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BIOTECHNOLOGY: AN ALTERNATIVE GOLDMINE

By

PROFESSOR R. A. BELLO

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BIOTECHNOLOGY: AN ALTERNATIVE GOLDMINE

An Inaugural Lecture Delivered at the
University of Lagos
On Wednesday, May 3, 2006

By

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1. INTRODUCTION

Biotechnology is a technology or group of technologies that is fast changing all facets of our life, from the food we eat to the way we live. Every aspect of living is being positively influenced by advents in Biotechnology.

What is Biotechnology? Biotechnology can be literally looked at as the use of biological processes to solve problems or make useful products. Biological processes have been used to solve problems for human beings for ages. Crops have been grown and animals raised to meet the food and clothing needs of human beings. Biological processes involving microorganisms have also been used for long to make useful products, like 'garri', bread, cheese, antibiotics and other biochemicals for medical uses.

However, in spite of this long use of biological processes or biotechnology to benefit mankind, Biotechnology seemed to have recently been receiving a lot of attention. Why is this so? The advances in the study of biology, in the last three decades, enabled the isolation and detailed study of the use of the smallest parts of the organisms, the biological molecules. This has led to the development of new technologies dealing with the art of manipulating the biological molecules to recreate themselves and for solving problems emanating from deficiencies in the basic building blocks. Hence, **Biotechnology is now being seen as the art of using cellular or molecular processes to solve problems or make useful products.** This new Biotechnology is more aptly looked at as a collection of biotechnologies, each capitalizing on the attributes of cells, such as their manufacturing capabilities and putting biological molecules, such as DNA and proteins to work for humans. New technologies get developed regularly. We now talk of: Monoclonal Antibody Technology, Cell Culture Technology, Protein Engineering Technology, Biosensor Technology, Cloning Technology, Recombinant DNA Technology and more recently Nanobiotechnology.

The creation of the sheep "Doly" was the first major publicized eye opener to what Biotechnology can be used for. Of course, much earlier, Biotechnology had enabled the genetic manipulation of seeds and plants for the production of pest-resistant strains for the production of bumper harvests in Agriculture, production of "superbugs" in Industrial Microbiology as well as for the production of antibiotics for medical uses.

The latest of the advances in Biotechnology enables the probing and studying of the bioproteins to the nano (10^{-9}) level. This is now enabling a better understanding of the causes and treatments of erstwhile recalcitrant disorders in the human system. Solutions are being seen to be feasible for disorders like cirrhosis, epilepsy and Parkinson's disease through cell transplants and for head and spinal cord injuries or degenerative diseases such as Alzheimer's disease up to cancer and other terminal diseases. In fact, the aging process is being explored. The ultimate is in the re-creation of human beings, which is being resisted on ethical grounds.

These breakthroughs in Biotechnology being achieved with recourse to the basic biological molecules seem to have had a mention in the scriptures. It is interesting to note that the Holy Quran, in surah 23 (Al Mu'minun) verses 13 – 14, vividly scientifically described the process of man's creation as follows:

“13 Then we placed him
As (a drop of) sperm
In a place of rest,
Firmly fixed.

14 Then We made the sperm
Into **clot of congealed blood**;
Then of that clot We made
A (foetus) lump; then We
Made out of that lump
Bones and clothed the bones
With flesh; then **We developed**
Out of it another creature.
So blessed be Allah,
The Best to create!”

The emphasis here is the description of the fact that all that is in the man as created is in the basic “clot of congealed blood” formed from the sperm. This is what recent advances in Mammalian Cell Culture Technology, particularly Embryonic Stem Cells Technology as well as the Somatic Cell Nuclear Transfer (SCNT) Technology seem to be delving into, where embryonic stem cells and somatic cells generated from the basic embryo and/or human

cell are being manipulated to therapeutically solve hitherto difficult medical problems, up to cancer as well as problems associated with aging.

In summary, Biotechnology now utilizes the knowledge of the biomolecules to develop better yielding crops in Agriculture, better understanding of the human aging process and treatment of erstwhile recalcitrant ailments like cancer in Medicine, creating 'superbugs' for cleansing the environment, and special strains of microorganisms for Industrial production processes.

For our own purposes and better understanding, we will look at Biotechnology through its applications and broadly categorize it into the following areas: (Fig 1.1)

- Agricultural
- Medical
- Industrial
- Environmental
- Regulatory Matters

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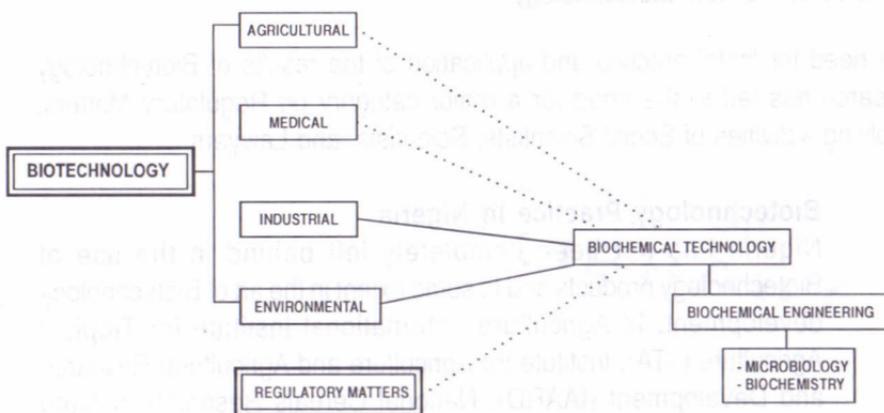


Fig. 1.1 *Biotechnology and Biochemical Engineering*

In Agricultural Biotechnology, gene manipulation and tissue culture development and propagation leading to improved seedlings, etc. are engaged in to obtain better yields per unit crop or animal to meet the food requirement of the fast growing world population.

In Medical Biotechnology, gene manipulation, leading to cloning of various organs/humans, 'super' microorganisms development for the production of better or more antibiotics, development of vaccines, etc are being carried out.

In Industrial Biotechnology, better ways of producing various biochemicals (e.g. alcohol, vitamins, etc) or organisms (yeast, etc) with the aid of genetic manipulation and/or media formulation are exploited.

Environmental Biotechnology involves keeping the environment safe for human use via degradation of hazardous materials biologically. Bioremediation of oil-polluted environment is a typical example.

As is seen from all these applications, the common front in the modern day exploit is being able to produce or manipulate genes and other biological molecules now up to the nano-level so as to produce organisms, plants or cells that would behave the way the researcher or applicant wants. This is captured in the new Biotechnology.

The need for 'safe' practice and application of the results of Biotechnology research has led to the need for a major category on Regulatory Matters, involving activities of Social Scientists, Scientists, and Lawyers.

1.1 Biotechnology Practice in Nigeria

Nigeria has not been completely left behind in the use of Biotechnology products and to some extent in the art of Biotechnology development. In Agriculture, International Institute for Tropical Agriculture (IITA), Institute for Agriculture and Agricultural Research and Development (IAARD), National Cereals Research Institute (NCRI), National Roots Crops Research Institute and other agricultural research institutions have, for decades, been developing and putting into use pest-resistant and better yielding strains of their plants. Maize farmers now buy seedlings rather than grow from old stocks. All these are examples of products of Biotechnology in use.

Various drugs and industrial products of Biotechnology are in the

Nigerian market. Similarly, medical practices, based on medical biotechnology development are in use in Nigeria (in vitro fertilisation, etc). Bioremediation of polluted environments is now being employed in the oil-polluted environments of the South-South zone of Nigeria. The various biotechnologies are also being put to use in active research at the Nigerian Institute for Medical Research and other medical research laboratories.

There are other primary Biotechnology practices that are basic to Nigeria. Examples are production of condiments (e.g “ogiri” from melon) production of alcoholic beverages (e.g “burukutu” from millet).

However, there is the need to face the challenges of modern Biotechnology and have a coordinated approach to the development and use of Biotechnology in our national life.

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2. BIOCHEMICAL ENGINEERING

How does a Chemical Engineer come into Biotechnology, which deals with microorganisms and biological molecules? Technology, generally, is the art of putting into application a scientific finding. This, thus, involves the application of engineering principles to scientific findings to make it available for general application (Fig 2.1).

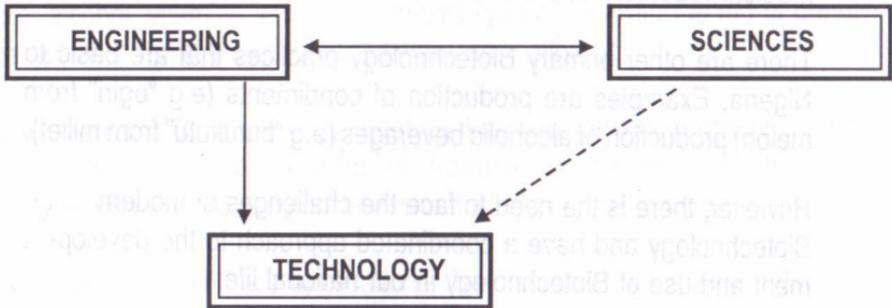


Fig. 2.1 Evolution of Technology

Biochemical Engineering is the first attempt at developing technology involving biological processes. As we all know, Technology is an art and is developed by Engineers, with inputs from related Sciences. After revolutionizing Chemical Technology in the 1950s, Chemical Engineering was called upon to adapt its Technology to biological processes, taking into cognizance, the peculiarity of biological processes. This gave birth to the specialization, Biochemical Engineering. Its first line of use was in the large-scale production of antibiotics and other industrial biochemicals. This is why Biochemical Engineering is usually defined as involving the industrial exploitation of microorganisms to produce more of itself and/or biochemicals. Hence, Biochemical Engineering is the Engineering basis of Industrial Biotechnology and to a large extent Environmental Biotechnology.

Advances in Biochemical Engineering can be better looked at from aspects affecting the development and operation of bioprocesses. As Chemical Engineers are often referred to as Process Engineers, so can Biochemical Engineers be seen as Bioprocess Engineers.

