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Inaugural Lecture Series 131

FATS AND LIFE

By

ONAJOBI, F. D.,
Professor of Biochemistry

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FATS AND LIFE

INTRODUCTION

The Journey to Ife

Mr. Vice-Chancellor, Sir, the Registrar, my colleagues, students, invited guests, ladies and gentlemen; it gives me great pleasure to stand before you all this afternoon to deliver this INAUGURAL LECTURE, the first to be given by a female member of staff in the Faculty of Science of this University. Around the middle of 1968, as I was nearing the completion of my Ph.D programme at the University of Edinburgh, I wrote applications for employment to the Universities of Lagos, Ibadan and Ife. The University of Ife (now Obafemi Awolowo University) immediately replied to say that my application was under consideration. Soon after this letter, Professor Syme, the then Head of Chemistry Department at Ife, visited me in Edinburgh and informed me that a department of Biochemistry was not in existence at Ife but the University was interested in my being the nucleus for starting one. A few weeks after this visit, I got a provisional letter of appointment from Ife. I was so much impressed by the speed with which the University treated my application that I made up my mind there and then that it had to be Ife for me. I therefore joined the University of Ife, as a member of Chemistry Department in March 1969. While in that Department, I, with other members of staff taught Chemistry for preliminary students and Chemistry for students of Pharmacy, Agriculture, Zoology and Botany. I taught my first Biochemistry course at Ife to Zoology students. I am happy to note that four of those Zoology students are now either Professors or Readers in the department of Zoology of this University.

Biochemistry at Ife

The University of Ife, (now Obafemi Awolowo University) decided, in its wisdom, to create, effective from 1969/70 session, a Department of Biological Sciences in which there were five units. The units were: Zoology and Botany (which were already in existence) Genetics, Microbiology and Biochemistry. It was from such a conglomerate that each unit developed its curriculum and awarded the different degrees until four of the units metamorphosed into separate departments in 1976. It was an uphill task developing a curriculum for Biochemistry in those days. Some of our senior colleagues in the older units of the Department of Biological Sciences felt that all the students in the Department, including Biochemistry students, had to take the same courses in the first two years, that is, the same "biological" Mathematics and Physics and the same Chemistry. Only Organic Chemistry, "lectures only", was allowed in year III, as a special favour for Biochemistry, Microbiology and possibly Genetics students. I give kudos to my colleagues in the unit of Biochemistry at that time, because, though we were young and supposed to be inexperienced (ordinary lecturers), we stood our ground and ensured that we wrote, and eventually got approved, a Biochemistry programme which compared favourably with any Biochemistry programme in the world. I make bold to say that our undergraduate programme is still one of the best in this country despite very inadequate funding in the past one and a half decades. We later added a postgraduate programme, which is equally of high standard. A number of our students are back in the department as lecturers/senior lecturers and one of them is the current Head of Department.

My colleagues (young and old) and I have also tried, up to the present time, to maintain discipline among our staff and students. I included staff because, if staff members are not disciplined, it will be impossible to inculcate discipline in students. Mr. Vice-Chancellor, Sir, Ladies and Gentlemen, I have given this background information about the development of Biochemistry at Ife so that you can have an insight into the background of my academic development at Ife which has led to this inaugural lecture.

The Title

Mr. Vice-Chancellor, Sir, the title of this inaugural lecture, FATS AND LIFE, implies that Fats have something to do with life, or that life has something to do with fats or that without Fats there cannot be life. I beg to submit, Sir, that it is all of the above.

What are Fats?

In a restrictive sense fats are defined as naturally occurring esters of glycerol and fatty acids which are solid at room temperature as opposed to oils which are similar esters but liquid at room temperature. In a broad sense the word fat can be a general term which is used synonymously with lipid. In this context, fats or lipids are compounds which are extractable from animal and plant tissues and microorganisms by organic solvents such as methanol, ethanol, ether, chloroform, benzene, acetone or mixtures of these solvents. The word, FAT in the title of this lecture is meant to be synonymous with LIPIDS and I crave your indulgence to use these two words interchangeably.

This lecture deals with fats which have direct effects on life but the use of some of these fats may affect life indirectly. Time will not permit me to go into details about such fats but I shall just mention some in passing. The following are some examples:

Fats (triacylglycerol) are used in making soap. We know that soap is essential for various cleaning purposes. Without the cleanliness offered by soap, our lives would be endangered by various microorganisms which thrive on dirt.

Fats contribute to the aesthetics of life, for example body creams, hand lotions and hair creams which are meant to prevent dryness with consequent scaliness of the skin are very rich in fats. A number of monoterpenes and diterpenes are components of essential (volatile) oils used in making perfumes.

Fats are used to make products which add to our comfort. For example various oils used in industries are fats. Rubber, without which there will be no tyres for our cars, among others, is a polyterpene. The list is endless.

What Is Life?

The *Oxford Advanced Learner's Dictionary of Current English* defines LIFE as the "ability to **function** and grow which distinguishes living animals and plants from dead ones and from rocks, metals etc." *The New Webster's Dictionary of the English Language,* International Edition, defines LIFE as "the state of an organism characterized by certain processes or abilities that include metabolism, growth, reproduction and response." While the first definition tells us in simple terms that an organism is dead when it stops **functioning**, the second definition gives us a little detail about what constitutes **functioning**.

In the course of this lecture, I hope to show that fats affect virtually every process that makes life possible and also to present my modest contribution to some FAT-related LIFE processes.

NATURE AND STRUCTURE OF FATS

Biological lipids, that is, fats extracted from tissues include the following major components: acylglycerols, (the major component of oils such as groundnut oil, palmoil etc) waxes, phospholipids (glycerophospholipids and sphingolipids), cholesterol and cholesterol esters, plant sterols and sterols of fungi, steroid hormones, bile acids, carotenoids, lipid- soluble vitamins and various terpenes (e.g camphor rubber). The structures of a few examples of these fat components are shown in Fig. 1 (a, b, c, d).

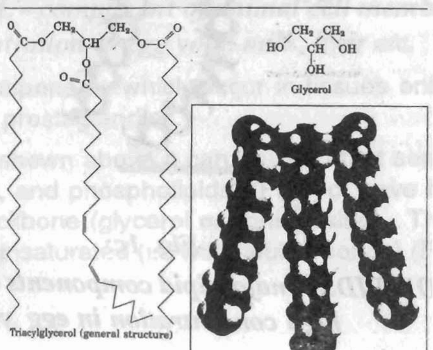


Fig. 1a:
TRIACYGLYCEROL - the major component of oils (olive oil, palm oil, groundnut oil, etc) and meat fat.

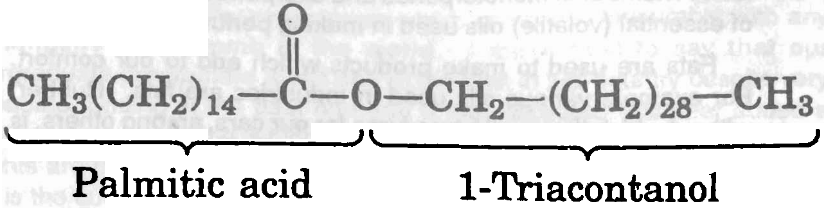


Fig. 1b:
Triacontanylpalmitate - A WAX

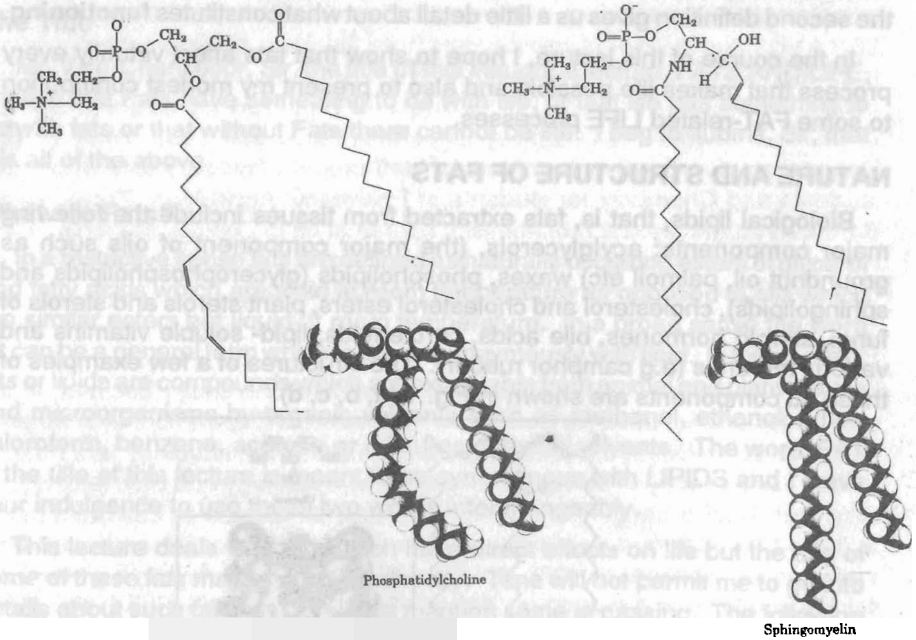


Fig. 1c:
PHOSPHOLIPIDS - major lipid components of cell membranes, also high concentration in egg yolk

