid development is attributed to the successful replacement of local stocks with genetically superior breeds and the transfer of technology. The emergence of the feedmilling industry has played an important role in their development and progress. Future expansion is geared to meeting local demand as well as for export. The poultry subsector, however, has a potential for expansion because of the local acceptance of poultry and poultry products. Major changes are being undertaken with poultry processing already an integral part of the broiler industry.

Unlike poultry and swine, the ruminant subsector is generally underdeveloped and the government has placed great emphasis on its development. The lack of productive breeding stock is the major constraint. Efforts are being made to increase the cattle population through increased import and artificial insemination services. Beef and dairy development programmes are being undertaken to upgrade local cattle through cross-

breeding with imported superior breeds. Milk production has increased substantially with the implementation of the dairy development programme for the smallholder farmer. The establishment of Milk Collecting Centres (MCC) has enabled smallholder dairy farmers to be organised into groups for more effective production and marketing of their produce. More than 80% of the local supply of beef is provided by the smallholder farmers although there are also a few feedlot operators. Goat and sheep production in West Malaysia are mainly undertaken by smallholder farmers with the primary objective for meat production.

Malaysia imports annually about 70% of its animal feedstuff requirements. The major importers are the feedmillers which produce mainly poultry and swine compounded feeds. The major local feedstuffs are palm kernel cake, soyabean meal, rice bran, fish meal, copra cake, wheat bran and molasses. It has been estimated that more than 5.8 million tonnes of agro-industrial by-products are available in West Malaysia. Attention is being given to using these by-products as animal feeds as there is no natural pastureland in Malaysia other than the small and scattered areas of mixed grasses and weeds on waste-land, roadside tables, fringes of rubber, coconut and palm oil estates and abandoned padi land.

CONSTRAINTS TO ANIMAL PRODUCTION

Although the livestock industry has made tremendous progress during the last three decades, it is not free from problems such as availability of feedstuffs, low reproductive efficiency and diseases.

Feed is the most expensive item in livestock production in Malaysia. Most feeding systems for ruminants in Malaysia incorporate a large proportion of fibrous materials and by-products from the agricultural industry. Attempts are being made to utilise these by-products, such as palm press fibre (PFF) from palm oil milling, by establishing feedlots close to the mills. At least 316 million tons of PPF are available in Malaysia annually and this quantity has the potential to meet the feed requirement of the ruminant industry. Unfortunately, the feeding value of PPF is relatively low, being highly lignified (21%) with low crude protein (6%) and is deficient in phosphorus and copper. Based on our present knowledge on by-product utilization by ruminants, reasonable growth and production cannot be achieved unless energy and protein are also provided. Under such a situation livestock farming is uneconomical.

One of the major problems in ruminant production in Malaysia is low reproductive efficiency. This includes losses which occur between conception and calving. About 50% of the losses occur from failures in conception, abortion and mortality of the young. Reproductive problems are often linked with diseases, nutritional deficiency and environmental constraints. The lack of good quality stocks is also a major constraint. The genetic resources of the local ruminant population (cattle, sheep, goat) are limited to support the expansion of the industry and the country has to import crossbred animals from Australia and New Zealand.

Loss due to disease is also a major problem in animal production. Profitable livestock production is only possible if major diseases are brought under control. Little information is available on the impact of various infectious diseases known to affect livestock in Malaysia. Neonatal calf mortality is a major cause of economic loss in cattle production. Field reports indicate that these losses are fairly high. Preliminary investigations revealed that bovine viral diarrhoea virus, rotavirus, coronavirus, parvovirus, Salmonella sp and E. coli are associated with such mortalities. Hog cholera is the most serious disease in swine. Rotavirus infection and transmissible gastroenteritis have been associated with neonatal diarrhoea, a major problem in some large farms. Although the poultry industry in Malaysia is fairly well-developed, loss due to disease is still a major problem. Newcastle

disease is a major source of loss faced by the industry. Other important poultry diseases include infectious bronchitis, avian coryza, mycoplasmosis and coccidiosis.