Typical bioprocesses of industrial importance are:

- production of biochemicals (vitamins, alcohol, etc)
- production of tissue culture
- industrial waste water treatment
- bioremediation processes.

In all these cases, the objective is to economically mass-produce the products or handle the wastes industrially on a large scale. While these processes can more readily be developed at the bench scale, it is the function of the Biochemical Engineer to develop an appropriate scenario to scale the process up to industrial size, based on the scientific results of Microbiologists, Biochemists, etc. Hence, in general, Biochemical Engineering is involved with Bioprocess Development.

2.1. Typical Biological Process

A typical biological process involving fermentation is shown in Fig. 2.2. Whether it is batch or continuous, it will generally have the following identifiable unit operations:

a) *Medium Formulation / Sterilisation Unit*

In this unit, the medium in which the microorganism is to grow maximally is prepared. This is based on results of previous work carried out on the characteristics of the organism, principally by Microbiologists.

Here, the basic feed components have to be supplied in the organic or inorganic forms. The use of organic compounds, which are in ready supply, is usually preferred in industrial processes as these usually supply the bulk of the micronutrients, which will have hitherto been supplied directly and more extensively. The medium must necessarily satisfy the carbon to nitrogen ratio as well as other needs for the growth of the organism.

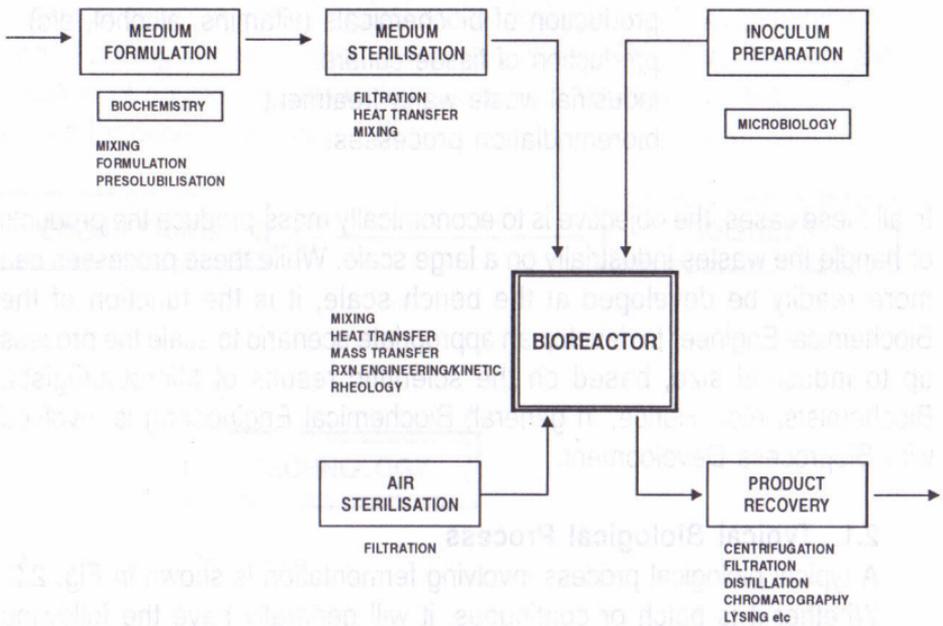


Fig. 2.2. General Schematic of a Typical Biological Process

Biochemistry of the components comes fully in use in the formulation of the medium while Microbiologists determine the optimal combinations of the components. In preparing the medium, usually in the liquid medium, mixing is employed and sometimes presolubilisation of the substrate (main feed component) is needed.

Where a sterile environment is required for the intended production, sterilization of the medium is essential to eliminate, within accommodation limit, unwanted microorganisms in the medium. This is either done 'in situ' in the bioreactor or in a separate sterilisation unit.

Sterilisation is usually carried out industrially via heating. Other methods used include Ultra-filtration, use of chemicals and radiation.

b) *Inoculum Preparation*

The inoculum is the base quantity of organisms required for transfer into the bioreactor to initiate and continue the production/growth process. The necessary microbiological cautions have to be taken and the organism has to be grown under the same conditions as exist in the bioreactor in the large scale. The medium used to produce the inoculum must necessarily be the same as the one used for the production process. It is desired that the inoculum be at least 10% of the working volume of the bioreactor.

In wastewater treatment processes, organisms present in the system (e.g. ponds) are usually employed for devouring the organic wastes in the wastewater and hence, inoculum addition may not be necessary. When the process is not microbial, e.g. enzyme processes, the use or development of inoculum is also not necessary.

c) *Air Supply / Sterilisation*

Many of the industrial processes utilise organisms needing molecular oxygen in their cycle. Where oxygen is needed (i.e. for aerobic processes), it cannot be supplied economically in large-scale processes as oxygen because of cost. It is obtained from air bubbled into the liquid. In fact, because oxygen is only 21% of air and because air and oxygen are slightly soluble in water, the supply of oxygen for aerobic processes is usually the basis for the design of the bioreactor.

When the process has to be aseptic, the possible contaminants from the air have to be removed to acceptable limits. Air sterilisation is carried out utilising filter beds of fibrous materials. Non-aseptic processes would not require the sterilisation of the air.

d) Fermentation In Bioreactor

The medium containing the key substrate(s) is transferred from the medium formulation unit or steriliser to the bioreactor either continuously or batchwise, depending on the type of process envisaged. This is then inoculated with the desired organism(s), pure or mixed.

Air is fed in, if required, and the desired metabolisation of the medium occurs in the bioreactor, whereby the substrates are transformed into the desired product(s). To achieve this, the environmental conditions in the bioreactor have to be appropriate for the desired fermentation. That is, the temperature, pH, dissolved oxygen level, foaming and other parameters have to be monitored and made appropriate to suit the needs of the fermentation.

e) Product Recovery

The product recovery stage involves the separation of the targeted product of the fermentation from other constituents of the fermentation broth and its subsequent purification to the desired level. Products of microbial processes are either intracellular (i. e. within the cells) or extracellular (outside the cell in the fermentation broth). Hence, the first exercise in product recovery is usually the separation of the cells from the broth through centrifugation, filtration, ultrafiltration, etc. With this, the cells are largely separated from the broth. If the product is intracellular, the cells are the useful product while the broth is a byproduct. The cells are broken open, through lysing, etc., and the content subjected to one or more separation processes (chromatography, absorption, extraction, etc) to get to the product. For extracellular products, the fermentation broth is the useful intermediate product, while the cells are byproducts. The broth is also subjected to one or more separation processes (distillation, extraction, absorption, chromatography, etc.) to get to the desired product and quality of the product.

As could be seen from Fig. 2.2, the process involves major contributions from Microbiologists, Biochemists and Biochemical Engineers, principally and collectively. When it comes to making the product available to the market in quantum, the role of Chemical Engineering comes in and this is the exclusive preserve of Biochemical Engineering. At this stage, the process developed at the laboratory or small-scale level has to be replicated to the large industrial scale. Then we talk about Scale-Up.

Hence, Bioprocess Development is in two parts, Process Development and Process Scale-Up. Process Development is primarily Science-based while Process Scale-Up is Engineering-based.

2.2. Bioreactors

Each of the stages described in Fig. 2.2 is referred to as a Unit Operation. The actual number and type of unit operations that will be involved in an Industrial Biotechnology process will depend on the nature of the process (Fig. 2.3). Is it aseptic and/or aerobic? Is the product desired extracellular or intracellular for microbial processes? Of all the unit operations that are in that typical process, the most important is the Bioreactor, where the biological conversions are expected to occur.

While existing Chemical Engineering equipment could easily be adapted for use in media formulation, medium sterilisation and product recovery, the configuration of the bioreactor depends largely on the type and nature of organism and/or product in focus. The main types of Bioreactors in use in the industry today are described below.

2.2.1. Stirred Tank Bioreactors

The Stirred Tank Bioreactor is the most used type of bioreactors. It consists of a vessel, usually jacketed and has a stirrer, powered by an electric motor, to effect stirring in the vessel (Fig 2.4a). Where aeration is desired, this is sparged into the vessel.

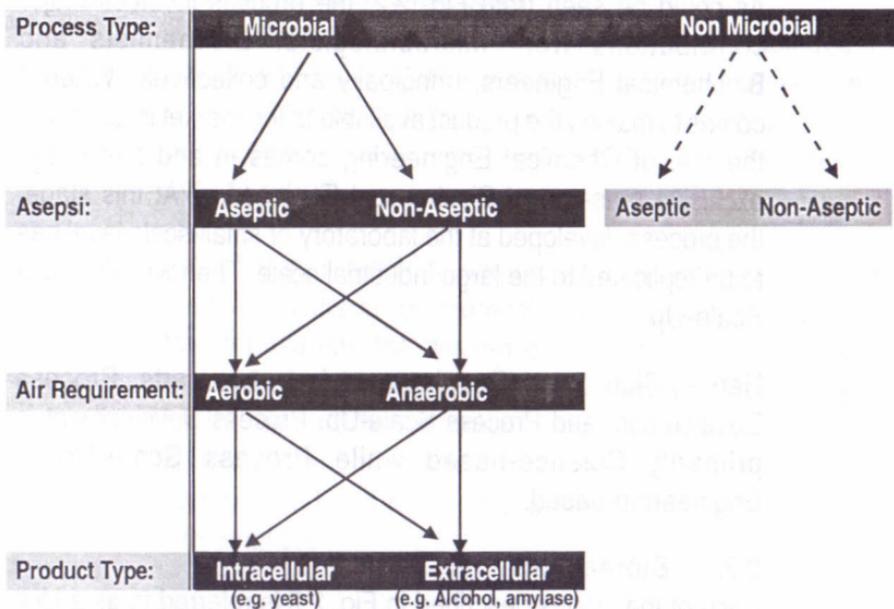


Fig. 2.3 Industrial Biotechnology Process Types

2.2.2. Pneumatic Bioreactors

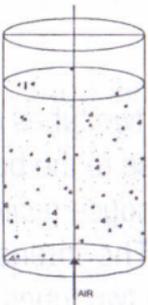
These classes of bioreactors utilise the advantage of the content of the bioreactor being normally sparged with air for the supply of oxygen in fermentations needing oxygen (aerobic fermentations). The bioreactors are designed to utilise the air as the supplier of oxygen as well as the mixing medium. There are two distinct types that have been fully developed for use. These are the Bubble Column and the Airlift Pneumatic Bioreactors (Fig. 2.4b).