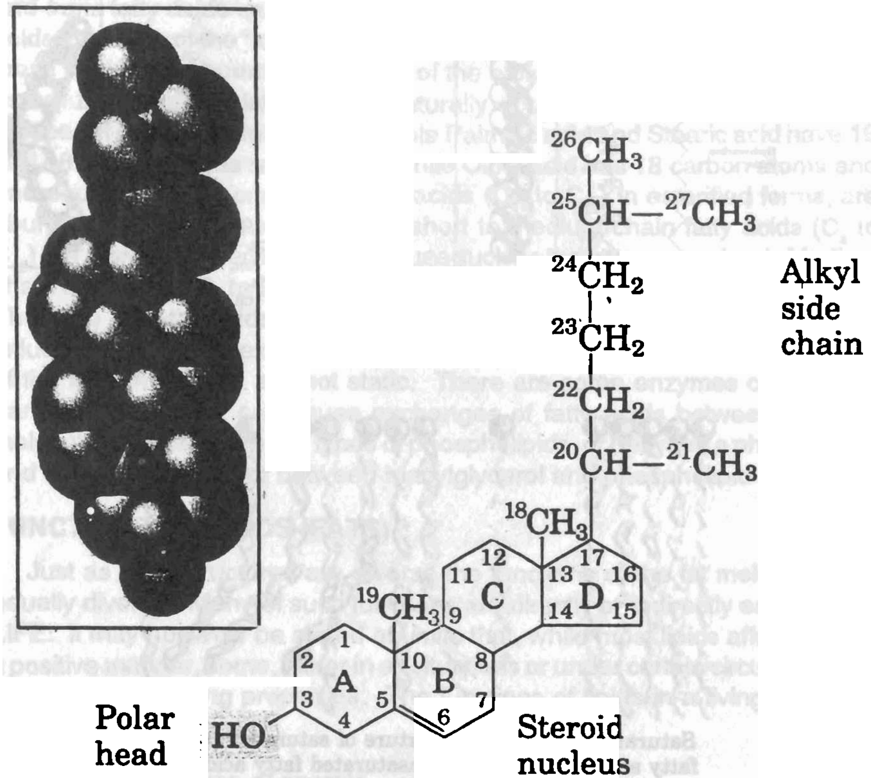


Fig 1d.
CHOLESTEROL - component of animal cell membranes, high concentration in egg yolk, milk, liver etc.

There are also lipid components which occur in tissues only in very small quantities, for example, prostaglandins.

From the structures shown above it can be seen that some of the lipids, Acyl glycerols (Fig. 1a), and phospholipids) (Fig. 1c) have long chain fatty acids esterified to a backbone (glycerol or sphingosine). These fatty acids are either saturated or unsaturated (i.e with double bonds) (Fig 2a,b).

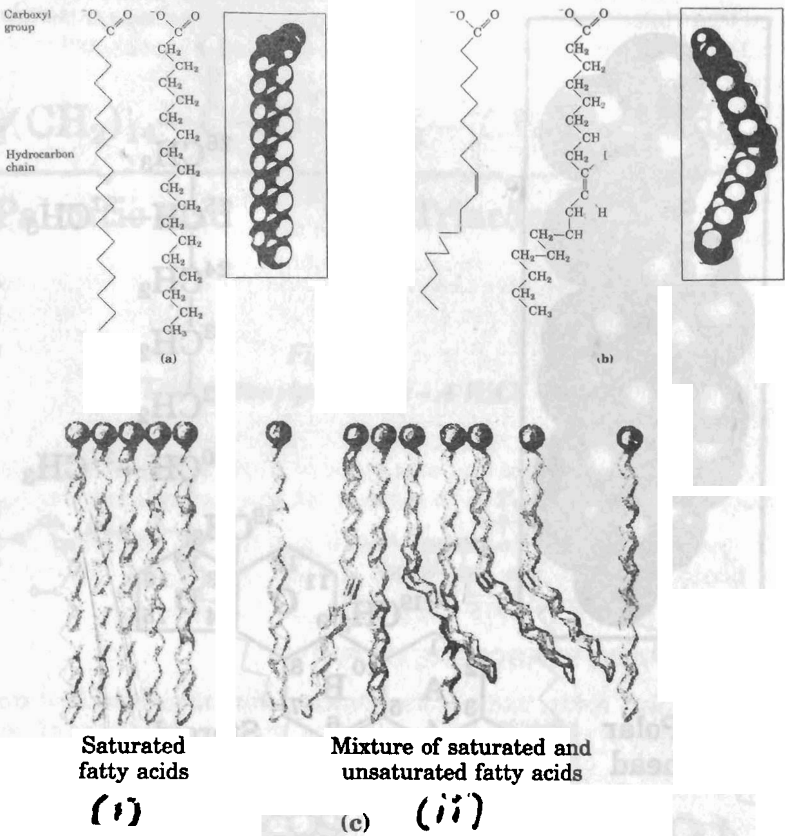


Fig. 2

a. FATTY ACID - saturated (stearic acid)
b. FATTY ACID - Unsaturated (oleic acid)
c. (i) Saturated fatty acids - closely packed
(ii) MIXTURE OF saturated + cis - unsaturated fatty acids - loose packing.

In nature, the configuration of the groups around the double bonds is normally *cis*, the *trans* configuration is rare except as transient metabolites. Saturated and *trans* fatty acids can be more closely packed, whereas unsaturated fatty acids, because of the "kink" in the structure are loosely packed (Fig. 2c). Such loose packing is important for some of the biological functions of these lipids as will be explained later. Most naturally occurring fatty acids have even-number of carbon atoms. For example Palmitic acid and Stearic acid have 16 and 18 carbon atoms respectively while Oleic acid has 18 carbon atoms and one double bond. Long chain fatty acids (C_{14} to C_{22}) in esterified forms, are abundant in most tissues whereas short to medium chain fatty acids (C_4 to C_{12}) are more restricted to certain tissues such as the mammary gland. Medium chain fatty acids (C_8 to C_{12}) are also abundant in coconut and palmkernel oils. The type of fatty acids esterified to a lipid compound (e.g phospholipid) influences, to a great extent, the functions of that lipid. The structures of some of the lipid molecules are not static. There are some enzymes called "acyl transferases" which can cause exchanges of fatty acids between the lipid molecules, e.g between two types of phospholipids, or between a phospholipid and cholesterol ester or between triacylglycerol and phospholipid etc.

FUNCTIONS OF LIPIDS (FATS)

Just as their structures are diverse the functions of the fat molecules are equally diverse. Many of such functions are directly or indirectly essential for LIFE. It may however be stated *ab initio* that, while most lipids affect LIFE in a positive manner, some, either in all situations or under certain circumstances, have life-threatening properties. The functions of lipids in a living organism include the following:

(a) *The provision of energy.*

When the fatty acid moiety of some of the lipid molecules, especially those of triacylglycerol, are catabolized (broken down), energy is made available ultimately in the form of Adenosine triphosphate (ATP) (Fig. 3),

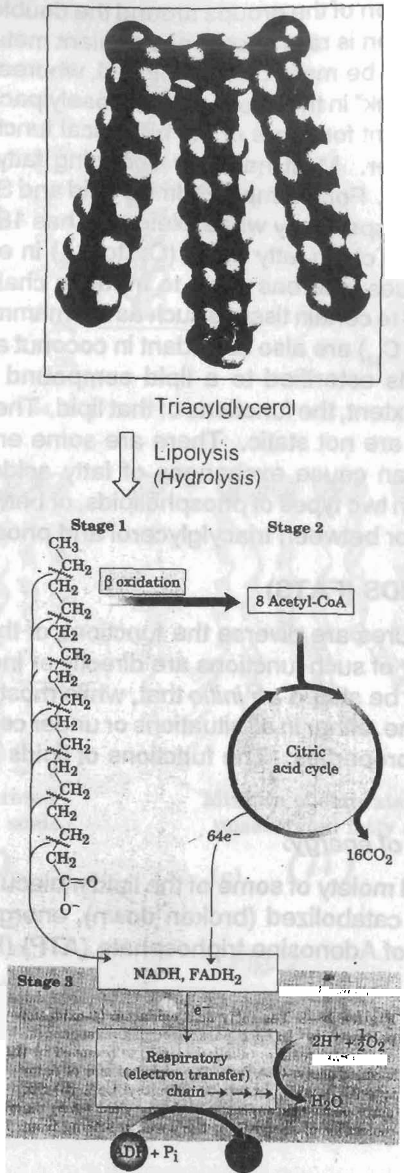


Fig 3.

