Arab Journal of Scientific Research, 18 (2), pp 73-80 (2000)

REVIEW PAPER

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Some Efforts of Saudi Arabia in Biotechnology

Abstract: With the advancement of science in different fields, the applications of biotechnology have increased, based on its use. Saudi Arabia, as one of the developing countries is using some biotechnological applications in agriculture, medicine, environment and petrochemicals. In Saudi Arabia, biotechnology has been used both in research and commercial applications. This paper illustrates the efforts made for research in biotechnology, such as in tissue culture, DNA studies in plants and desulfurization of oil. It also shows some of the industrial applications of biotechnology that are suitable for Saudi Arabia and the Gulf area. It also shows the efforts being made to transfer the basic knowledge of biotechnology and the techniques that have commercial returns.

عرض لجهود تبني تطور التقانات الحيوية في المملكة العربية السعودية

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المستخلص: مع تقدم البحث العلمي في مجال التقانات الحيوية ، تعددت تطبيقات هذه التقانات وتعددت مسمياتها حسب المجال الذي تستخدم فيه ، والمملكة العربية السعودية كإحدى الدول النامية لم تفوت الفرصة في استخدام هذه التقانات في كل من الزراعة ، الطب ، البيئة بالإضافة الى الصناعات النفطية ، ويأتي استخدام المملكة لهذه التقانات على المستويين البحثي والتطبيقي التجاري . تعرض هذه الدراسة الجهود المبذولة في أوجه النشاط البحثي في مجالات التقانات الحيوية بدءا من تقنية زراعة الأنسجة والتعامل مع المادة الوراثية DNA الى تحسين مواصفات النفط . كما تعرض هذه الدراسة بعض التطبيقات الصناعية للتقنيات الحيوية المناسبة لدول المنطقة والجهود المبذولة لنقل وتوطين المبادئ الأساس لعلوم التقانات الحيوية أو تقنيات حيوية محددة والمردود التجاري المتوقع

Introduction

Biotechnology is nowadays a strong tool in the hands of scientists for use to promote many aspects of biological applications. It is a resultant of a group of science fields; it is partly biochemistry as it deals with promoters and inhibitors, microbiology as microorganisms are widely used as tools of transformation, and molecular biology as genetic materials are the most common tools of biotechnology.

Saudi Arabia as a developing country has endeavored to benefit from biotechnology. Biotechnology in agriculture is becoming increasingly important in the development process in Saudi Arabia. Because of the significant role of the private sector in biotechnology, this new technology brings with it important and complex intellectual property issues.

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There are many research components within most of plant biotechnology programs, such as the molecular biology of plant viruses, transgenic virus resistance and plant transformation and micropropagation. In most cases the objective of research in plant biotechnology is the improvement in disease and insect resistance, the improvements in environmental sustainability and in yield and quality of field crops. Other than insect and disease resistance, some labs have directed their efforts towards producing transgenic plants to eliminate some common fruit problems such as browning, or to analyze gene expression events during fruit ripening in order to improve fruit quality.

Many countries conduct research to help in conservation of natural resources, crop production and protection, animal production and protection, post harvest quality and use, human nutrition, and management systems. (Department of Economic Studies, 1998). In the context of Saudi Arabia, a developing country with vast arid lands, arid climate and abundant petroleum resources, there is more justification to make use of this technology to enhance oil recovery and to reduce environmental pollution. Recently, biotechnological techniques have been used to remove sulfur from fossil fuels

by biocatalytic desulfurization (BDS). In addition bioremedation has also been applied to help in cleaning up the environment.

Research centers have started research to diagnose local commonly inherited diseases in order to reduce the increased number of patients. Other research has been started to use biotechnology in gene therapy and early discovery of diseases. On the other hand, forensic departments have begun using DNA fingerprinting in their crime investigations, using updated methods and instruments.

Pharmaceutical research centers have started technology transfers to produce certain bio-products using biotechnology methods. Other companies support this biotechnology movement by producing the required oligonucleotides and enzymes.

Since biotechnology in the country is in its early stages, researchers are trying to apply the latest techniques and methods such as biosensors, surface plasmonresonance and transgenic methods.