2.2.2.1. Bubble Column Pneumatic Bioreactor

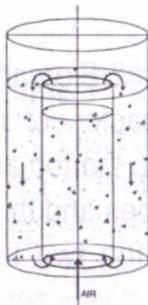
The Bubble Column is well-known in the Chemical Process Industry. It consists of a vertical column with air sparged at the base. The air forms bubbles rising through the content of the column. As the bubbles rise, they generate eddies and turbulence around themselves enabling the desired mixing at the immediate environment of the bubbles. The mixing so generated is not as intense and uniformity throughout the column cannot be assured. Also the fluid is virtually static and no macro-movement of the liquid occurs.



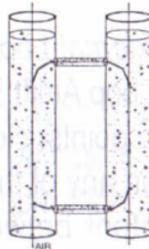
(a) STIRRED TANK BIOREACTOR



(i) BUBBLE COLUMN BIOREACTOR

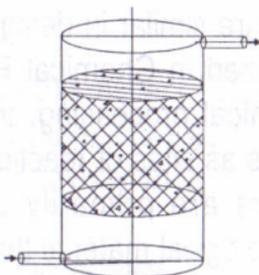


(ii) CONCENTRIC-TUBE AIRLIFT BIOREACTOR



(iii) EXTERNAL-LOOP AIRLIFT BIOREACTOR

(b) PNEUMATIC BIOREACTOR



(c) PACKED-BED BIOREACTOR

Fig. 2.4 DIFFERENT TYPES OF BIOREACTORS

2.2.2.2. Airlift Bioreactor

The static nature of the liquid in the Bubble Column was improved upon in the Airlift Bioreactor design. A circulation of the liquid is generated by creating a pressure difference between the sparged leg of the bioreactor and the downcomer leg. The intensity of the circulation is dependent on the type and the ratio of the cross-sectional areas of the downcomer to that of the riser (Fig.2.4b). There are two

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major types of Airlift Bioreactors. These are the Concentric-Tube Airlift Bioreactor (CT) and the External-Loop Airlift Bioreactor (EL).

2.2.2.2.1. *Concentric-Tube Airlift Bioreactor*

In the Concentric-Tube Airlift Bioreactor, two concentric tubes are placed one inside the other. The liquid is made to circulate through the annulus between the two tubes and in the smaller tube. The path followed will depend on whether the air is sparged in the annulus or in the smaller tube. The macro-circulation of the fluids enable macro-mixing of the fluid content apart from the micro-mixing generated around each air bubble.

2.2.2.2.2. *External-Loop Airlift Bioreactor*

The External-Loop Airlift Bioreactor consists of two tubes connected together at two points, close to the top and close to the bottom. The air is sparged in any of the tubes and this will induce recirculation of the liquid content between the two tubes. The intensity of the circulation depends on the relative sizes of the two tubes.

2.2.3. ***Packed-Bed Bioreactors***

Packed-Bed Bioreactors are similar in design and concept with the packed-bed reactors utilized in Chemical Process Industries (Fig 2.4c). Whereas for chemical processing, the packings are either catalysts on inert supports as sites of reactions, the packings in the Packed-Bed Bioreactors are primarily used as supports for immobilising the active biological material that is responsible for the biological process (i.e. enzyme or microorganism).

These bioreactors are finding increasing use in the industry. It enables the enzyme to remain on the support and be reused as many times as possible, improving the economics of the processes. Similarly, immobilisation of microorganisms has been finding increasing application where the products desired are not adversely affected by immobilisation.

3. CONTRIBUTIONS TO KNOWLEDGE

My contributions to this wide area of endeavour will be discussed in two segments. This section will focus on the contributions to the academic evolution of Biotechnology, while the next chapter will concentrate on my contributions to the development of Biotechnology and practice in Nigeria.

In this section, we shall discuss the results and contributions of the fundamental researches carried out and their impact on the art of Biotechnology. This will be done in two segments. The first will highlight the major contributions in Bioreactor Design, while the second section will discuss work done on Process Development and Design.

3.1. Bioreactor Design

As was mentioned earlier, the nature or type of vessel used for carrying out the desired biochemical transformations in Industrial Biotechnology influences the economics of the operation. Hence, the selection of the appropriate bioreactor quite often becomes major in a bioprocess. Hence, research works continue to be extensively carried out to characterise and modify bioreactors to suit new requirements in Industrial Biotechnology.

The contributions in this aspect have been in the characterisation and evolution of the Airlift Bioreactors as well as in the use and characterisation of the immobilised enzyme/whole cell bioreactors.

3.1.1. Airlift Bioreactors

Our pioneering works on these types of bioreactors (Bello et al. 1980; 1982; 1984; 1985a; 1985b) were able to investigate theoretically and experimentally all the intrinsic and physical characteristics of this class of pneumatic bioreactors for the first time and position it for industrial use.

There are two basic requirements of any contactor being considered for use as a bioreactor. One is its mixing ability and next is its oxygen transfer capability or ability to ensure the organisms in the bioreactor will be able to get enough oxygen for its metabolism in an aerobic

application. Until the advent of these and similar works, only the Stirred Tank had enjoyed the full status of a good mixer and contactor. However, it utilises a motor for stirring while the Airlift Contactor utilises the same air sparged into it to effect the circulation and mixing, thus creating a potential economic advantage.

Bello et al. (1984) were able to show that the airlift contactors were intermediate mixers of the order of three times better than bubble columns and three to five times worse than stirred tank contactors (Fig 3.1). This helped to position the Airlift Contactors for use in fermentations not requiring intense agitations (e.g. tissue culture fermentations).

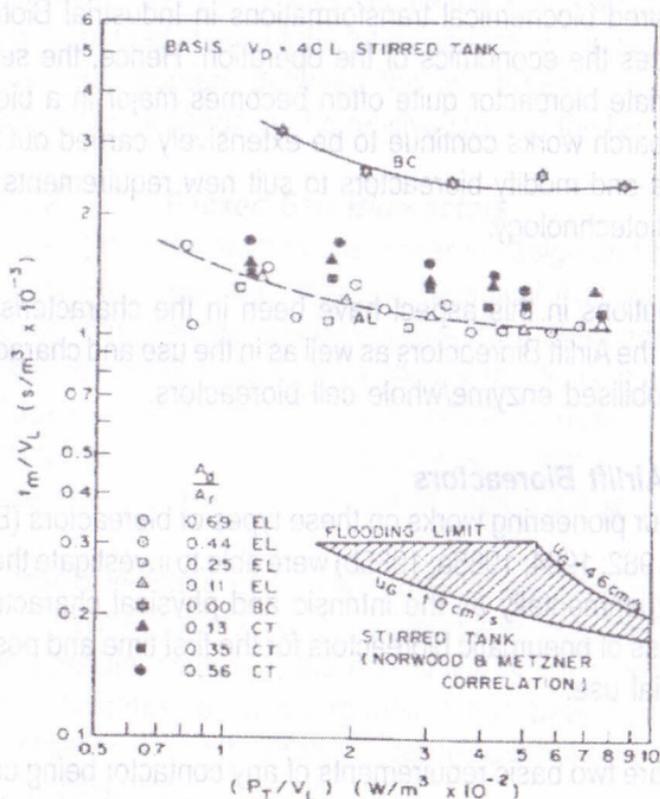
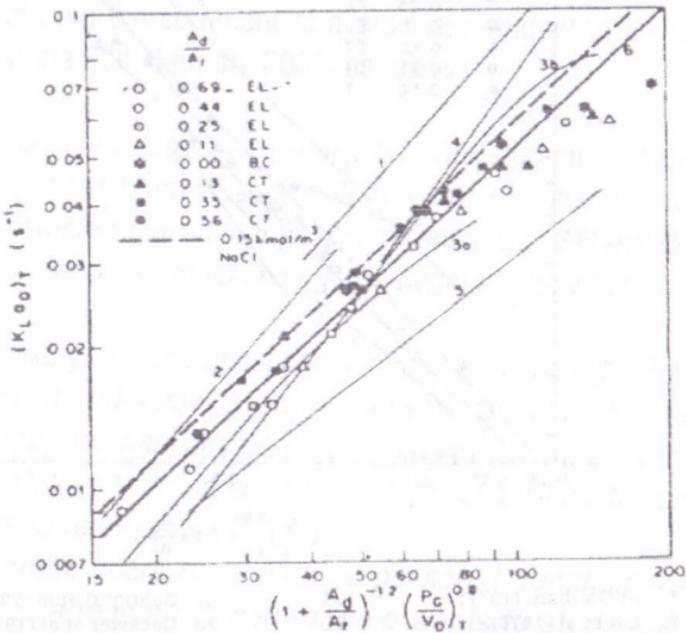


Fig. 3.1 Comparison of the Mixing Capabilities of various types of Contactors (Water)

On the mass transfer capability of the airlift contactors, Bello et al (1985a, b) investigated the intrinsic properties of the airlift contactors and pneumatic contactors in general, through energy and momentum balances and established that the volumetric oxygen mass transfer coefficient, $(K_L a_D)_T$, varies with the geometric ratio of the downcomer and riser $(1 + A_d/A_r)$ and the pneumatic power per unit volume $(P_G/V_D)_T$ as given in eq. 3.1.

$$(K_L a_D)_T = K(1 + A_d/A_r)^{-1.2} (P_G/V_D)_T^{0.8} \quad 3.1$$

where K was obtained to take a value of $5.5 \times 10^{-4} (\text{m}^3 \text{W}^{-1})^{0.8} \text{s}^{-0.2}$. Equation 3.1 was found to agree well with data obtained in airlift contactors as well as bubble columns as shown in Fig 3.2. Hence, equation 3.1 can be used to predict volumetric oxygen transfer coefficient in pneumatic contactors.