Generation of energy (ATP) from a fat molecule

which can then be used (directly or indirectly) for various energy requiring processes in the organism, such as muscular movement, transport of molecules across membranes, biosynthetic processes, nerve conduction and transmission, bioluminescence in the firefly (*tannan-tannan* in Yoruba) etc. Although carbohydrates and proteins also produce energy when catabolized, fats give more than twice as much energy as either of these two on weight for weight basis.

(b) *As components of biological membranes*

The major components of biological membranes are lipids and proteins with carbohydrates occurring in minor quantities. Apart from the cell membrane (plasma membrane) which demarcates one cell from other cells or from the surroundings, there are internal membranes which demarcate the different compartments of the cell from one another. These include the membranes of the nucleus, endoplasmic reticulum, mitochondria, Golgi apparatus, lysosomes, various vacuoles and chloroplasts in plants (Fig. 4).

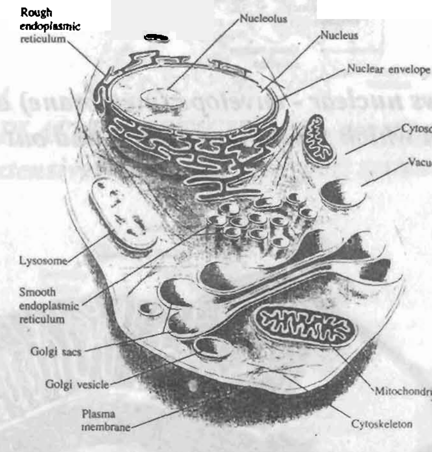


Fig. 4a

ANIMAL CELL - showing various membranous organelles

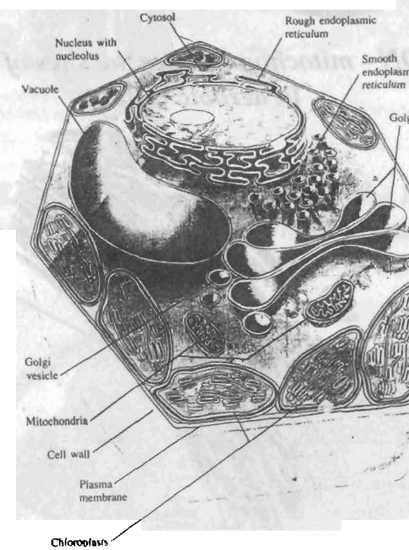


Fig. 4b

PLANT CELL - showing various membranous organelles.

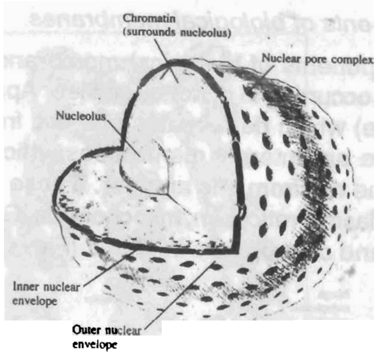


Fig 5a.

***NUCLEUS** - shows nuclear - envelope (membrane) and nuclear pore complex through which substances pass in and out of the nucleus.*

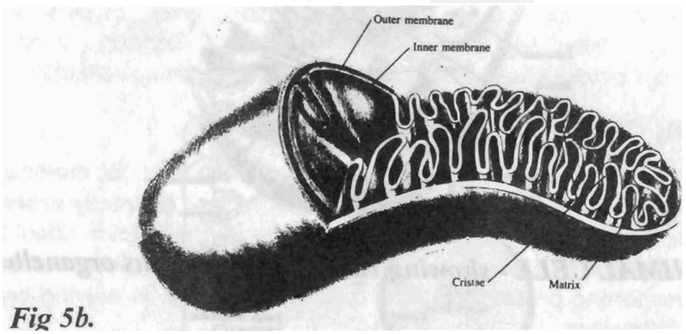


Fig 5b.

***MITOCHONDRION** - mitochondria are the sites of energy production in aerobic cells.*

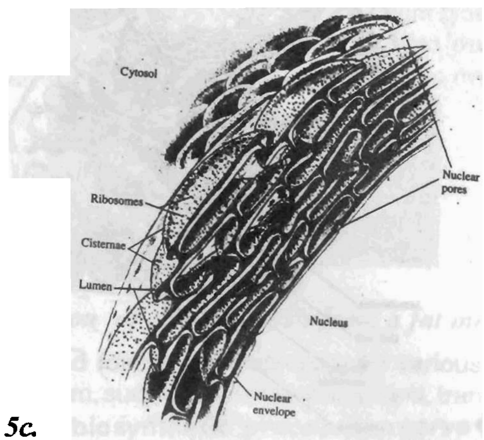


Fig 5c.

***ROUGH ENDOPLASMIC RETICULUM (ER).** Ribosomes bond to the surface of the membranes of the rough ER carry out protein systhesis.*

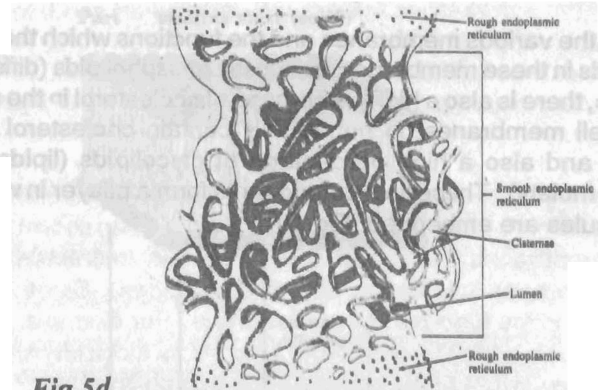


Fig 5d.

***SMOOTH ENDOPLASMIC RETICULUM** - constitutes part of a cell's extensive membrane transport system.*

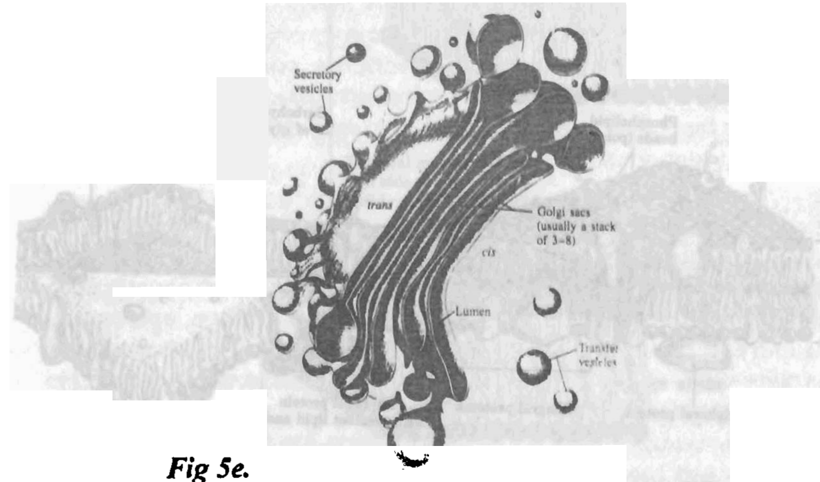


Fig 5e.

***GOLGI COMPLEX.** - closely associated with the ER, modifies and transports carbohydrate and lipid precursors.*

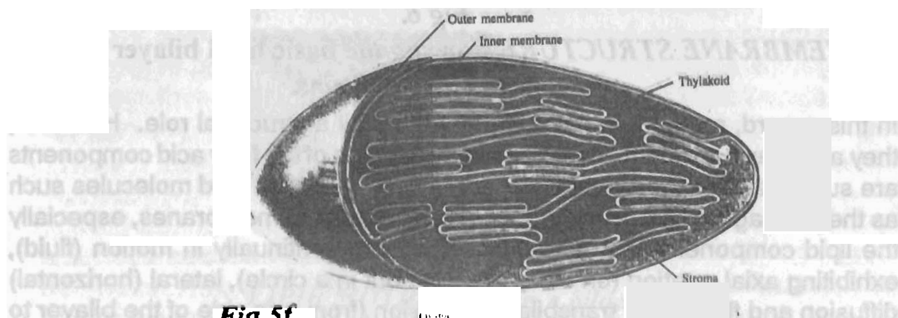


Fig 5f.

***CHLOROPLAST.** - site of photosynthesis.*

Fig 5a-f show the various membranes and the functions which they perform in cells. The lipids in these membranes are mostly phospholipids (different types). In animal cells, there is also a high percentage of cholesterol in the membranes while plant cell membranes do not usually contain cholesterol but contain other sterols and also a high percentage of glycolipids (lipids containing carbohydrate moiety). These lipid components form a bilayer in which various protein molecules are embedded (Fig. 6).