DEVELOPMENT OF ANIMAL BIOTECHNOLOGY

Until a few years ago, the application of biotechnology in animal agriculture was very limited. However, recent developments in biotechnology have shown its potential in animal health and production. Most of these activities are very much at the preliminary stages of development. Research institutions such as Universiti Pertanian Malaysia (UPM), Department of Veterinary Services (DVS) and the Malaysian Agriculture Research and Development Institute (MARDI) are engaged in research related to animal biotechnology. Some advances have been made in the development of veterinary vaccines and rapid diagnostic techniques for animal diseases. Through the cloning technique, a heat-tolerant oral Newcastle disease vaccine has been developed and this vaccine can be used to vaccinate village chickens. The enzyme-linked immunosorbent assay (ELISA) technique has also been developed for the diagnosis of important diseases of livestock. Work on monoclonal antibodies has been initiated. The use of monoclonal antibodies in ELISA and other assay systems has not only increased the sensitivity of the assay but also has provided a means of obtaining reproducible results. Genomic studies of DNA viruses with restriction endonucleases have been initiated. Analysis of structural proteins of viruses and bacteria using polyacrylamide gel electrophoresis with or without Western blotting are in progress.

Studies have also been conducted to identify microorganisms in the rumen of cattle and buffaloes in terms of cellulose degradation and higher capacity for survival as well as to elicudate their nutritional requirements and to grow them under laboratory conditions. These information together with established recombinant DNA techniques will be used to create more efficient organisms for microbial digestion in the rumen.

The technique of embryo transfer has been developed at various institutions in Malaysia. Using combinations of exogenous hormones, successful superovulation of cattle and goats has been achieved with the production of an average of 8–12 ovulations from both ovaries. Improved techniques on non-surgical collection of embryos have been developed.

History was created when the National Science and Technology Policy was formulated to include the development of biotechnology in the national five year development programme from 1986 to 1990 (Fifth Malaysia Plan, FMP). The policy reads:

> "The National Science and Technology Policy shall focus on the promotion of scientific and technological self-reliance in support of economic activities through the upgrading of research and development (R & D) capabilities by the creation of an environment conducive to scientific creativity and the improvement of scientific, educational and other relevant infrastructure."

Guided by the above policy, a strategy for the development of science and technology called "Intensification of Research in Priority Areas (IRPA)" was implemented. The major objective of IRPA is to develop strategic planning on national development through upgrading of basic research as well as applied research in exploitable areas of science in support of sectorial economic growth. Priorities on R & D in IRPA are placed under the categories of agricultural, industrial, health and strategic research. Activities related to animal biotechnology are covered under agricultural as well as industrial research. Basic research relating to biotechnology is covered under strategic research.

In addition to the development of biotechnology under the IRPA programme, the Fifth Malaysia Plan has also a provision for the establishment of a National Biotechnology Programme under the National Council for Scientific Research and Development. A Na-

tional Biotechnology Committee (NCB) was formed to plan and coordinate all activities of the programme. The functions of NBC are:

(i) to advise the government on matters pertaining to policy on research, funding and incentives to industries

(ii) to monitor new developments in biotechnology and to relate them to national needs

(iii) to facilitate and promote cooperation in R & D between research institutions and industry

(iv) to establish guidelines on a code of ethics and safety in all aspects of biotechnology development.

Five priority research sub-programmes were identified, namely molecular biology, industrial research, medical, animal and plant biotechnology.

NATIONAL ANIMAL BIOTECHNOLOGY PROGRAMME

The long term objectives of the animal biotechnology programme are:

(i) to contribute to the advancement of the livestock industry by consolidating the resources of institutions working on biotechnology which are directed to specific target problems in animal health and production

(ii) to initiate training of scientists who will contribute to developing the manpower requirements in animal biotechnology

(iii) to promote cooperation and collaboration in research and training on animal biotechnology among national organizations and between national and international organizations.