- | | | |
|-------|---|------------|
| 1. | Schugerl et al (1977) | BC |
| 2. | Gasner (1974) | CT (Split) |
| * 3a. | Kawagoe and Robinson (1980) | EL |
| * 3b. | Kawagoe and Robinson (1980) | BC |
| 4. | Botton et al (1980) | CT |
| 5. | Onken and Weiland (1980) | EL |
| 6. | This Work (Water & 0.15 kmol/m ³) | EL+CT |

Fig. 3.2 Correlation of overall volumetric mass transfer coefficient, $(K_L a_D)_T$, with specific power input $P_G/V_D)_T$ (data points for water).

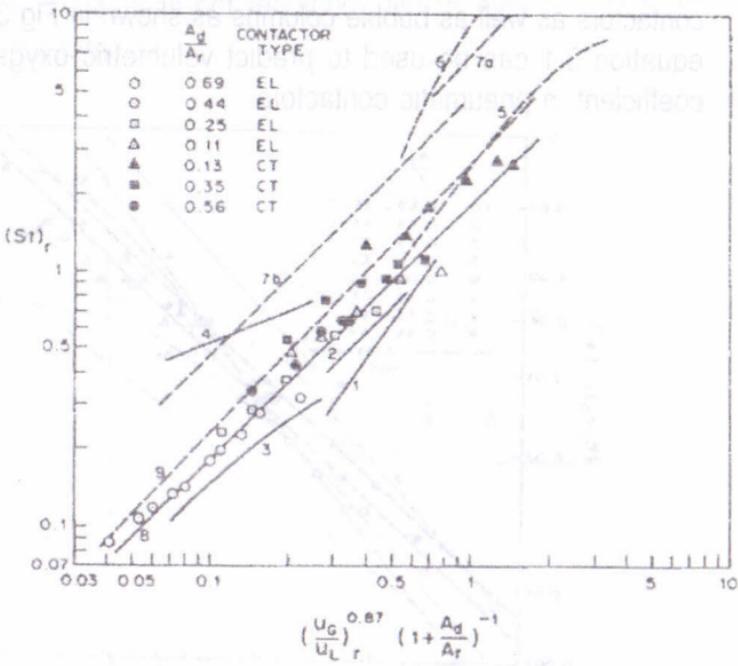
* $(K_L a_D)_T$ calculated from $(a_D)_T$ measurements (Kawagoe & Robinson (1980)) and K_L values of Calderbank and Moo-Young (1961).

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In Bello et al. (1985 b), dimensional analysis was performed on all parameters affecting volumetric mass transfer coefficient in airlift contactors and they established that:

$$St_r = \frac{(K_L a_D)_r H_D}{(U_L)_r} = C \left(\frac{U_G}{U_L} \right)_r^{0.90} \left(1 + \frac{A_d}{A_r} \right)^{-1} \quad 3.2$$

and C has the value of 2.28. Equation 3.2 also correlated all data available on pneumatic contactors as shown in Fig 3.3 and so can be used to predict the volumetric mass transfer coefficient of the pneumatic contactor



- | | | | |
|--|----|---|-------|
| 1. El Gabbani (1977) | CT | 6. Schugerl et al (1977) | BC |
| 2. Lin et al (1976) | EL | 7a Deckwer et al (1974) | BC |
| 3. Kawagoe & Robinson (1980) | EL | ($u_L = 1.67 - 2.21$ cm/s) | |
| 4. Onken & Weiland (1980) | EL | 7b Deckwer et al (1974) | BC |
| 5. Alvarez-Cuenca and Nerenberg (1981) | BC | ($u_L = 0.63$ cm/s) | |
| ($u_L = 7.5$ cm/s) | | 8. This Work (Water) | EL+CT |
| | | 9. This Work (0.15 kmol/m ³) | EL+CT |

Fig. 3.3 Dimensionless correlation of the volumetric mass transfer coefficient data in airlift contactors (water and salt solution).

* $(K_L a_D)_r$ calculated from $(a_D)_r$ measurements and K_L values of Calderbank and Moo-Young (1961).

These fundamental works thus provided the needed insight into the operations of pneumatic contactors in general and airlift contactors in particular and provided the needed design equations for use in the design of pneumatic bioreactors. It should be mentioned that pneumatic bioreactors are now in commercial uses for large scale fermentation and even on the bench scale for laboratory uses and the contributions earlier mentioned were pertinent to this being feasible.

The work also provided better insight into the mechanism and operation of the then suspended ICI airlift fermentor (Kubota et al., 1978) for sewage treatment.

The import of our contributions in this regard can be better appreciated from the comment of a graduate student in an e-mail received on the 30th January 2001, as follows:

"My name is Jaime Arturo Calvache and I am student of chemical engineering in the National University of Colombia (south America) and I am interested in airlift reactors. In my university we have device at bank level, and we would like a lot to begin to study this type of reactors.

I want to make you some questions and also if it is possible I would like to request you some favors. Is possible to obtain for my an electronic copy in format pdf (or the one that you believe convenient) of your Ph. D. thesis "A characterization study of airlift contactors for applications to fermentations".

Although some years have already passed, I consider that your work is a reading forced for who wants to study this type of reactors.

I hope not cause to you any inconvenience. I am of you very grateful for your attention.

Thanks for your time.

JAIME ARTURO CALVACHE

(jeacalvache@yahoo.com)"

3.1.2. Immobilised Enzyme Bioreactors

My other contributions in the area of bioreactor design are on the characterisation of immobilised enzyme and immobilised whole cells bioreactors. The emphasis here was to utilise resources that are within reach, in Nigeria, for the processes in consideration.

In the immobilisation studies, a packed bed type of bioreactor (Fig 2.4c) is used. The enzyme or whole cells to be immobilised are attached to some support, which will constitute the basic packing in the bioreactor. The immobilisation may be with or without the use of a binding agent. For the immobilisation studies, palm wood chips were used as the support. The palm wood chips used were those of the palm tree (*Raphia hooker*), which are readily available, and are naturally porous for entrapment of the enzymes or cells. Also the palm wood would pose no danger to food items as it is the "natural bioreactor" for the production of palm wine, which is an acceptable natural drink.

Generally, enzymes, which are catalysts for biochemical reactions, are very expensive. Any process, which can get them utilised more than once, improves the economics of that process.

The lactose-lactase system was studied. This was based on the immediate needs of a dairy plant. Generally, lactose has some problems associated with it in industrial processing. First is lactose crystallisation (salting out) during storage of sweetened condensed milk and frozen ice cream. The other is lactose intolerance, which has been established in a lot of animals and human beings. Hence, in the industry, during the processing of milk or milk products for human consumption, lactose in the milk is usually hydrolysed via the action of lactase. The hydrolysis of lactose by the lactase interestingly yields sweeter simpler sugars (glucose and galactose), which makes the product sweeter and also even reduce the overall requirement of sweeteners. This makes the process more profitable.

Various polymeric materials, normally used in food preparations were tried, in various concentrations as binding agents for the lactase. Packed beds of the lactase, immobilised on the palm wood chips were used as the bioreactor for the hydrolysis of lactose.

The works (Ogunbayo and Bello, 1986, 1993; Olagesin et al., 1987) were able to establish that cremodensin, a polymeric material used as filler in the dairy industry, as well as Gum Arabic were very good binders for lactase on palm wood chips. The resulting bioreactors were found to be stable and reuseable over various times, batchwise or for a long time for continuous operation. Fig 3.4 is for cremodensin, and Fig. 3.5 for Gum Arabic. Fig 3.6 shows a typical run with dairy milk.

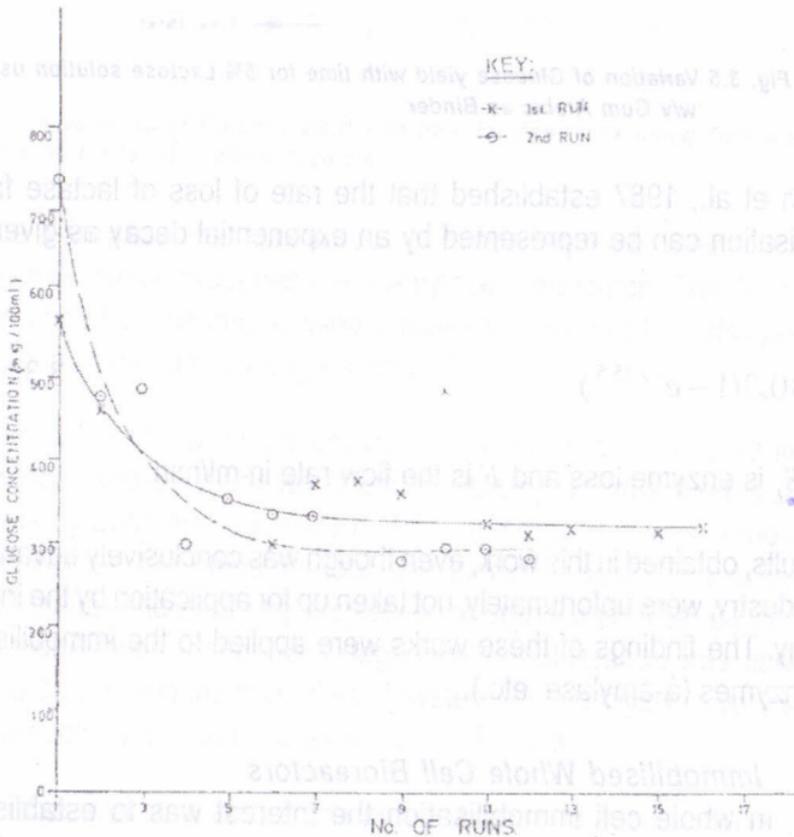


Fig. 3.4 Stability of the Cremodensin Immobilisation

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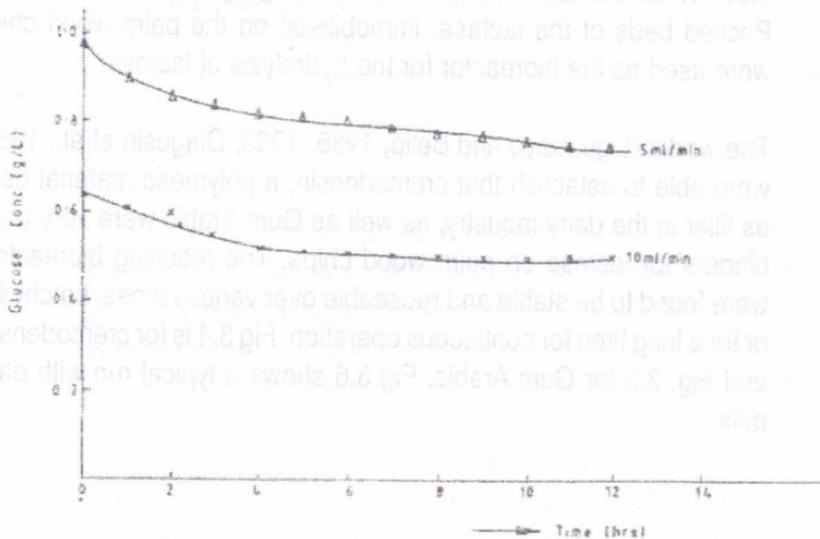