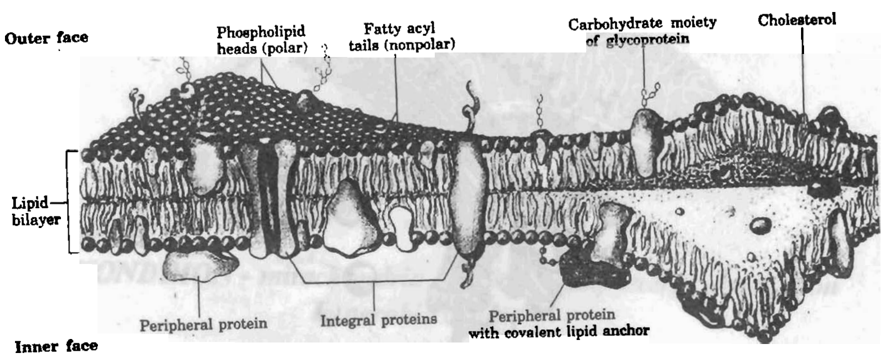


Fig 6.

MEMBRANE STRUCTURE showing the* basic lipid bilayer *plus proteins and glycoproteins.

In this regard, membrane lipids are said to play a structural role. However, they also play functional roles. For example some of the fatty acid components are substrates for the synthesis of some very important lipid molecules such as the prostaglandins. The components of biological membranes, especially the lipid components are not static. They are continually in motion (fluid), exhibiting axial rotation (on the same spot but in a circle), lateral (horizontal) diffusion and flip-flop or transbilayer diffusion (from one side of the bilayer to another) (Fig. 7).

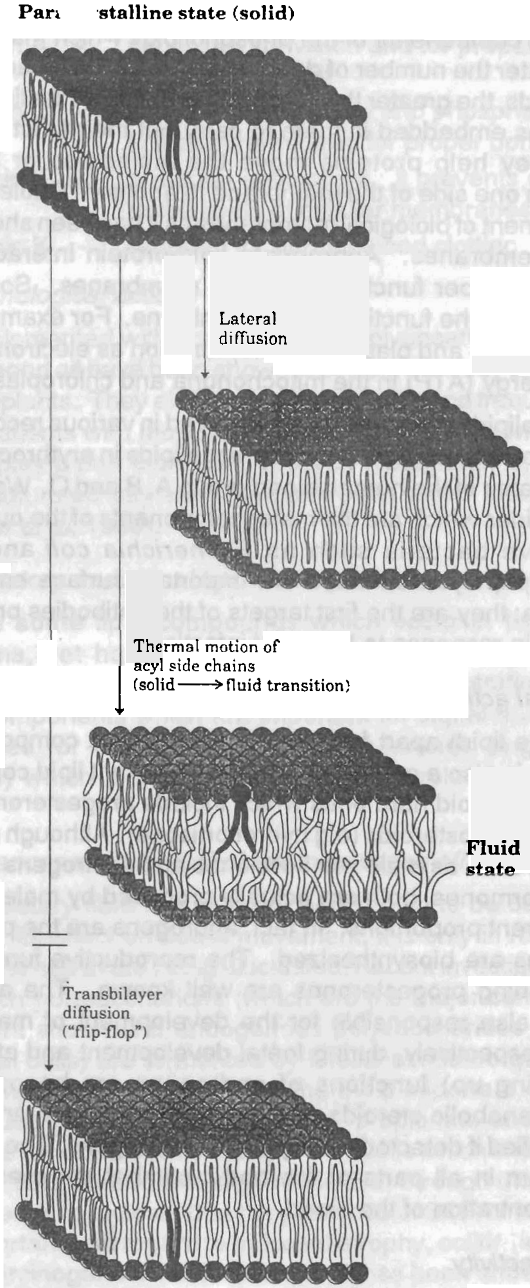


Fig 7.

LIPID MOTION within a bilayer

It is the fatty acid components of the phospholipids which make possible the fluidity. The greater the number of double bonds in the fatty acid components of the phosphilipids, the greater the fluidity. This fluidity of the lipid components helps the proteins embedded in them to carry out their functions effectively. For example they help proteins move the molecules or ions they are transporting from one side of the membrane to another. Cholesterol is a very important component of biological membranes as it has been shown to regulate fluidity of the membranes. Appropriate lipid-protein interactons are also important for the proper functioning of cell membranes. Some lipids also participate directly in the function of the membrane. For example, some lipid quinones (ubiquinone and plastoquinoine) function as electron carriers in the production of energy (ATP) in the mitochondria and chloroplasts.

Some sphingolipids are known to be involved in various recognition events at the cell surface. For example, glycosphingolipids in erythrocyte membrane are the determinants of the human blood group A, B and O. We also have the Lipopolysaccharides which are the major components of the outer membrane of gram-negative bacteria such as *Escherichia coli* and *Salmonella typhimurium*. Lipopolysaccharides are important surface entities of gram-negative bacteria: they are the first targets of the antibodies produced by the immune system in response to bacterial infection.

(c) *Hormonal activity*

Cholesterol, (a lipid) apart from being an important component of animal cell membranes, is also a precursor of some important lipid compounds such as bile acids and steroid hormones which include progesterone, androgens, oestrogens and corticosteroids (e.g hydrocortisone). Although androgens are sometimes referred to as male sex hormones and oestrogens are referred to as female sex hormones, both are actually produced by males and females, although in different proportions. In fact, androgens are the precursors from which oestrogens are biosynthesized. The reproductive functions of these hormones, including progesterones are well known. The androgens and oestrogens are also responsible for the development of male and female characteristics respectively, during foetal development and at puberty. The anabolic (building up) functions of androgens are becoming common knowledge: the anabolic steroids which many sports men and women take (and get disqualified if detected) are synthetic androgens. The corticosteroids affect metabolism in all parts of the body, combat stresses and regulate electrolyte concentration of the blood.

(d) *Vitamin activity*

Vitamins A, D, E and K are lipids and are usually referred to as fat-soluble vitamins. Each of these vitamins (like all vitamins) is important for one life process or the other. However, because the lipid soluble vitamins can be stored (mostly in the liver), they can be toxic when taken in excess. The

functions of these fat-soluble vitamins are as follows:

- Vitamin A - necessary for vision and for proper growth and development
- Vitamin D - important for calcium and phosphate metabolism. It is thereforerequired for proper bone formation.
- Vitamin E - a natural antioxidant. It prevents oxidative damage to the lipids of cellular membranes.
- Vitamin K - required for normal blood clotting

(e) *Immunological actions*

Diets supplemented with rich sources of polyunsaturated fatty acids, such as sunflower seed oil have been shown to protect the body against the rejection of organ transplants. They also reduce the severity and frequency of replapses suffered by patients with multiple sclerosis, a disease in which autoimmunity is thought to play a part (Johnson, 1985). Prostaglandins, synthesized from some polyunsaturated fatty acids have also been shown to have immunological actions (White *et al*, 1990).

(f) *Regulatory and signal transducing effects*

There are some lipid compounds which occur in tissues in very low concentrations, yet have very important biological roles. For example, phosphatidyl inositol, which occurs only in small concentrations, is metabolized to produce components which are important for signal transduction in cells, and substrates for the synthesis of eiocasanoids (e.g prostaglandins, leukotrienses) which play important regulatory roles in a variety of tissue functions.

(g) *Anticancer and blood cholesterol lowering effects.*

Although dietary fibre has always been known to be beneficial to health, with regard to its effect on bowel movement, it is only in recent times that its other benefits to health are being elucidated. Recent investigations have shown that non-starch polysaccharides (which are the major component of dietary fibre), resistant starch and endogenous polysaccharides (from mucus and shed epithelial cells) are fermented by intestinal microorganisms, especially in the colon, to produce substances, the most important of which are *short chain fatty acids* (SCFA) such as acetate, propionate and butyrate. These SCFAs are rapidly absorbed by the epithelial cells which line the colonic lumen and some of the absorbed SCFA go to the liver through the portal circulation. There is evidence to indicate that the presence of SCFAs in the colon may be clinically important with regard to mucosal atrophy, colitis (inflammation of the colon) and carcinogenesis. For example, it has been shown that n-butyrate, and, to a lesser degree, propionate inhibit the growth of various colon cancer cell lines and favour differentiation. In animals with induced metastatic colon cancer, n-butyrate reduces spread of the cancer (Sheppach, 1998).

Dietary fibre, probably on account of its conversion to SCFA, has also been shown to significantly decrease total serum cholesterol, and low density lipoprotein cholesterol, thus consequently reducing cardiovascular diseases (Anderson *et al*, 1984; Zafrallah *et al*, 1991).

Thus it is now evident that dietary fibres are beneficial to health on account of their conversion in the gut to some fat molecules, the short chain fatty acids.

(h) *Pharmacological actions*

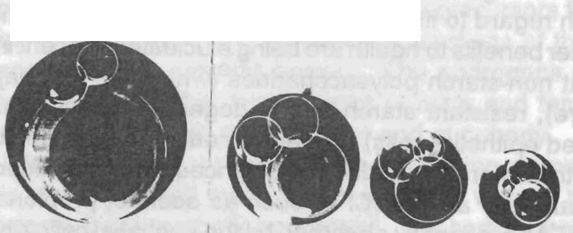
The prostaglandins are good examples of naturally occurring fat components which have important pharmacological actions. On account of this, some of them are used as drugs. A number of other drugs are lipids or lipid derived. Examples are menthol, steroids, etc.