The immediate objective of this programme is to develop expertise in biotechnological techniques which can be applied to research in animal health and production. Initially, the animal biotechnology programme will concentrate on development of techniques for disease diagnosis and control. Local researchers should become familiar with many of the modern biotechnological techniques which include:

a) Enzymeimmunoassay (EIA, ELISA)

b) Polyacrylamide gel electrophoresis (PAGE) and Western blotting

c) Genome analysis

d) Dot blot ånd *in situ* hybridization

e) Southern blotting

f) Molecular cloning and probing

g) Gene sequencing

h) Hybridoma technology

Research activities undertaken cover the following areas:

(i) examination of microbes through the PAGE technique and analysis of the immunogenic and pathogenic components with or without the immunoblotting technique

(ii) genome analysis using restriction endonucleases

(iii) production of monoclonal antibodies against these microbes and their utilisation in the development of immunoblotting and enzyme-linked immunosorbent assay (ELISA) for diagnostic purposes.

FUTURE RESEARCH PRIORITIES

In Malaysia, the major areas of priority for future research in animal biotechnology are genetics, reproduction, nutrition, health and disease control.

Genetics and Reproduction

One of the most serious problems in ruminant production is low reproductive efficiency or loss which occurs between conception and weaning. Detailed studies on diseases, infertility and sterility in ruminants should, therefore, be conducted. Increased productivity can be achieved through the application of embryo transfer (ET) technique. ET is an established field technique involving the use of superovulation followed by fertilization *in vivo*, flushing out the embryos and then inserting them into the recepient animal. This technique, when combined with recombinant DNA, will enhance the genetic potential and adaptation of the embryo. The introduction of desirable genes will permit animals to resist or be more tolerant to certain environmental challenges such as specific diseases or harsher climatic conditions. The combination of recombinant DNA methods with ET will yield dairy bulls of higher breeding value for milk. With recent advances in molecular genetics, it is now possible to isolate, clone and characterize specific genes and their flanking regions. The cloned genes can then be reintroduced into animals. Various strategies exist for transferring such cloned DNA sequences into animals. Microinjection of cloned DNA into zygotic nuclei has been the preferred method in recent years. It is also possible to infect zona-free preimplantation embryos with retroviruses which transfer genetic materials to the host via the normal life cycle of the virus. Post-implantation embryos may be transformed by the injection of viral particles into the embryo. Gene transfer in mammals has been accomplished in mice, rabbit, sheep and pigs. Adequate mapping of the genome of domestic animals remains a necessary initial step before certain inherent problems of animal production can be tackled using recombinant DNA. Recombinant DNA is only fruitful if complete information on the manipulated genome is available.

Monoclonal antibody technology provides a much needed mechanism for improving methods of selective breeding. Conventional methods of producing typing reagents have provided a limited but important view of the antigenic polymorphic determinants present on white blood cells which can be used to define gene systems for selective breeding. Monoclonal antibody technology has great potential and can serve as a mechanism for identifying not only gene systems that influence susceptibility to infectious diseases but also those that control desirable performance traits. Consequently, the following areas in genetics have been identified for future research:

a) Establishment of a genomic library of local farm animals through chromosome and gene mapping

b) Identification and transfer of germplasm associated with resistance to disease

c) Identification of genetic factors related to reproduction

d) Determination of genetic markers for identification of different breeds of farm animals.

In reproduction, future research areas related to animal biotechnology include:

a) Embryo transfer for increased female reproductive rates

b) Embryo manipulation including preservation, sexing and splitting

c) Genetic modification of embryo through embryo fusion, nuclear transfer and direct gene transfer

d) Gamete manipulation including gamete preservation, sexing and *in vitro* fertilization.