Fig. 3.5 Variation of Glucose yield with time for 5% Lactose solution using 50% w/v Gum Arabic as Binder

Olagesin et al., 1987 established that the rate of loss of lactase from the immobilisation can be represented by an exponential decay as given in Eq. 3.3.

$$E_l = 30.3(1 - e^{-F/5.5}) \quad 3.3$$

where E_l is enzyme loss and F is the flow rate in ml/min.

The results, obtained in this work, even though was conclusively advantageous to the industry, were unfortunately, not taken up for application by the interested company. The findings of these works were applied to the immobilisation of other enzymes (α -amylase, etc.).

3.1.3. Immobilised Whole Cell Bioreactors

In whole cell immobilisation the interest was to establish more economical modes of hydrolysing starch. Normally α -amylase can be used directly to hydrolyse starch. Rather than harvest and purify

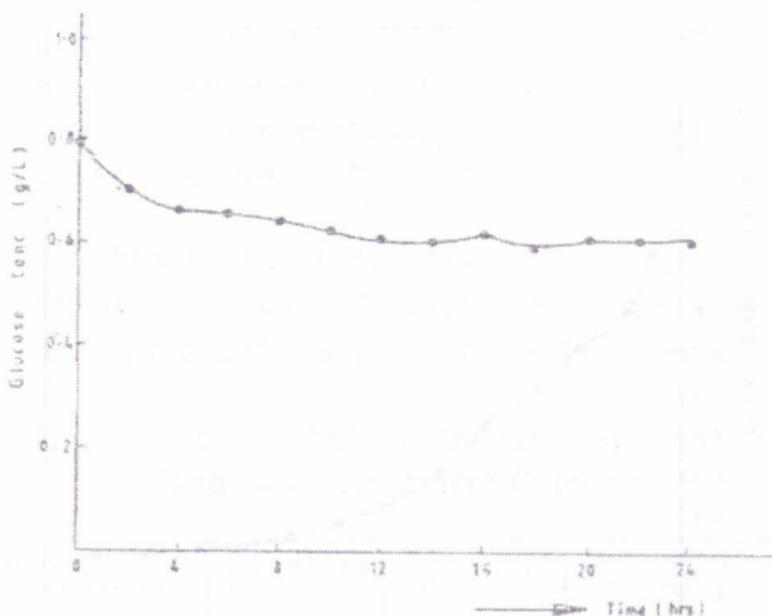
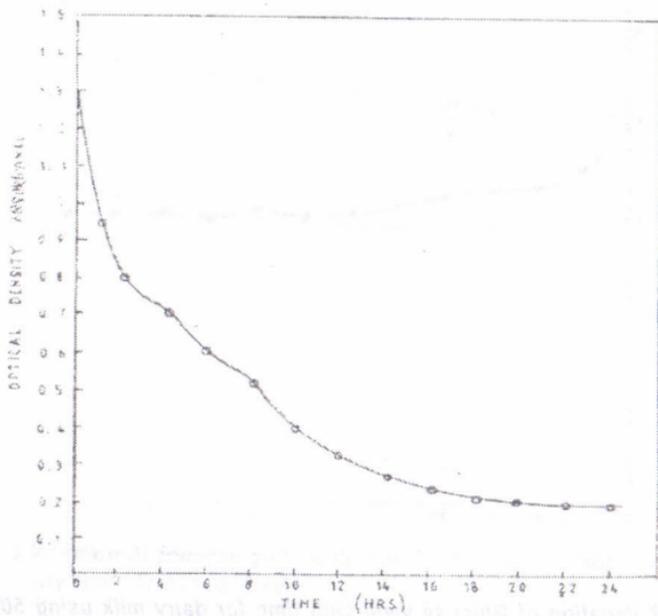


Fig. 3.6 Variation of Glucose yield with time for dairy milk using 50% w/v gum arabic as binder at 5 ml/min feedrate

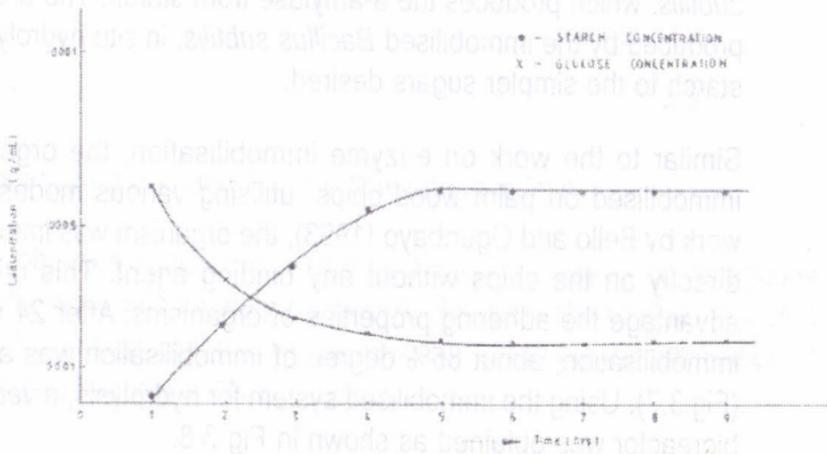
the α -amylase, the work set out to immobilise the organism, *Bacillus subtilis*, which produces the α -amylase from starch. The α -amylase produced by the immobilised *Bacillus subtilis*, in situ hydrolyses the starch to the simpler sugars desired.

Similar to the work on enzyme immobilisation, the organism is immobilised on palm wood chips, utilising various modes. In the work by Bello and Ogunbayo (1993), the organism was immobilised directly on the chips without any binding agent. This utilises to advantage the adhering properties of organisms. After 24 hours of immobilisation, about 85% degree of immobilisation was achieved (Fig 3.7). Using the immobilised system for hydrolysis, a very stable bioreactor was obtained as shown in Fig 3.8.

Further improvement on the immobilisation and exploration of the mode of immobilisation had shown us that enhancement of the immobilisation can be achieved with the use of some aldehydes and ketones as enhancing agents. Ogunbayo and Bello (2005)



3.7 Retention of *B.Subtilis* in the packed bed reactor during immobilisation



3.8 Starch and Glucose concentration during Hydrolysis of starch with the immobilised cells Bioreactor

reported that the best enhancement was obtained when the support was treated, as opposed to treating the cells or both of them. Glutaraldehyde gave the best enhancement, followed by Buteraldehyde and Methyl ethyl ketone gave the least enhancement (Table 3.1). These results suggest that (CHO....NH₂) bonding occurs between the cells and the polar compounds.

With these findings, we have been able to develop and characterise immobilised whole cell bioreactors which can be used for various applications, particularly for starch and food processing problems.

Table 3.1 The Extent of Immobilisation with each of the Binding Enhancement Chemical

Chemical	Glutaraldehyde	Butyraldehyde	Formaldehyde	Methyl ethyl ketone	Untreated
Extent of Immobilisation (%)	79.4	75.8	72.2	62.4	54.2

3.2. Process Development and Design

Apart from the design of bioreactors, our works had included the utilisation of the bioreactors in developing new processes.

3.2.1. Synthetic Palmwine Production

The process involved the use of an immobilised yeast packed bed bioreactor to simulate natural palmwine production. This process was developed during the period when Nigeria was awakened to develop and utilise locally available materials and facilities. This was in the post 1983 era, when importation of barley malt for brewing was banned and palmwine became very popular as an indigenous drink. FIIRO was bottling palmwine and training entrepreneurs on how to bottle and preserve palmwine. The continuing availability of the palmwine to be bottled was of concern. The continuing destruction of the palm trees upon tapping and the increasing demand was the motivation to simulate palmwine industrially.

The synthetic palmwine was produced in a process using packed bed bioreactor with *Saccharomyces cerevisiae* immobilised on the palm wood chips used as the packing in the bioreactors. The details are reported in Bello and Ogunbayo (1990).

The chromatograms of the synthetic palmwine and the natural palmwine are shown in Figs. 3.9 and 3.10. The key components in the wine are as in Table 3.2. The acetic acid concentration was similar to that in natural palmwine, so was the alcohol content. The chromatogram showed one component being absent in the synthetic palmwine, which was in the natural wine. Nevertheless, a taste panel certified the taste and odour of the synthetic palmwine to be similar to those of natural palmwine.

This process is established and can be utilised when the Nigerian economy calls for it.