TRANSPORT OF LIPIDS IN THE BLOOD

Various components are carried in the body from organ to organ and from one tissue to another, dissolved in the plasma of blood. Lipids, being insoluble in water, cannot on their own dissolve in the plasma, they are helped to do so by certain proteins. Therefore the lipids are carried round in the blood as entities called **lipoproteins.** These are a combination of certain proteins (called apoproteins) linked to various types of lipids by non-covalent forces. There are four main types of lipoproteins. These are:

(a) Chylomicrons
(b) Very low density lipoproteins (VLDL)
(c) Low density lipoproteins (LDL), and
(d) High Density Lipoproteins (HDL)

Fig. 8



	Chylomicrons	VLDL	LDL	HDL
Protein	2%	7%	21%	47%
Cholesterol	7%	20%	47%	18%
Triglycerides	85%	55%	9%	7%
Phospholipids	6%	18%	23%	28%
Atherogenic risk	slight	high	very high	protective factor

Fig 8.

LIPOPROTEINS - relative sizes, and composition of the lipoproteins

depicts the relative sizes and the concentrations of these lipoproteins in the blood. The chylomicrons carry exogenous (dietary) fat, which is mainly triacylglycerol from the intestine to other tissues, especially muscles, adipose tissue and finally to the liver. The VLDL carry endogenous (synthesized in the liver) triacylglycerol to tissues after which they are converted, first to Intermediate Density Lipoproteins (IDL) and finally to Low Density Lipoproteins. The LDL carry cholesterol to peripheral tissues while HDL carry cholesterol from peripheral tissues to the liver. Goldstein and Brown got a nobel prize for their elucidation of the following:

(1) how low density lipoproteins are taken up by cells through receptors on the cell membrane,
(2) how the LDL cholesterol is utilized by the cell,
(3) how the LDL cholesterol regulates cholesterol synthesis in the cell, and
(4) how problems associated with the uptake mechanisms can lead to elevated blood cholesterol and consequently atherosclerosis.

Fig. 9

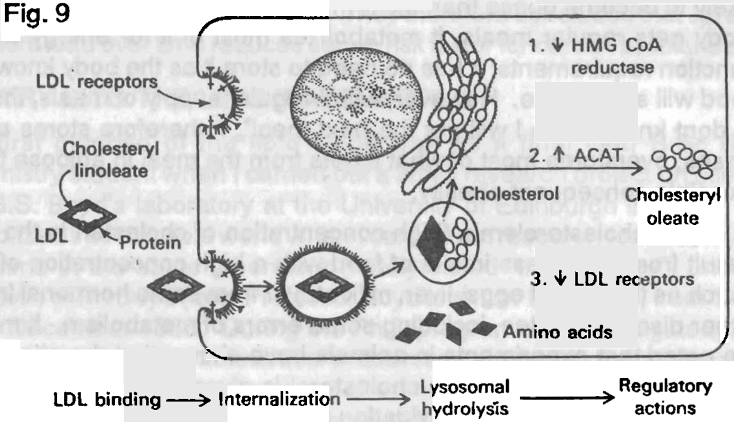


Fig 9.

Scheme of Low Density Lipoprotein (LDL) uptake through receptors on a cell membrane.

depicts some of these processes (Brown and Goldstein, 1976; 1984).

Atherosclerosis is the formation of plaques, resulting from the depositon of various components on blood vessel walls (particularly arterial walls). Prominent among the deposited components are cholesterol and cholesterol esters presumably derived from LDL. Such atherosclerotic plaques narrow the *arteries* and may even occlude them and stop blood flow. A combination of atherosclerotic plaque and thrombus formation (blood clot), particularly in coronary arteries, can lead to coronary heart disease and even cardiac arrest. There are many risk factors which may increase the incidence of atherosclerosis and coronary heart disease, these include cigarette smoking, diabetes mellitus, high blood pressure, lack of exercise, obesity, hypercholesterolemia (high blood cholesterol) and hereditary factors.

Obesity is usually classified as a secondary risk factor exhibiting its effect through concomittant hypertension, diabetes and hyperlipidemia (high concentration of lipid in the blood). The risk factors which are directly associated with lipids are obesity and high concentration of cholesterol in the blood. Obesity is the excess storage of fats, mainly triacylglycerol, in the adipose tissue of the individual. This may result from excess intake of fats in the diet or from excess intake of carbohydrate which can be converted to fatty acids and then to triacylglycerol and stored. It may be noted that the word "excess" is not absolute in this context. What is just adequate for one individual may be excess for another. Obesity is also influenced by other factors such as hormones, hereditary traits, age, physical excercise and whether or not the individual eats small meals at regular intervals (even more than three times a day) or large meals irregularly (once or twice a day). Experiments in animals have shown that the latter individual (who eats large meals irregularly) is more likely to become obese than the former. The rational for this is that, when the body gets regular meals, it metabolizes most of it for energy and other life function requirements; it has no need to store it as the body knows that more food will soon come. However, with irregular supply of meals, the body says "I dont know when I will get the next meal", it therefore stores and in some cases, overstores most of what it gets from the meal in adipose tissues, with possible consequent obesity.

Hypercholesterolemia (high concentration of cholesterl in the blood) may result from an excess intake of food with a high concentration of cholesterol (such as the yolk of eggs, liver, milk etc) or from some hormonal imbalance or other diseased states, including some errors of metabolism. It may however be noted that experiments in animals have shown that the observed arterial damage when a diet rich in cholesterol is given should be attributed, not to cholesterol itself, but to its oxidation products. Although cholesterol is vital to the life of an animal including human beings (for cell membranes, steroid hormones, bile acids, etc) there is abundant synthesis of cholesterol in the body. Many animal tissues, especially the liver, adrenals, intestine, the gonals and the skin synthesize cholesterol at a fast rate. Those tissues which synthesize cholesterol at a slow rate may obtain extra cholesterol from the receptor mediated intake of LDL into their cells.

Apart from the amount of cholesterol in the diet, it has also been shown from epidemiological studies, that the type of fatty acids (that is fatty acids esterified to the triacylglycerol) in our dietary lipid influences the level of cholesterol in the blood. High ratios of polyunsaturated fatty acids to saturated fatty acids have been shown to decrease the level of blood cholesterol and LDL while low ratios have been associated with high blood cholesterol, increased LDL and high risk of developing atherosclerosis and coronary heart disease. (Brown, 1969; Krombout *et al* 1985). For example, some studies

showed that there has been an increase in the incidence of heart diseases in Japanese who migrated to the USA from their country where, the incidence of coronary heart disease is low, their dietary fat is low with a very high ratio of polyunsaturated to saturated fatty acids. Their blood cholesterol pattern changed at the same time from a characteristically low Japanese level to the typically much higher level of the USA (Thelle, 1993).

However the effect of polyunsaturated fatty acids on atherogenesis is apparently not straightforward. It has been shown that these fatty acids as well as the cholesterol in LDL get modified by oxidation. Such oxidatively modified lipoproteins are atherogenic. Thus while dietary polyunsaturated fatty acids may retard atherogenesis by lowering plasma levels of LDL, they may, at the same time, promote atherogenesis through their susceptibility to oxidative modification (Steinberg *et al*, 1989).

It has also been reported that nibbling, under fasting condition, decreases serum cholesterol as well as the incidence of cardiovasular disease (Jenkins *et al* 1995). The investigators suggested that these effects are partly attributable to a reduced concentration of insulin. They therefore concluded that spreading the nutrient load over time reduces serum risk factor for cardiovascular disease.

MY ENTRY INTO THE LIPID (FATS) WORLD

My first glimpse of the lipid world was as a final year B.Sc (Hons) Biochemistry student when I carried out a small research project on bile acids in Dr. G.S. Boyd's laboratory at the University of Edinburgh in 1965. I was fully baptized into this lipid world when I carried out research towards my Ph.D programme in the same laboratory (fondly called "the Boydery") under the supervision of Dr. Boyd (later Professor Boyd and now deceased) from October 1965 to December 1968. During the Ph.D programme I investigated, (using ^{14}C-mevalonic acid, a radioactive precursor), cholesterol and lipoprotein metabolism by subcellular fractions of rat liver. I discovered, then, that the apoprotein of serum á-lipoprotein (High density lipoprotein) exerted a regulatory role on cholesterol synthesis by the liver. The apoprotein did this by causing an accumulation of squalene, one of the intermediates of cholesterol synthesis, thus inhibiting the synthesis of cholesterol (Boyd and Onajobi, 1969; Onajobi & Boyd 1970). This was a novel form of control and therefore constituted a very significant finding.