The Current Situation in Saudi Arabia

In agriculture, where plants and animals are facing diseases and environmental stresses, biotechnology is a good tool to solve such problems. The cash crops of Saudi Arabia, such as date palm, wheat and vegetables, are facing many problems related to their productivity and quality, e.g., insects that are affecting date palms such as red weevil (*Rhynchophorus ferrugineus)* are destroying thousands of trees, especially in the Eastern Province. Saudi Arabia is one of the leading countries in date palm production. Out of 13 million date palm trees grown in different areas of the country, more than 77% are considered to be at production stage, covering an area of 93.825 hectares and producing 589,000 tons of dates (USDA 1990). The production is distributed among more than 400 cultivars including 50-60 commercially important cultivars. Most plant tissue culture activities are geared towards the date palm (Table 1). Tissue culture research was first started in 1982 at King Faisal University Date Palm Research Center. Since then public and private labs and research activities have increased to reach more than 6 public labs and 5 private labs authorized by the Ministry of Agriculture and funded by Saudi Arabian Agricultural Bank. Over 17 applications have been submitted to the Ministry of Agriculture as commercial tissue culture labs (Asharq Al-Awsat, 1999) Other than just micropropagation, some labs are developing some cultivars, e.g., salt tolerant ones (Abu El-Nil M. 1989). Some other crops are also being given attention in terms of *in vitro* research. At King Saud University, Riyadh, applied research has been funded by King Abdulaziz City for Science & Technology (KACST) to study potato diseases and production of pathogen-free potato clones via tissue culture. KACST also has funded many research projects related to biotechnological applications (Tables 2, 3 and 4) (Al-Khalifah and Alani, 1998). The first activity of plant biotechnology research and application might have been the micropropagation of date palm that started 1982 in King Faisal University–Al-Hofuf. In 1986 the Date Palm Research Center developed a protocol for somatic embryogenesis and in 1995 an organogenesis protocol was established. The latter is highly recommended to eliminate mutations which are highly unwanted in the date palm business. Plant biotechnology at KACST started with the establishment of a tissue culture lab in 1996. The Tissue Culture Lab Program has included *in vitro* culture of important cultivars of date palm and their DNA fingerprinting through RAPD analysis. Both embryogenesis and organogenesis protocols are under study. Shoot tips and leaf primordia from two to three year old offshoots have been used as explants. Murashige and Skoog media supplemented with 2,4-D, Kinetin, 2ip and NAA in different combination were used for the development of callus and embryogenic callus. Regeneration of some cultivars was achieved through embryogenesis. DNA fingerprinting of date palm cultivars through RAPD analysis is also in progress. Out of 140 RAPD primers (Operon) initially screened for reproducible and polymorphic DNA amplification, through PCR, 42 primers were selected for DNA fingerprinting. These 42 primers are now being applied for the identification and assessment of genetic diversity among the different cultivars of date palm. This assessment can be used as a data base for further research on date palm identification.

Scientific Meetings and Conferences in Biotechnology

KACST, in cooperation with other institutions, has arranged or participated in many scientific activities in this field. In November, 1984, the Saudi Society for Biological Sciences organized the first Arab Gulf conference on biotechnology and applied microbiology in collaboration with the Arab Bureau of Education for the Gulf States. This was followed by two conferences in 1987. In April 1987

Table 1. Institusions in Saudi Arabia Working on Research and Applications of Plant Tissue Culture

Institution	Financial Resources	Activities Started in	Main Activities
Date Palm Research Center, Hofuf.	KACST & King Faisal Univ.	1992	• Training and research • Development of 2 tissue culture protocols for date palms • Field trials of tissue culture date palms. • Hosted three national symposiums on date palms.
Plant Production Department King Saud Univ. Riyadh	KACST & King Saud Univ.	1983	• Training and research • Development of tissue culture protocols for arak (*Salvadora persica*), date palm, pomegranate, potato, and strawberries.
Plant Production Department King Saud University Qassim.	KACST & King Saud Univ.	1994	• Training and research • Development of tissue culture protocols for arak (*Salvadora persica*), date palm, pomegranate, potato, and strawberries.
Pharmaceutical Department King Saud Univ. Riyadh.	KACST & King Saud Univ.	1997	• Production of active metabolites by tissue culture.
National Agricultural and Water Research Center, Riyadh.	Ministry of Agric.	1989	Research • Serological typing of potato virus diseases using ELISA. • Development of a tissue culture protocol for potato. • Induction of drought/salt tolerant wheat lines.
Tissue Culture Lab, Environmental Scientific Institute, KACST, Riyadh.	KACST & Japanese Cooperation	1997	Research • Development of tissue culture protocols for date palm and salt tolerant plants • Classifying date palm tree polymorphism.
Private Companies Saudi American Plant Development, Dammam and other 5 private labs.	Escagenetics Co. USA Revenue from sales	1992	Research • Development of 2 tissue culture protocols for date palm. • Field trials of tissue culture date palms. • Technology development • Micropropagation of date palm. • Commercial production. • Sales of micropropagated date palms to farmers.