Table 3.2 Comparative Characteristics of the Palmwine

		SYNTHETIC PALMWINE	NATURAL PALMWINE (This Work)	NATURAL PALMWINE (Literature)
1.	Acetic Acid Concentration	0.017–0.021	0.020	0.020 (FIIRO, 1982)
2.	Total Solids (g/100ml)	4.22–5.50	6.59–8.70	7.5–9.39 (FIIRO, 1982)
3.	Alcohol Content (%)	8.15	7.9	0.5–7.1 (Bassir, 1968)

3.2.2. Starch Hydrolysis

For better and ease of design, deeper understanding of the basic processes of the breakdown of the starch components to the simpler sugars, are necessary. This will also enable better understanding and distinction between different types of starch.

COLUMN — SE 30
 COLUMN TEMP — 70°C (constant)
 PRESS of carrier gas (PSI) — 15 PSI
 CHART Speed — 0.16 cm/min
 FLOW RATE — 5°C/min
 SENSITIVITY — 5×10^3

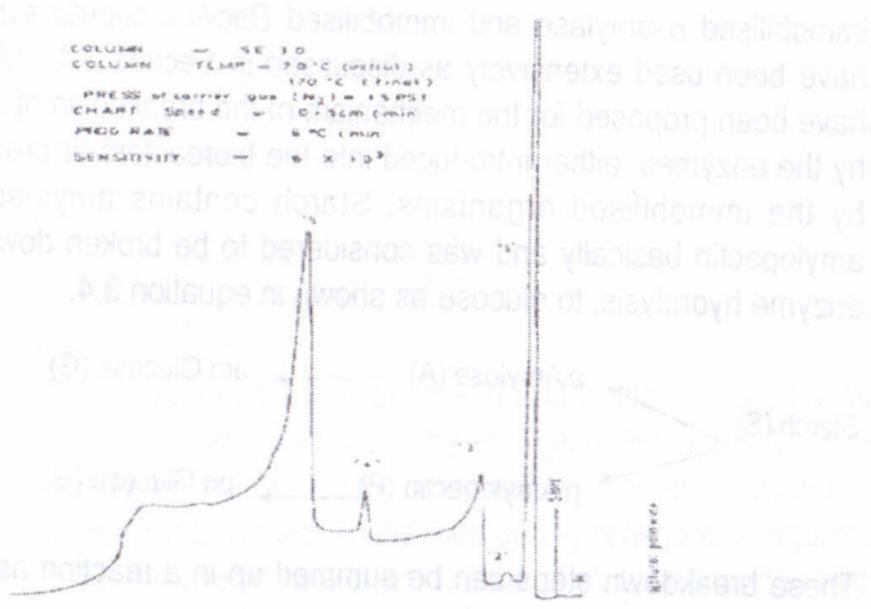


Fig. 3.9 Chromatogram for Natural Palmwine

Column — SE 30
 Column Temp — 70°C (constant)
 Press of carrier gas (PSI) — 15 PSI
 Chart speed — 0.16 cm/min
 Rate — 5°C/min
 Sensitivity — 5×10^3

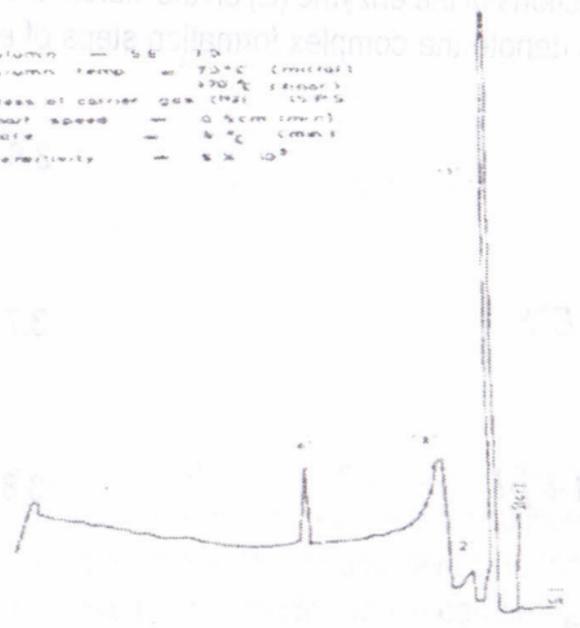
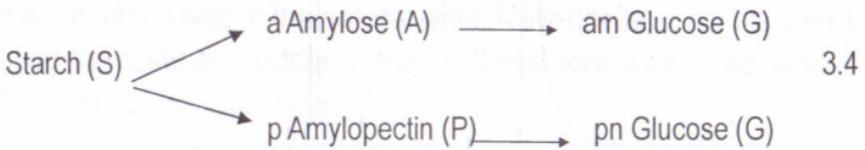


Fig. 3.10 Chromatogram of Synthetic Palmwine

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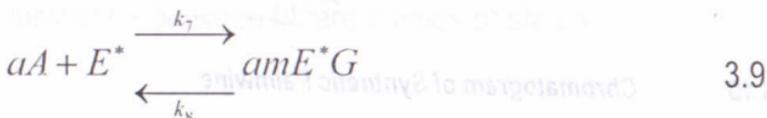
The works on starch hydrolysis involved developing cheaper and novel means of hydrolysing starch as well as understanding the mechanism of the breakdown for process design purposes. Both immobilised α -amylase and immobilised *Bacillus subtilis* systems have been used extensively as discussed in Section 3.1. Models have been proposed for the mechanism of the breakdown of starch by the enzymes, either introduced into the bioreactors or produced by the immobilised organisms. Starch contains amylose and amylopectin basically and was considered to be broken down, via enzyme hydrolysis, to glucose as shown in equation 3.4.

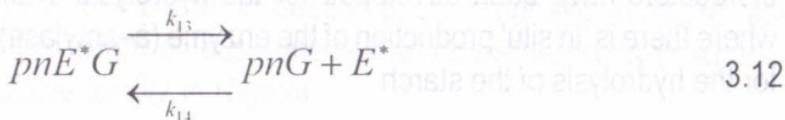
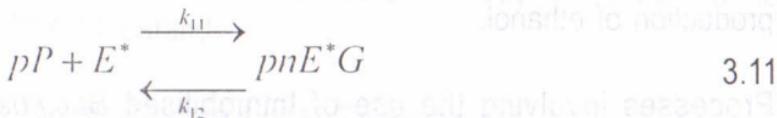
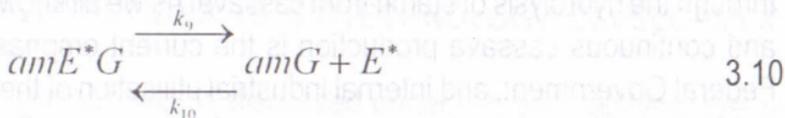


These breakdown steps can be summed up in a reaction as:



For the catalytic actions of the enzyme (E) on the starch, the following elementary steps denote the complex formation steps of enzyme:





A similar scheme was proposed and found suitable for mixtures of amylose and amylopectin by Park and Rollings (1994). By writing the equations for the rate of formation of the products or degradation of reactants in each of the elementary reactions in equations 3.6 to 3.12, the overall rate of production of glucose from the hydrolysis of starch as well as the overall rate of degradation of starch were obtained as in equations 3.13 and 3.14, respectively.

$$\frac{dC_G}{dt} = \frac{\left[k_9 \frac{k_7}{k_8} C_A^a - k_{10} C_G^{am} + k_{13} \frac{k_{11}}{k_{12}} C_P^p - k_{14} C_G^{np} \right] K_A C_{E0}}{\left[1 + K_A + K_B C_A^a + K_C C_P^p + \frac{C_A^a C_P^p}{K_D C_E} \right]} \quad 3.13$$

$$\frac{-dC_S}{dt} = \frac{k_3 K_A C_S C_{E0}}{\left[1 + K_A + K_B C_A^a + K_C C_P^p + \frac{C_A^a C_P^p}{K_D C_E} \right]} - \frac{k_4}{K_D} C_A^a C_P^p \quad 3.14$$

Figure 3.11 shows a comparison of the prediction by this model and experimental data for glucose production during hydrolysis of starch with α -amylase. The results gave credence to the mode of breakdown proposed in the model, which can be utilised to predict the glucose formation in a particular process.

The implication and application of this work is in its direct use in the current drive to produce ethanol in large quantities in the country

through the hydrolysis of starch from cassava. As we all know massive and continuous cassava production is the current emphasis of the Federal Government, and internal industrial utilisation of the cassava will be more beneficial for the economy. A major use will be in the production of ethanol.

Processes involving the use of Immobilised *Bacillus subtilis* bioreactors have been developed for the hydrolysis of the starch, where there is 'in situ' production of the enzyme (α -amylase) required for the hydrolysis of the starch.

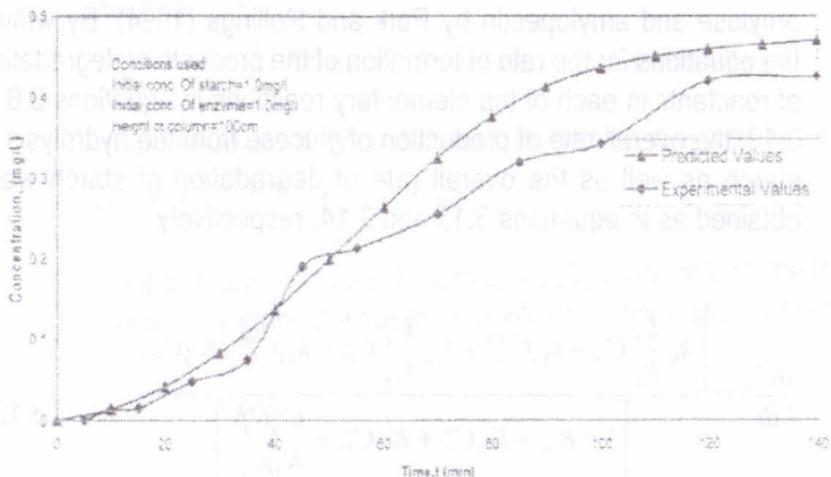


Fig. 3.11 Comparison of experimental and predicted values of glucose production during starch hydrolysis

4. CONTRIBUTIONS TO BIOTECHNOLOGY DEVELOPMENT IN NIGERIA

This aspect will be discussed under two perspectives. We will look at the contributions from the academic viewpoint as well as the professional stand.