LIPID WORK AT IFE:

CONTINUED INTEREST IN CHOLESTEROL AND LIPOPROTEINS

On joining the University of Ife (now Obafemi Awolowo University) in 1969, I first digressed a bit from the lipid world by joining the Grassland Research Project (based in the Faculty of Agriculture) on which I went on an International Atomic Energy Agency fellowship to the University of Fort Collins in Colorado, USA for one year. When I was there I studied sulphate uptake and metabolism by corn roots. On returning to Ife, I continued for sometime on similar lines, investigating factors which affected ATP-sulphurylase activity in rice roots.

However I soon went back to my "first love", i.e carrying out research on lipids. I reentered this field by investigating the level of total serum cholesterol and the cholesterol associated with the LDL (low density lipoprotein) plus VLDL (very low density lipoprotein) in some healthy Ife residents. Before this investigation, the normal serum cholesterol levels were well known for various populations in the Western World (Heiss *et al*, 1980). Work carried out at the UCH, Ibadan also showed the normal amount of cholesterol associated with HDL (High Density Lipoprotein) (Taylor & Agbedana, 1983), but there was no report on the amount of cholesterol associated with LDL and or VLDL in a Nigerian population. Yet it was important to have both values because the higher the concentration of plasma LDL in an individual, the greater the risk of arterial and coronary heart diseases whereas HDL protects the individual against such diseases. (Miller and Miller, 1975).

For my investigation, I analyzed the serum of 248 apparently healthy Nigerian subjects. The group included a few lecturers but mostly fresh students registering at the Health Centre, school children, farmers, traders and house wives. Three European lecturers resident at Ife at that time were also sampled for comparison.

The results showed that while the mean of the total serum cholesterol level of the three Europeans studied was 208 ± 32 mg/100ml, which compared well with values obtained for Europeans in Europe or in the U.S.A., much lower values, averaging 124 ± 28 mg/100ml was obtained for the Nigerian subjects. Also the LDL + VLDL cholesterol was much lower (75 ± 18 mg/100ml for female and 66 ± 16 mg/100ml for male subjects) than those obtained for the Europeans (118 ± 20).

Table 1

Comparison of Total Serum Cholesterol and LDL + VLDL Cholesterol In Normal Nigerians and Europeans

Nationality	**Nigerian**	**European**
Number in Sample and Sex	15 (Male)	3 (Male)
Age range (years)	41-60	36-58
Total Serum Cholesterol (mg/100ml)	129 ± 25	208 ± 32
LDL + VLDL Cholesterol (mg/100ml)	73 ± 18	118 ± 20

Table 1 compares the values for these Europeans and Nigerian men of

similar age group. The cholesterol levels (total or in the lipoproteins) increased with age, just like in Western subjects. However the ratio of LDL + VLDL cholesterol to total serum cholesterol was significantly higher (P< 0.01) in female subjects (0.59) than in male subjects (0.55) (Onajobi, 1987). This is opposite to what obtains in Western subjects (Heiss *et al*, 1980).

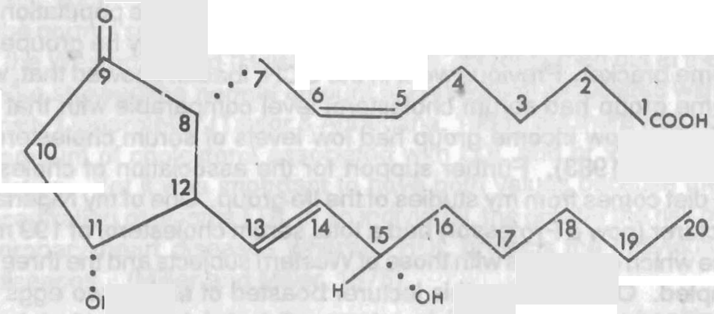
The low level of serum cholesterol in the sampled Ife population is probably associated with diet as most of the tested subjects may be grouped in the low income bracket. Previous work in the UCH, Ibadan showed that, while a high income group had serum cholesterol level comparable with that of Western subjects, a low income group had low levels of serum cholesterol (Taylor & Agbedena, 1983). Further support for the association of cholesterol levels with diet comes from my studies of the Ife group. One of my Nigerian subjects, a lecturer (now a Professor) had a total serum cholesterol of 199 mg/100ml, a value which compares with those of Western subjects and the three Europeans sampled. On interview, this lecturer boasted of eating two eggs a day on a permanent basis. When he was lectured on the dangers of such practice, he immediately reduced his egg intake to one a day. These days, being older and wiser, he now takes an average of just about two eggs in a week.

INVITATION TO RESEARCH ON PROSTAGLANDINS

Although I did not carry out any research on lipids during my one-year IAEA Fellowship period in the USA in 1970/71 sesson, a remark by Dr. Cleon Cole, an agronomist in whose laboratory I spent the year was apparently to guide my interest later in another field of lipid research. Being fascinated by a new (at that time) publication on PROSTAGLANDINS, he asked "Funmi, do you think you can find out, while you are here, if plants synthesize or contain prostaglandins"?. "In one year? Impossbile". I retorted. "One needs many years to carry out such a novel investigation" I explained. At that time prostaglandins had only been found in mammalian tissues and a coral, *Plexaura homomalla*. Back in Ife, that conversation kept cropping up in my mind until I decided to act on it. The next question was "which plant do I investigate?" Again, a chance remark, this time by a friend's mother on the efficacy of *Ocimum gratissimum* (Efinrin) for various ailments, influenced my decison to investigate this plant.

What are Prostaglandins and What do they do?

The PROSTAGLANDINS (PGs) are a group of cyclic, oxygenated, fats, usually with 20 carbon atoms, with a carboxylic acid moiety and one or more double bonds (Fig. 10).



PGE$_2$

Fig 10.
A PROSTAGLANDIN

They were originally isolated from the prostate glands but have since been found in virtually every mammalian tissue, in marine organisms including corals, in insects and more recently in a few plants, fungi and algae (Samuelsson *et al*, 1978; Stanley-Samuelsson, 1994; Ali *et al*, 1990). They generally act locally rather than circulating to distant sites of action. They have a variety of physiological and pharmacological actions and they are very potent, being active at nanogram (10^{-9} gram) or even picogram (10^{-12} gram) levels. There are different types of prostaglandins, named according to the functional groups on the five-membered ring and according to the number of double bonds on the side chains. They all belong to the group of lipid compounds generally termed EICOSANOIDS. Other members of the eicosanoids include the Prostacyclin, Thromboxanes (TX), Leukotrienes (LT), Hepoxilins and Lipoxins. The common feature of the eicosanoids is that they are all biosynthesized from common polyunsaturated fatty acid substrates such as Arachidonic acid (C20:4). The fatty acid precursors are usually located on carbon 2 of phospholipids. Thus phospholipase A$_2$, an enzyme which hydrolyses fatty acids from position 2 of phospholipids, plays a very important role in making substrates available for eicosanoid biosynthesis (Fig. 11).

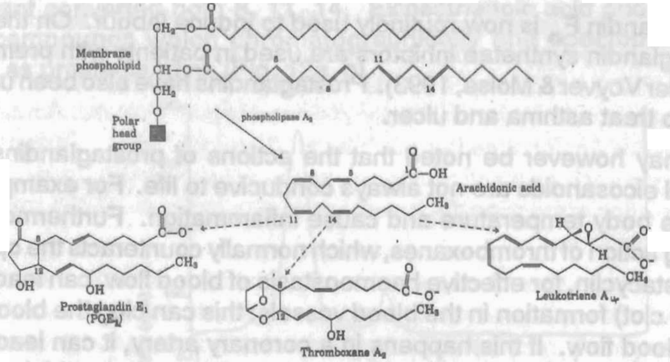


Fig 11.
Release of Arachidonic acid from a phospholipid and its conversion to PROSTALGLANDINS, THROMBOXANES and LEUKOTRIENES

The prostaglandins, thromboxanes and prostacyclin are mostly formed by an enzymic pathway known as the CYCLOXYGENASE pathway while the Leukotrienes, Hepoxilins, Lipoxins and some hydroxy plus hydroperoxy derivatives of arachidonic acid are formed by the LIPOXYGENASE pathway. Two types of cycloxygenases (COX) have actualy been discovered: the constitutive enzyme (COX-1) and the inducible enzyme (COX-2). There are also different Lipoxyganeses. For example the 5-lipoxygenase and the 12-lipoxygenase are involved in the biosynthesis of Leukotrienes and hepoxilins respectively.

As mentioned above, the biological actions of prostaglandins are many and varied. They play important regulatory and signalling functions in the reproductive, respiratory, circulatory, excretory, secretory, immune, blood clotting and central nervous systems. Through their stimulatory effects on smooth muscles, they affect blood pressure, parturition, gastrointestinal movement and lung function etc. (White *et al*, 1990). In plants, the prostaglandins have been shown to aid fruit ripening and hasten the time of flowering (Attrep *et al* 1980). From the above mentioned list of actions, (which is far from being exhaustive) it can be seen that the prostaglandin is the equivalent of what the Yoruba herbalist calls "GBOGBONSE" (meaning a drug that cures all ailments). We may therefore refer to prostaglandins as the "GBOGBONSE OYINBO".