Source: ESCWA (1997), and updating by N. Al-Khalifah (KACST, 1999)

Table 2. Annual Research Program Projects Related to Biotechnology

Title	Institution	Granted Budget	Status
Induced Genetic Mutation in Wheat by Diethyl Sulfate.	KSU	168.000	Finished
Potato Diseases and Production of Pathogen-Free Potato Clones Via Tissue Culture in Saudi Arabia.	KSU	883.375	"
Genetic Epidemiologic Studies of Selected Neurologic Diseases in Saudi Children.	KFSHRC	479.000	"
Induction and Selection of Salt and Drought Tolerant Lines of Wheat by Plant Tissue Culture.	KSUG	625.000	"
Studying the Productivity of Native Chickens and the Possibilities of their Genetic Improvement in the Kingdom of Saudi Arabia.	KFUH	810.160	"
Molecular Basis of Inherited Neurological Diseases in Saudi Arabia.	KFHNG	789.000	Ongoing
Epidemiological Study of Deafness in Childhood in Saudi Arabia.	KSU	1.482.000	"
Purification and Characterization of Prokallikrein and Kallikrein from Camel Pancreas.	KKMA	844.700	Finished
Biotechnological Production of Biologically Active Metabolites by Plant Cell Culture Techniques.	KSU	720.720	Ongoing
Applications of Recombinant DNA Technology in Medicine – On the Look for Genetic Markers for Non-Communicable Diseases.	KSU	2.130.760	"
Surveillance of Antibiotic-Resistant Bacteria in M.O.H Hospitals.	MHELT	1.008.600	"
Genetic Engineering Techniques as a Tool to Identify some Economical Date Palm (*Phoenix Dactylifera L.*) Cultivars in Saudi Arabia.	KFUH	1.867.000	"
Recombinant DNA Probes and Polymers Chain Reaction for Detection of Brucella Infection in Humans.	KFSHRC	759.500	"
Phytochemical and Biological Evaluation of Saudi Plants.	KSU	2.766.336	Finished
Aspects of Human Haemoglobins and Haemoglobinopathies in Arabian Peninsula Studies at Genetic and Molecular Levels.	KSU	6.473.900	"
Utilization of Saudi Dates and their By-Products in Biosynthesis of Antibiotics.	KSU	704.450	"

Table 3. Limited Grants Program Projects Related to Biotechnology

Title	Institution	Granted Budget
Patterns of Susceptibility or Resistance of Local Clinical Isolates to Commonly Used Antibiotics Correlation with Antibiotics Consumption with Mech.	KSU	80.000
Routine Use of Prophylactic Antibiotics in Cesarean Section: A Multi Center Prospective Double-Bond Placebo-Controlled Randomized Clinical Trial.	KAU	72.766
Residues of Diethylstilbesterol (DES) and Antibiotics in Milk, Meat and Eggs.	KFU-H	99.580
Screening and Identification of Resistant Plasmids in Multi-Drug Resistant Gram-Negative Bacteria Isolated from Riyadh Area.	KFU-H	84.900

Table 4. Annual Research Program Newly Submitted Projects Related to Biotechnology

Title	Institution	Requested Budget
Imaging Pancreatic βcell mass with radiohalogenated synthetic somatostatin non-peptide agonist.	KFS-Hosp	981.000
Identification of MHC class I and II alleles by sequence based typing in major tribes of Saudi Arabia.	KFS-Hosp.	2.042.499
Genetic basis of male infertility in Saudi Arabian population	KFS-Hosp	721.900