4.1. Adaptation to Local Environment

As had been shown in Section 3, our emphasis in all our research has been to adapt all our materials and considerations to what are readily available locally in Nigeria.

In our development of the Packed Bed Bioreactors used for the immobilised enzyme and immobilised whole cell studies, our consideration for the use of palm wood chips, rather than other artificial polymeric supports, as are used elsewhere, was based on the need to develop processes that will be Nigerian, will be economically viable locally and will find ready acceptability in both our environment and internationally.

The process established for producing palmwine utilised the Packed Bed Bioreactor technology to simulate the palm tree. It embedded the organisms naturally available in the palm tree juice for the natural palmwine production through immobilisation on palm wood chips in a controlled environment.

The advantage of this is that when fully commercialised, the throughput for a production plant will not be limited to whatever a palm tree can produce or how many palm trees are available for tapping or whether palmwine tappers are available.

Our works on starch hydrolysis took advantage of the fact that most of our major agricultural products are starch-based. The transformation of starch into the various raw materials, which could be feeds to the chemical, pharmaceutical and food processing industries, are yet to be embarked upon. The various sources of starch, from grains to the roots offer enough base for a virile industry. This, we believe, is bound to come.

If cassava production is embarked upon on the scale being prompted and promoted by the Federal Government mainly for exportation of the raw chips, entrepreneurship will surely lead to value addition locally to the cassava chips. This may not be far to come, as the mass production of the cassava will assure the needed volume of raw feed to integrated cassava plants in the country.

For the benefits of the general audience, starch is used for the production of adhesives, various pharmaceutical products like glucose, dextrose, dextrans, maltose, as well as ethanol (gasohol), etc.

Our processes for starch hydrolysis will ensure an economical breakdown of the starch to the simpler sugars, which will feed the production of the various pharmaceutical and food products.

4.2. Professional

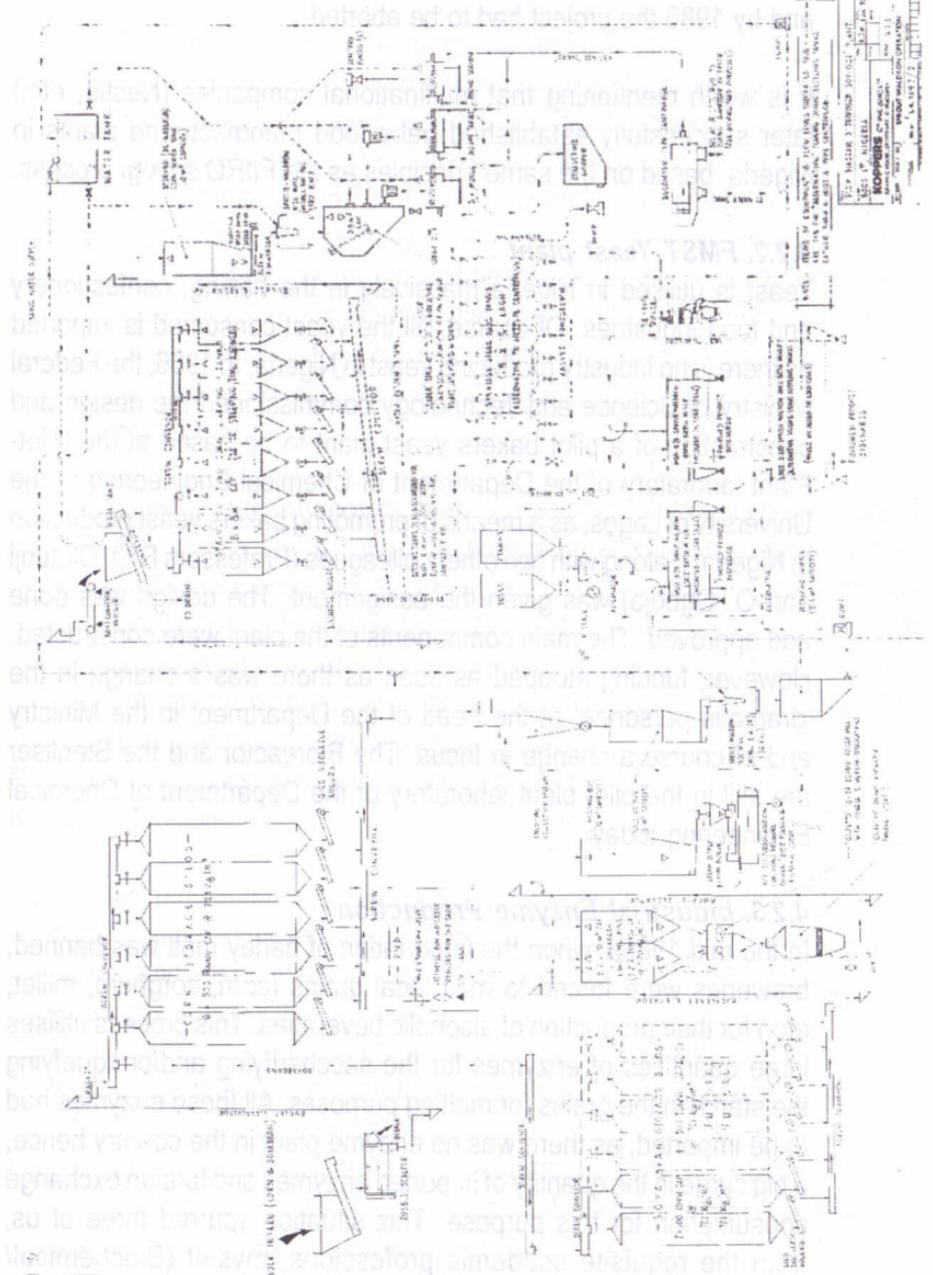
I have been involved in various projects aimed at developing the biotechnology industry, over the years. A few of them will be mentioned here, mainly to highlight the kind of bottlenecks the growth of biotechnology, particularly industrial biotechnology, had faced and would still face, if the emphasis on its development is not given the right push.

4.2.1. The BOGS Soyogi plant

In 1983, a Nigerian entrepreneur bought a license from FIIRO to produce soyogi, a fortified corn based baby food. The FIIRO soyogi production process was then at a pilot scale but the product was acclaimed. The onus was on me as the lead consulting engineer to scale up the FIIRO process.

The scale-up was successfully carried out and attested to by the Sprout-Waldron Division of Koppers Co. Inc. (UK) Limited (Fig 4.1).

The company, BOGS Food Limited, after all the preliminary works and with adequate fund could not realise the project because of the problem of import licence then. After meeting all the requirements for the import licence issuance for the project, it was shocking to find that, for a project that was to source its raw materials totally locally, only about 40% of the amount required for the importation of the needed equipment was approved. All attempts to get a redress failed



and by 1986 the project had to be aborted.

It is worth mentioning that multinational companies (Nestle, etc.) later successfully established baby food manufacturing plants in Nigeria, based on the same principles as the FIRO soyogi process.

4.2.2. FMST Yeast plant

Yeast is utilised in Nigeria massively in the baking, confectionery and food industries. Of course, all the yeast consumed is imported as there is no industry producing yeast in Nigeria. In 1986, the Federal Ministry of Science and Technology commissioned the design and construction of a pilot bakers yeast plant to be based at the Pilot-Plant laboratory of the Department of Chemical Engineering of the University of Lagos, as a means of promoting bakers yeast production in Nigeria. I, along with two other colleagues (Professors F. O. Olatunji and O. Ogboja) was given the assignment. The design was done and approved. The main components of the plant were constructed. However, funding stopped as soon as there was a change in the 'dramatis personae' at the head of the Department in the Ministry and of course a change in focus. The Bioreactor and the Steriliser are still in the pilot plant laboratory of the Department of Chemical Engineering today.

4.2.3. Industrial Enzyme Production

In the mid 1980s, when the importation of barley malt was banned, breweries were forced to malt local grains (corn, sorghum, millet, etc.) for their production of alcoholic beverages. This process utilises large quantities of enzymes for the saccharifying and/or liquefying the starch in the grains for malting purposes. All these enzymes had to be imported, as there was no enzyme plant in the country hence, a big surge in the quantity of imported enzymes and foreign exchange consumption for this purpose. This situation spurred three of us, from the requisite academic professions, myself (Biochemical/ Process Engineering), Professor O. Amund (Microbiologist) and Professor O. Omidiji (Cell Biologist/Biochemist), to get together for the local production of bacterial amylase, based on very research results already obtained with local raw materials. This was in 1991.

My duty as the Process Engineer and a Biochemical Engineer was to design and scale-up the process for a 500-ton enzyme plant and package it for investment. This was readily done. The total project cost as at January 1991 was N30million (or \$3.45million at an exchange rate of N8.70 to \$1.00), based on a feasibility report concluded by Coopers & Lybrand. The study gave a return on capital employed at 35% in the first year, 41% in the second, 36% in the third, etc. The profit margin was projected at 29%, 50%, 56%, 61% and 62% in years 1 to 5, respectively, based on 50%, 60%, 70%, 80% and 80% utilisation in the first, second, third, fourth and fifth year, respectively.

However, the promoters, then, found it difficult to obtain investors in the sector. The project was presented at various investment fora with no success. Hence, the project, which could have commenced production in 1992, is yet to see the light of the day. Over 2000 tons of the enzyme is still being imported into this country as at today without any attempt to produce a kilogram, even though all that are necessary for its production are available locally.

Possible reasons as adduced by Bello (2000) for the project not seeing the light of day include:

- (1) The big multinational brewing and food companies are usually tied to purchasing enzymes and other raw materials from their principals or their agents and are often not interested in investment in local production, even when this is financially rewarding.
- (2) The importing companies would rather protect their commercial businesses than invest in production, particularly in an economy that has hitherto been commerce favoured.
- (3) Lack of confidence in the ability of Nigerian experts to pool together an enzyme business, considered to be specialised by the usually uninformed and quite often helpless (where they are informed) Captains of Nigerian Industries and those with investable funds.
- (4) Biotechnology has not been seen as a major business sector in Nigeria, unlike in the developed economies and as such, it has not been receiving

appropriate attention and the patronage it deserves.