It is now known that the prostaglandins are able to have such a wide range of actions because they act in many tissues by regulating the synthesis of the intracellular messenger, cyclic AMP (cAMP). Because the latter mediates the action of many hormones, the prostaglandins are able to affect a wide range of tissue and cellular-functions, that is, the **Prostaglandins affect virtually every life process.** Many of the biological actions of the prostaglandins have found wide applications in clinical practice. For example, in Western countries prostaglandin $F_{2\alpha}$ is now routinely used to induce labour. On the other hand, prostaglandin synthetae inhibtors are used in patients with premature labour (Van-der Veyver & Moise, 1993). Prostaglandins have also been used in clinical trials to treat asthma and ulcer.

It may however be noted that the actions of prostaglandins or those of related eicosanoids are not always conducive to life. For example some PGs elevate body temperature and cause inflammation. Furthermore the blood-clotting action of thromboxanes, which normally counteracts the opposite action of Prostacyclin, for effective haemeostasis of blood flow, can lead to thrombus (blood clot) formation in the blood vessels: this can clog the blood vessel and stop blood flow. If this happens in a coronary artery, it can lead to a cardiac arrest. Aspirin, a non-steroidal antinflammatory drug, which is sometimes recommended in low doses by doctors for preventing heart attacks and strokes, has been shown to function by inhibiting cycloxygenase-1 (COX-1) in platelets, thus preventing the synthesis of thromboxane A_2, the thrombus formation promoting eicosanoid (Vane, 1994). Moreover some leukotrienes are involved in the allergic and hypersensitivity reactions obtained in some individuals who are said to have anaphylactic shock, as a result of bee stings, certain drugs or various other agents. Anaphylactic shocks can be fatal if not well managed.

The plant, Ocimum gratissimum

Ocimum gratissimum (Linn) Labiatae, is a herbacious plant grown all over West Africa and in many other tropical countries of the world. It is called *EFINRIN* in Yoruba, *Chianwu Ahuji* in Igbo and *Daido yatagida* in Hausa. Its extracts are used traditionally for various medicinal and therapeutic purposes such as for fever, coughs, diarroea, dysentery, conjuctivitis, rheumatism etc (Oliver, 1960; Ayensu, 1978). Sofowora and others, in the Faculty of Pharmacy at Ife, have investigated the essential oil (volatile oil) of this plant and shown that the oil contains mostly thymol which is responsible for its antimicrobial activity (Sainsbury & Sofowora, 1971). The leaves of this plant are also sometimes used in cooking for flavouring purposes.

Biosynthesis of prostaglandin-like compounds by Ocimum gratissimum leaves

Methods which had been used to study prostaglandin synthesis in manmalian tissues were adapted for these studies.

Initially I used the leaves from young Ocimum gratissimum plants grown from seeds in the Green House (in the Faculty of Agriculture) but later young leaves of plants grown in my garden were used. These leaves were homogenized in Tris-HCl buffer or phosphate buffer and subjected to centrifugation at 20,000g in a refrigerated high speed centrifuge. Three different methods were used to test if the 20,000g supernatant could convert arachidonic (C20:4) or eicosatrienoic acid (C20:3) to Prostaglandin-like products.

Using these different methods, I found that the O. gratissimum 20,000g supernatant converted both 8, 11, 14. Eicosatrienoic acid and Arachidonic acid to compounds which chromatographically and spectophometrically behaved as prostaglandins (Fig. 12a, b).

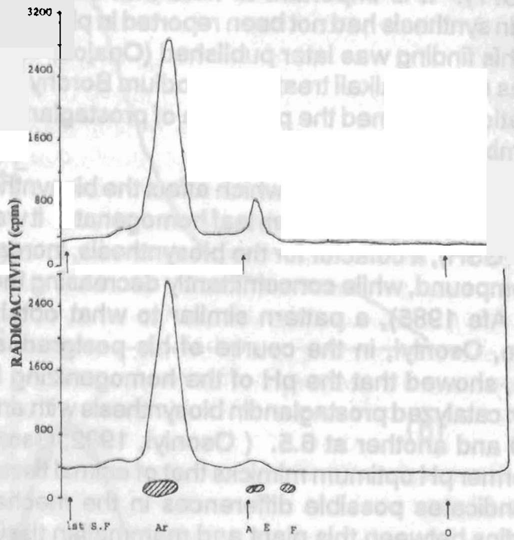


Fig 12a.

Radiotic of total lipid extract from incubation of 14c arachidonic acid with O. Gratissimum leaf homogenate
TOP: Incubation with fresh homogenate
BOTTOM: Incubation with boiled homogenate
A, E & F = Prostagladins A,E & F respectively; AR = Arachidonic axid O = Origin 1st S. F. = 1st Solvent Front.

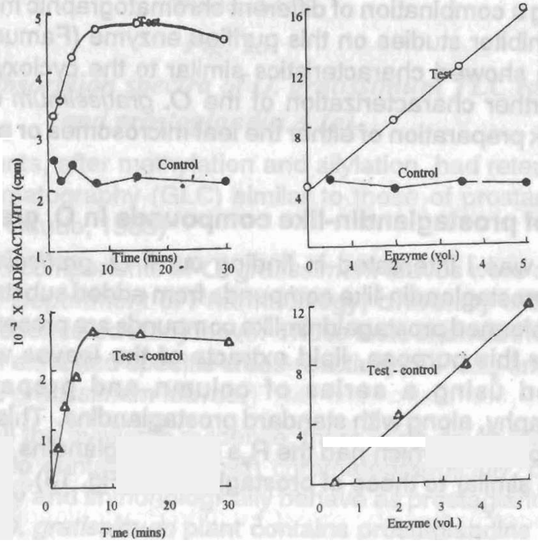


Fig. 12b.

Effect of incubation time and amount of enzyme (from O. Gratissimum) on the formation of prostalglandin-like components.

I first reported this novel finding at the 20th International Conference on the Biochemistry of Lipids held in Aberdeen Scotland in September, 1977. (Onajobi, 1977). It is important to note that before my research findings, prostaglandin synthesis had not been reported in plant tissues. A more detailed account of this finding was later published (Onajobi 1984). Various chemical modifications such as alkali treatment, sodium Borohydride ($NaBH_4$) reduction and methylation confirmed the presence of prostaglandin E-like product in the incubation mixture.

We also investigated factors which affect the biosynthesis of prostaglandin-like compounds by *O. gratissimum* leaf homogenate. It was shown that reduced glutathione (GSH), a cofactor for the biosynthesis, increased the production of PGE-like compound, while concomittantly decreasing the PGF-like compound (Onajobi & Afe 1985), a pattern similar to what obtains in animal tissues. Furthermore, Osoniyi, in the course of his postgraduate studies under my supervision, showed that the pH of the homogenizing buffer affected the *O. gratissimum* catalyzed prostaglandin biosynthesis with an optimum pH between 7.5 and 8.0 and another at 6.5. (Osoniyi, 1992; Osoniyi & Onajobi, 1998). While the former pH optimum mimicks that of animal tissues, the other optimum at pH 6.5 indicates possible differences in the mechanism of formation of prostaglandins between this plant and mammalian tissues.

Attempts have been made to purify the *O. gratissium* PG-like compounds synthesizing enzyme system. In the first place, using ultracentrifugal fractionation (centrifuging at very high speed - up to 110,000g) we located the enzyme system in the microsomal fraction (Onajobi, Ajayi and Nwakolo, 1986) similar to its location in animal tissues. Furthermore, Famurewa, in his postgraduate studies, under my supervision, was able to purify this enzyme system using a combination of different chromatographic methods. He carried out some inhibitor studies on this purified enzyme (Famurewa and Onajobi, 1996) which showed characteristics similar to the cycloxygenase of animal tissues. Further characterization of the *O. gratissimum* enzyme system is awaiting bulk preparation of either the leaf microsomes or at least the 20,000g supernatant.

Presence of prostaglandin-like compounds in O. gratissium leaves

Not only was I interested in finding out if *O. gratissimum* leaves would synthesize prostaglandin-like compunds from added substrates, I also wanted to know if preformed prostagaldnin-like compunds are present in *O. gratissimum* leaves. For this purpose, lipid extracts of the leaves were obtained and fractionated using a series of column and preparative thin layer chromatography, along with standard prostaglandins. This led to the isolation of lipid components which had the R_fs of prostaglandins on TLC and had UV absorbance similar to those of prostaglandins (Fig. 13).