KACST organized a workshop on utilizing the energy of biomass (organic waste) in the Arab countries in collaboration with the Federation of Arab Scientific Research Councils. In December 1987 KACST sponsored the National Seminar on Genetic Engineering and Biotechnology in collaboration with UNIDO and King Saud University in Riyadh. The seminar ended with many recommendations for utilizing and employing biotechnology applications in the Kingdom. Based on these recommendations the National Committee of Genetic Engineering and Biotechnology was initiated. Presentations of the workshops and the seminars were published by KACST in Proceedings No 45 and 28 respectively. In March 1990, King Saud University (KSU), in collaboration with KACST, organized the symposium on DNA Technology and Genetic Engineering in Human Diseases, which was published by KACST as Proceedings No. 65. In October 1993 KACST and KSU organized the Symposium on Medical Genetics in the Setting of Middle Eastern Populations. Following that, the Symposium on Genetic Disorders in Arab Populations, which presented a wealth of indicative information, together with the first Gulf Symposium on Genetic Disorders were sponsored by KACST and organized by KSU in November 1997. Since 1993 KACST, in collaboration with the Petroleum Energy Center of Japan, has organized an annual lecture series on Biotechnology and Membrane Separation, discussing the results of research carried out at KACST. During the past two decades King Faisal University has organized three great symposiums on the date palm (March 1982, March 1986 and January 1993) where extensive research work on date palm *in vitro* culture was presented and included in the three proceedings of such activities.

National Committee on Genetic Engineering and Biotechnology

The National Committee on Genetic Engineering and Biotechnology was initiated in 1992 and reestablished in 1999. The committee consists of seven members from different governmental organizations and specializations. Many activities have been organized, such as monthly lectures covering the biotechnology fields and building a national database for information about specialists, organizations, equipment and research activities related to biotechnology. The committee is the national focal point of bio-safety. It also participates and communicates with the international biodiversity and bioethics committees.

Future Anticipations

The unlimited demands on biotechnology make every country look for means of adopting some of its applications. Because it is costly and of a sophisticated nature, there are limitations to applying biotechnology in many countries. In every field of science where biotechnology can be applied, scientists are aspiring to adopt it. In agriculture, there is a high demand for conserving the natural resources by reducing water and soil pollutants and adapting plants to the stressful conditions of Saudi Arabia. Crop production in terms of quantity and quality is limited by heat, drought, and salt stress; therefore, plants need to be engineered to adapt to such conditions. Resistance to diseases, pests, insects and weeds can be increased. Animal production and protection can be improved by implementing reliable preventive measures against livestock diseases, improving diagnostic tests and improving biocontrol organisms used against livestock insects and pests. Farm products can be improved to be of the best marketability by enhancing non-food uses and developing new uses for surplus products. Finally, biosafety, management systems and other benefits of biotechnology are also in demand.

Saudi Arabia is currently working on a long term national plan for science and technology. Biotechnology is included in this plan. A group of specialists in this field is working on setting up this part of the plan. It will cover appropriate technologies for the Kingdom, such as plant improvement, gene therapy, and oil desulfurization.

Solving Some Environmental Problems

Saudi Arabia has major issues with its petroleum resources:

1. The refinery wastes, oily sludges, tank residues and oil contaminated soils are considered among the most dangerous for the environment in Saudi Arabia. Oily waste is the residue of cleaning and restoration of crude oil tanks and other process equipment in refineries. It is a mixture of oil emulsion with naphtalenic compounds, water, waxes and iron oxide. The waste carries a high risk of environmental pollution. Biodisposal, also known as landfarming, presents an inexpensive and successful example of using biotechnological techniques to solve such problems (Alani, 1992).

   This application uses soil aerobic microorganisms to biodegrade the oily waste in the upper soil zone to carbon dioxide and water. In 1982, the Arabian American Oil Company (ARAMCO) considered landfarming for disposal of waste. Therefore, a pilot landfarm was established at Ras Tanura Refinery to evaluate this treatment method and to develop techniques that would be used in Saudi refineries.

   The biodegradation of the sludge was completed after two months at the biodegradation rate of 475,000 liters per hectare. In 1984, the first sludge application was made and ARAMCO reached the conclusion that land treatment was the safest, most cost effective and environmentally acceptable waste management technology available for the tankage wastes generated as part of its refinery operation (Ala ud Din 1989).

2. Saudi Arabia is a major producer of crude oil and natural gas and accommodates the largest oil reserves in the world. It should consider the biotechnological process to enhance oil recovery. In some fields, Saudi crude oil contains numerous heterocyclic organic sulfur compounds such as dibenzothiophene (DBT) and its alkalyted derivatives. These compounds which are becoming one of the major sources of acid rain due to sulfur emission during combustion, can be easily degraded by hydrodesulfurization (HDS), which is being applied in refineries worldwide.