The few examples of feasible and economically viable Biotechnology projects given above show:

- (a) The multidisciplinary nature of Biotechnology, particularly Industrial Biotechnology.
- (b) The expensive nature of Biotechnology practice and projects.
- (c) The profitability of Biotechnology projects.
- (d) Protection and safeguard by the producing nations.
- (e) The need for special attention to be focused on the need for investment in Biotechnology in Nigeria.

The production of Bakers yeast and bacterial enzymes are still money spinning ventures, which are still relevant to the Nigerian economy, particularly with the drive for diversification of the economy. The local production of the enzymes, needed for starch hydrolysis, will be essential for the success of the ethanol production drive from our agricultural materials being currently undertaken by the Nigerian National Petroleum Corporation (NNPC). The ethanol is needed by NNPC as a blend for the gasoline to enable the stabilisation of fuel costs.

5. SUGGESTIONS AND RECOMMENDATIONS

An attempt has been made at bringing to the fore the emerging technologies in Biotechnology, their apparent applications and uses. From the foregoing, it is essential that Nigeria braces up to being part of the evolution of the emerging Biotechnology practices and not just be a consumer of its products.

The presentation also highlighted attempts at putting to practice Industrial Biotechnology and the bottlenecks encountered, which had set the nation decades back in the utilisation of common and feasible Industrial Biotechnology practices, even though these are goldmines for the economy.

Suggestions and recommendations for the way forward will be made under three broad headings viz: Biotechnology Research and Development, Biotechnology Applications and Biotechnology Education.

5.1. Biotechnology Research and Development

5.1.1. Biotechnology is multidisciplinary in nature and cooperation between researchers of the cognate disciplines has to be encouraged and enabled to achieve top rated research and development of applications. The joint use of equipment and facilities for research in Biotechnology are necessary because of their expensive nature. A vehicle for the collaboration needed in Biotechnology research at the University of Lagos is the Biotechnology Research Group, which is already in place. This body needs the support, recognition and the backing of the University for its evolution and upgrade as necessary into a Centre or Institute, to enable it attract appropriate resources from agencies locally and internationally for top rate researches in Biotechnology. A Biotechnology laboratory, with the basic minimum the University can input is immediately desired. This can be further enhanced with resources to be sourced elsewhere.

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5.1.2. Biotechnology is advancing fast and it cuts across virtually all disciplines (Engineering, Science, Medicine, Agriculture, Social Sciences, Law). The applications of the advances in Biotechnology to researching and finding solutions to problems that are African, be it medical, industrial, environmental or agricultural should be of utmost priority to the University of Lagos. This kind of activity will catapult the University to a unique status worldwide. To achieve this fast, it is here suggested and recommended that expertise in the new technologies (proteomics, nanotechnology, etc.) should be developed immediately through recruitment and training in these specialties, as a matter of policy.

5.1.3. At the national level, the Federal Government is highly commended for realising the potentials of Biotechnology for national development and for setting up the National Biotechnology Development Agency (NABDA). This centre should be for coordination of activities in Biotechnology research and applications. It should network all government departments and research institutes as well as tertiary institutions for an effective and coordinated Biotechnology programme for the nation. It is recommended that research in Biotechnology should be concentrated in tertiary institutions and selected research institutes in their areas of accredited specialisations. In fact, because of the expensive nature of facilities for Biotechnology research, it is recommended that zonal research centres should be established in tertiary institutions and research institutes, in each aspect of Biotechnology (medical, industrial, agricultural, environmental), based on their areas of specialisation. These research facilities will then be available to researchers within each zone.

5.1.4. For immediate advancement in Biotechnology, the Federal Government should as a matter of urgency establish a Biotechnology Research Fund for the direct funding of

research in Biotechnology. This fund should be coordinated by the National Biotechnology Development Agency (NABDA) and disbursed for researches in line with national priorities.

5.2. Biotechnology Applications

5.2.1. A database of all activities in Biotechnology (research, production, marketing, etc) needs to be established as a matter of urgency to enable appropriate planning, coordination and non-duplication of efforts nationally. This will enhance networking and should be immediately effected by the National Biotechnology Development Agency (NABDA).

5.2.2. In a similar vein, culture banks of all microorganisms, tissues, and all other biotechnology cultures need to be established at various designated research centres nationally. This will form a basis for standardisation, non-repetition as well as progressive and coordinated research. The National Biotechnology Development Agency (NABDA) should immediately fund the establishment of these culture banks and should have their documentations as part of the Biotechnology database.

5.2.3. Research Institutes should be strengthened to concentrate on applied researches and applications of the results of researches in their areas of biotechnology specialisation.

5.2.4. For a quick realisation of the benefits of Biotechnology, it is recommended that national priorities will have to be identified, then the basic and applied research objectives on the national priorities established and activities in these areas spread out nationally but funded and coordinated centrally at the National Biotechnology Development Agency (NABDA). For example, Industrial Biotechnology research group can be established with all stakeholders involved. The group then reviews and establishes national priority areas in Industrial Biotechnology,

identifies the activities necessary to realise established goals, set targets and fund basic and applied researches aimed at realising the goals through competitive proposals.

5.2.5. Biotechnology is a goldmine in the developed economies as well as developing economies that are upright like India. Investment in Biotechnology applications has to be induced and encouraged by Government through its policies. This is not too difficult to achieve over a number of years. Brewing Technology was forced to look inwards, upon the ban on importation of barley malt and now malt local grains. We are now much better off for it. In the pharmaceutical sector, gains are now being made in local production of drugs, based on positive policies.

To start with, Nigeria, as a matter of urgency should not be importing yeast, with all the agricultural raw materials available for its production as well as the know-how. Similarly, the most frequently used enzymes, like the amylases are ripe for production within the country. Similarly, local production of fermentation-based antibiotics can be readily carried out. Decisions, similar to those taken on malt barley will see the necessary investments into these areas, which would witness the addition of a very virile Biotechnology Sector to our Stock Exchange, as it is in all the vibrant economies. It should be realised that the producer nations will continue to encourage our status as the dumping market of their own products, if the right policies are not immediately put in place.

5.3. Biotechnology Education

5.3.1. To enhance Biotechnology development in Nigeria, programmes in Biotechnology are ripe for establishment. However, because of the multidisciplinary nature of Biotechnology and the infant level of the practice of Biotechnology in the country, University programmes should currently be at the postgraduate level. The University of Lagos should as a matter of urgency support and promote a postgraduate programme in Biotechnology to enable it take

the driver's seat in Biotechnology research. It is recommended that such a programme should be put together and coordinated by the 'Biotechnology Research Group'.

5.3.2. First degree programmes in Biotechnology should currently be discouraged in Nigeria for now. This is because the graduates of such programmes would not have full grounding in any of the basic sciences and may run into problems with job prospects, judging from the current level of Biotechnology practice in the nation. It is suggested that curriculum experts should vet curricula of such programmes for their relevance to the students' aspirations and future prospects.

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CONCLUSION

In conclusion, it was brought to the fore that Biotechnology has become one of the frontline technologies today because of the advances made in cell and molecular biology, where various technologies up to nanotechnology are being developed and used to understand and manipulate biological molecules for unprecedented uses in medical, agricultural, industrial and environmental aspects of our life.

It has also been seen that Nigeria is not completely devoid of Biotechnology practice, use and research. It is just that, due to the level of the economy, activities and investments which could boost research and development in Biotechnology are hitherto not in place and for Nigeria to develop and catch up with the needed technology to feed its people, solve peculiar health problems and industrialise, it has to evolve policies and strategies that will encourage investment in Biotechnology activities.

The basic technology and wherewithal for developing Industrial Biotechnology processes are within our reach. With appropriate motivation and support, it is possible for many biotechnology products, like bakers' yeast and saccharifying enzyme (α -amylase), antibiotics, currently consuming large foreign exchange due to import, to be produced in-country as the raw materials and the technologies are readily available.

The Federal Government has taken the right step in bringing Biotechnology to the fore as one of its three priorities (others being Information Technology (IT) and Communication). It has also taken the right step in forming a National Biotechnology Development Agency (NABDA). As has been shown, Biotechnology is a multidisciplinary technology and getting appropriate results in the application of Biotechnology in the various sectors (Agriculture, Medicine, Industry, Environment) demands coordination at the Centre but effective decentralisation into appropriate zonal Centres established for each of the sectors of Biotechnology. Appropriate policies, funding and direction to achieve quick and tremendous

growth and results from the application of Biotechnology are necessary to back this up.

University of Lagos should, as a matter of urgency, take the driver's seat and be in the forefront in at least three of the areas of application of Biotechnology (viz: Medical, Industrial and Environmental) through active and coordinated collaborative researches in the various areas. The University is called upon to endorse, appropriately fund and encourage the Biotechnology Research Group, as the vehicle for this and for the establishment of a multidisciplinary postgraduate programme in Biotechnology.

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7. ACKNOWLEDGEMENTS

First of all, I like to give all my thanks to the Almighty Allah and acknowledge all His mercies upon my family and myself all these years. I cannot recount how many of His interventions in my life I have had. All I want to say is "Alhamdu Lillahi".

I was born to parents who valued education so much, even though they did not receive formal education and who deprived themselves of all luxuries and even meals to see me through secondary education. My early days were full of the love and support in our town, Iboro, Yewa North of Ogun State, where it all started and I owe all I am today to my late father, the late Alhaji Tijani Ishola Bello ('ina Lilahi wa wa ina Lilahi rajiun') and my eversupportive mother, Alhaja Bintu Abeke Bello. I am happy that one of them is alive to witness today. My uncles are not left out of this. They all contributed to my secondary education fees in those days. I acknowledge the contributions of the late Mr Yusuf Bello and Alhaji Sunmonu Bello. I am grateful to all of them.

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