Nutrition

Most feeding systems for ruminants in Malaysia incorporate a large proportion of fibrous by-products from the agricultural industry. Unfortunately, the feeding values of agro-based by-products are relatively low and as such large amounts of the by-products are left to waste. The inability of the ruminant to utilize these by-products is primarily a problem of solubilization by rumen organisms of the cell wall component of padi straw, palm-pressed fibre, etc. The microbiology of the rumen is complex. It consists of a variety of species of bacteria, protozoa and fungi. Their primary function is to degrade cellulose. The initial rate of solubilization of cellulose is the primary limitation to its rate of utilization. The factors that influence the rate of solubilization of cellulose are (i) the rate of colonization of feed particles by microbes (ii) the extent of ligno-cellulose in the cell wall which protects cellulose from digestion and (iii) the rate of production of cellulase by the rumen organisms. If rumen organisms can be modified to increase cellulase production and/or increase ligno-cellulose breakdown, then both the extent and rate of digestion in the rumen will then increase allowing higher feed intake and, therefore, higher animal productivity.

Recombinant DNA technology has been applied to produce altered bacteria with abilities to perform a number of new functions. It is possible to use such a technique to modify rumen organisms to increase the rate of digestion and digestibility of agro-based by-products. A small increase in digestibility of these by-products through the introduction of organisms altered by this technique will benefit the livestock industry enormously. Therefore, the research areas in nutrition which have been identified are:

a) Screening and characterization of rumen microbes for cellulolytic activities

b) Genetic modification of rumen microbes for enhanced lignocellulose utilization

Health and Disease Control

Biotechnology has already made a substantial contribution to animal health in the areas of vaccine production and diagnostic methods. The introduction of genetic engineering has made it possible to produce effective vaccines against livestock diseases. Using such a technique, it is possible to synthesize selected viral components in bacteria. The development of better, cheaper and safer vaccines involves (i) the identification and characterization of immunogenic antigens and (ii) synthesis and production of such antigens through recombinant DNA. These synthesized viral components can then be used for safe and effective vaccine production. Attempts are being made to develop new vaccines for diseases such as Newcastle disease, fowlpox, infectious bronchitis and haemorrhagic septicemia by the application of genetic engineering. The development of hybridoma technique has increased the possibility of defining the antigenic determinants on the surface of the virus which are of primary importance for the induction of im-

munity against disease. Monoclonal antibodies can also be used for purifiction of viral vaccines by the immune absorption technique.

Recent advances in immunology and molecular biology have contributed towards the improvement of diagnostic methods. The advent of antibodies monoclonal has provided an important tool for effective identification of diseases. Through the use of monoclonal antibody technology, it is now possible to identify antigenic differences amongst viruses and bacteria. For example, antigenic variation of surface antigens within a virus type is frequently encountered. The host immune response discriminates between these antigenic types into serotypes. An animal immune to one serotype is usually susceptible to infection by another serotype of the same virus. It has always been clear that an ability to differentiate between strains or serotypes would be an extremely important diagnostic tool. In biotechnology, monoclonal antibodies are useful in detecting antigenic differences which have been masked or could not be detected with polyclonal antisera. Other biotechnological techniques that can be applied to differentiate viral isolates include comparison of viral structural proteins by polyacrylamide gel electrophoresis and comparing viral nucleic acids by electrophoresis after endonuclase digestion of genome. We can also expect methods, such as sequencing the base of nucleic and amino acids, to be applied in the future for diagnostic work.

Future research areas in animal health and disease control, therefore, should include:

a) Vaccine development through modified pathogen or clone immunizing antigen

b) Monoclonal antibodies for application in diagnostics, vaccination and separation technology

c) Nucleic acid probes for use in diagnosis of infectious diseases

d) Genomic analysis of animal viruses

ISSUES RELATING TO ANIMAL BIOTECHNOLOGY

There has been considerable public and political interests in the field of biotechnology because of reported "breakthroughs" of possible great significance. Most research and teaching institutions in Malaysia have plans or programs for harnessing biotechnology for national development. It is important that all of these institutions understand realistically the potentials and problems associated with biotechnology research. Many issues have to be considered before the new technology can be utilized to solve problems in animal health and production successfully. The issues are as follows:

Education and training

The most important component of any successful animal biotechnology programme is trained personnel. Training should include a solid background in veterinary science followed by graduate level work in microbiology, biochemistry and molecular biology without sacrificing traditional areas of importance in veterinary medicine and animal science. Professor David Baltimore, a Nobel Laureate from the Massachusettes Institute of Technology, stated that:

> "Approximately 30 years is needed, starting with early maturing through a long period of apprenticeship at graduate school and post-doctoral work, to develop a researcher capable of handling modern biotechnology. Those of us who train people in modern biology know that the most important experience is acquired when things go wrong. One must be in a situation to see how many different things can go wrong and how you can get around those things to learn how to solve the problems. One of the saddest recurrence is

when someone who is inexperienced and is working in a relatively isolated area spend six months making the same mistake because he does not know it is a mistake."

One of the most important constraints in the development of animal biotechnology research in Malaysia is the lack of trained personnel. They are few in numbers and are scattered in the various research and teaching institutions. One way to overcome this problem is to stimulate interaction between university departments and research institutes involved in animal biotechnology. These interactions may take many forms such as joint research projects and long-term bilateral collaboration in teaching and research. It is also essential that the most appropriate research programs be identified and related training be undertaken. This will involve:

(i) workshops on priorities, resource allocations and implementation strategies

(ii) participation in national and international conferences by researchers

(iii) long-term research manpower development at both the graduate and postdoctoral levels

(iv) training of technicians through short courses.

The National Biotechnology Programme under the National Council for Scientific Research and Development should be the agency for facilitating the development of manpower and training through the support of well-designed training programs, attachment of scientists from developed countries and awards to identify qualified personnel from national research and teaching institutions.

Infrastructure

Biotechnology research is continually dependent on infrastructure. A successful programme will require equipped and functional laboratory facilities, well-equipped libraries and continual supply of consumables. One of the biggest problems is the acquisition of materials from abroad. A thorough evaluation of the minimal requirements for success and a plan to deal with local constraints should be part and parcel of the R & D programme in biotechnology. A continual support of funds is, of course, crucial.

CONCLUSION

We are in the era of biotechnology. If Malaysia is to reap the benefits of this technology, it needs local capabilities, the acquisition of which requires tremendous commitment. One possibility for accomplishing this is the pooling of resources from various institutions to establish laboratories that can tackle local problems. Ideally there should be improved collaboration between the sciences and engineering and between the researchers in public institutions and industry. Greater government support for fundamental as well as applied research is desirable.

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RINGKASAN

BIOTEKNOLOGI HAIWAN – PERSPEKTIF MALAYSIA.

Sehingga beberapa tahun kebelakangan ini, penggunaan bioteknologi dalam pertanian ternakan adalah sangat terhad. Perkembangan terbaru dalam bioteknologi walau bagaimanapun telah menunjukkan keupayaan penggunaannya dalam kesihatan dan produksi haiwan. Kebanyakan aktiviti-aktiviti ini masih lagi di peringkat permulaan. Di Malaysia terdapat tiga bidang utama penyelidikan sehubung dengan peranan bioteknologi dalam kesihatan dan produksi haiwan. Ini adalah genetik dan reproduksi, pemakanan dan kesihatan haiwan. Penyelidikan bioteknologi melibatkan teknologi penyelidikan yang sungguh kompleks dan teknik-teknik bermutu tinggi yang belum digunakan dalam sains biologi. Adalah penting kepakaran dalam teknologi ini perlu dibentuk dahulu sebelum projek-projek penyelidikan tempatan jangka panjang dan yang memerlukan perbelanjaan yang tinggi dapat dijalankan. Kesan bioteknologi ke atas industri ternakan adalah sangat luas. Kegunaannya dalam pertanian ternakan dan perubatan veterinar sungguh ketara. Penggunaan bioteknologi di Malaysia boleh membawa kepada hasilan dan kaedah-kaedah yang berguna.