Microbial desulfurization may provide an improved biotechnological technique. It can take place under milder refinery processes compared with HDS, which is carried out under severe conditions such as extremely high temperature and pressure. Moreover, it can make a selective cleaning carbon-sulfur bond in heterocyclic organic sulfur compounds without destroying the carbon skeleton. Almost all the previous research work has investigated microorganisms grown at normal temperatures, usually in the vicinity of 30° C.

Refining processes are accompanied by high temperature. Consequently, the treated petroleum fractions must be allowed to cool down to normal temperature for microbial desulfurization to proceed. Moreover, the rate of chemical reaction is generally increased with increased reaction temperature. It is therefore advantageous to use bacteria that withstand higher temperatures than ambient temperatures. This can be achieved by screening thermophilic bacteria from the environment. Many soil samples have been collected in Saudi Arabia and experiments have been conducted on enrichment culture by using some semi-synthetic media containing DBT as a sole source of sulfur.

Several kinds of bacteria grown at 30°C have been isolated. These bacteria are thermophilic, aerobic and are capable of converting DBT to 2-hydroxybiphenyl. It is very useful to find new desulfurizing bacteria in terms of improvement of the existing desulfurizing gene. It is also important when a patent right is exercised. Knowing these factors, the screening was done using soils which were collected from the suburban area of Riyadh and Dhahran, and the medium on which DBT was made as the only sulfur source, which metabolizes DBT and produces 2-HBT, was obtained. It contained the same DBT metabolic activity, metabolic intermediate and sulfur transport system as KA251R. Therefore, it is assumed that both KA251R and SAT01 hold the same genes related to DBT degradation. So far, new desulfurization genes have not been obtained.

DNA Research Applications

Using DNA in forensic applications was started in the mid 1980s, mainly in the DNA Finger Print Unit-Forensic Laboratory, Ministry of Interior, which was established in 1985, initially with one person and a thermocycler. Nowadays there are very well qualified and trained researchers. They use updated equipment and materials. DNA finger print unit investigations include murder, rape, paternity,personal identification, and other applications.

Commercial Applications

Pharmaceutical Research

There are three pharmaceutical companies in Saudi Arabia, one of which is Saudi Pharmaceutical Industries and Medical Applications (SPIMACO). SPIMACO is a joint-stock company with a fully paid up capital of $160 million. It was established in January 1986 with the main objective of setting up an advanced pharmaceutical industry in Saudi Arabia, for the local production of medicines. Production started in the first quarter of 1990 with six products and increased to over 90 products in 1998. Production capabilities include production of oral solids, oral liquids, dry powders, injectables, ointments, creams, suppositories, and various other forms.

Recently SPIMACO started a joint project with King Abdulaziz City for Science and Technology (KACST) to produce medicines locally using biotechnology. They are planning to invest more than $20 million to transfer and use biotechnology in the pharmaceutical production field. Biotechnology transfer projects are facing difficulties such as importing required knowledge, equipment, and materials. However, qualified personnel and cooperation with foreign biotechnology companies can overcome these difficulties.

Gulf Biotech

Gulf Biotech Company is a part of the Dallah Group, established in 1998. Their mission is to meet the specifications for custom synthetic oligonucleotides and to deliver purified products within 72 hours. They aim at supporting the research community with high quality services and complete satisfaction. All oligonucleotides are quality tested and the identity is guaranteed. Gulf Biotech has their

own direct collaboration with distinguished biotech laboratories and universities in order to get scientific support and the latest information on advancement. They use the latest equipment and western technology and techniques in the DNA manufacturing process. Gulf Biotech started with oligonucleotide synthesis and they plan to start production and packaging restriction enzymes soon (depending on the demand). Their products cover synthesis of the following:

- Sequencing primers
- Short DNA duplexes with internal restriction site
- Stop linkers
- Linkers
- Phosphorylated linkers
- Viral primers and probes
- Bacterial primers and probes
- Human genomic primers and probes

Nowadays the company synthesizes hundreds of varieties of oligonucleotides in good quality and identity. However, researchers and scientists require full or at least most of the restriction enzymes and DNA/RNA purification kits in order to meet their goals without spending weeks waiting for a single enzyme.

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(Received 21/12/1999, in revised form 21/01/2001)