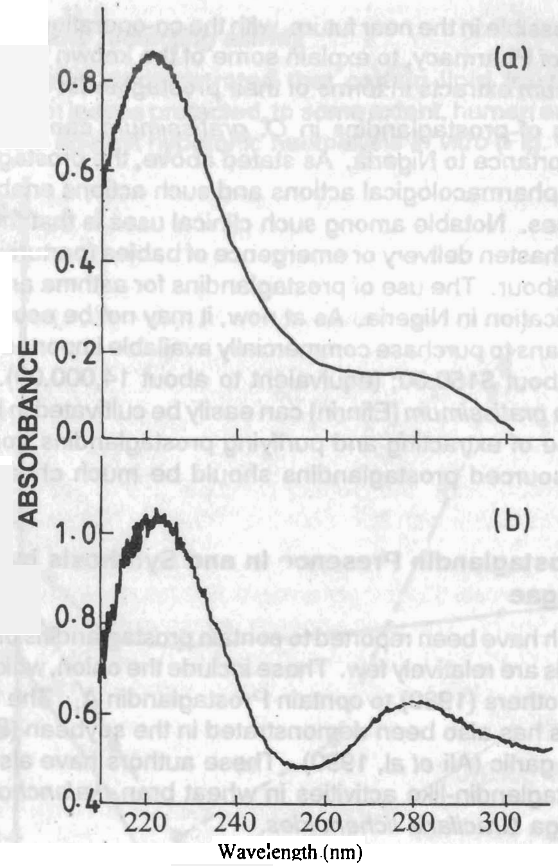


Fig. 13.
Ultraviolet (UV) absorption spectra of O. gratissimum TLC raction (b) and prostaglandin A (a).

Two of the components, after methylation and silylation, had retention times on Gas Liquid Chromatography (GLC) similar to those of prostaglandins E and A. (Onajobi and Okudo, 1985)

Such isolated lipid components of *O. gratissimum* leaves were also tested by Famurewa at the Department of Pharmacology, University of Edinburgh, during a World Bank sponsored study leave. These tests showed the presence of compounds which exhibited specific cross-reactivity to PGE_2-antibody and PGF_{2a}-antibody in *O. gratissimum* leaves.

Therefore, from all the available evidence, there is no doubt that *Ocimum gratissimum* leaves do contain fats which chromatographically, chemically, spectrophotometrically and immunologically behave as prostaglandins. Thus it is certain that the *O. gratissimum* plant contains prostaglandins as well as enzymes which synthesize them.

It may be possible in the near future, with the co-operation of some members of the Faculty of Pharmacy, to explain some of the known therapeutic actions of *O. gratissimum* extracts in terms of their prostaglandin content.

The finding of prostaglandins in *O. gratissimum* can be of clinical and economic importance to Nigeria. As stated above, the prostaglandins have a wide range of pharmacological actions and such actions enable their use for clinical purposes. Notable among such clinical uses is that they are used as an injection to hasten delivery or emergence of babies (parturition) when there is prolonged labour. The use of prostaglandins for asthma and ulcer will also find wide application in Nigeria. As at now, it may not be economically viable for most Nigerians to purchase commercially available imported prostaglandins - 5mg costs about $150.00; (equivalent to about 14,000.00). On the other hand, *Ocimum gratissimum* (Efinrin) can easily be cultivated in large quantities for the purpose of extracting and purifying prostaglandins from their leaves. Such locally sourced prostaglandins should be much cheaper than those imported.

Reported Prostaglandin Presence In and Synthesis by Other Plants, Fungi and Algae

Plants which have been reported to contain prostaglandins or prostaglandin-like compounds are relatively few. These include the onion, which was reported by Attrep and others (1980) to contain Prostaglandin A_1. The biosynthesis of prostaglandins has also been demonstrated in the soybean (Bild *et al*, 1978) in onions and garlic (Ali *et al*, 1990). These authors have also reviewed the finding of protaglandin-like activities in wheat bran, *kalanchoe blossfediana* and the red alga *Gracilaria lichenoides.*

I have also shown that the leaves of *Capsicum frutescens* (ata wewe - small pepper), *Sida rhombifolia, (Osepotu), Euphorbia pulcherima and Carica papaya* (pawpaw) possess oxidases similar to prostaglandin synthetase (Onajobi, 1985), but more confirmatory experiments still need to be carried out on these.

Other Active Lipid Components In O. gratissimum Leaves

(a) *Smooth-muscle Contracting Lipid-soluble Principles*

In the course of hunting for prostaglandins in *O. gratissimum* leaves, I discovered that two purified lipid fractions of the leaf homogenate had smooth muscle contracting activity as evidenced from the observation that they contracted guinea pig ileum and rat colon; one of them also raised, for a short period, the arterial blood pressure of anaesthetized rats (Onajobi, 1986). Such smooth muscle contracting activity could have relevance to some of the traditionally known medicinal activities of *O. gratissimum* extracts.

Cell-membrane protecting activity

We have also demonstrated that certain lipid fraction of *O. gratissimum* leaves protected, to some extent, human erythrocyte membrane against hypotonic haemolysis *in vitro* (Fig. 14)

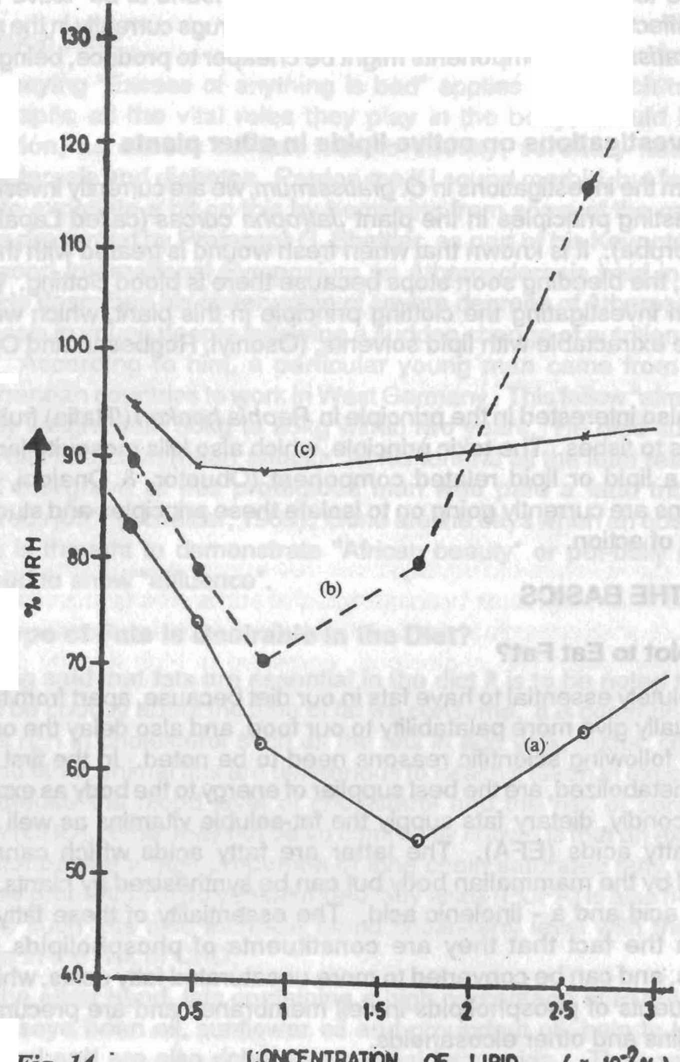


Fig. 14.

Membrane protecting activity of lipid fractions of O. gratissimum (a) & (b) - show protective acivity (c) - no protective activity.

(Igiran 1990). The effect was however biphasic, inhibiting the haemolysis at low concentrations but increasing haemolysis at high concentrations. Such biphasic effects on erythrocyte haemolysis have been described for some drugs such as local anaesthetics and tranquillizers. (Isomaa *et al*, 1986).

The antihaemolytic fractions however still need to be purified. If such purified fractions are tested on experimental animals and found to be active *in vivo*, they might effectively replace some antihaemolytic drugs currently in the market, as the *O. gratissimum* components might be cheaper to produce, being locally sourced.

Current Investigations on active lipids in other plants

Apart from the investigations in *O. gratissimum*, we are currently investigating some interesting principles in the plant *Jatropha curcas* (called Lapalapa or Botuje in Yoruba). It is known that when fresh wound is treated with the latex of this plant, the bleeding soon stops because there is blood clotting. We are interested in investigating the clotting principle in this plant, which we have shown to be extractable with lipid solvents, (Osoniyi, Rogbesan and Onajobi, 1996).

We are also interested in the principle in *Raphia hookeri* ((Rafia) fruit which is poisonous to fishes. The toxic principle, which also kills mosquito larvae, is apparently a lipid or lipid related component (Obuotor, & Onajobi, 1998). Investigations are currently going on to isolate these principles and study their mechanism of action.

BACK TO THE BASICS

To Eat or Not to Eat Fat?

It is absolutely essential to have fats in our diet because, apart from the fact that fats usually give more palatability to our food, and also delay the onset of hunger, the following scientific reasons need to be noted. In the first place, fats, when metabolized, are the best supplier of energy to the body as explained earlier. Secondly, dietary fats supply the fat-soluble vitamins as well as the essential fatty acids (EFA). The latter are fatty acids which cannot be synthesized by the mammalian body but can be synthesized by plants. They are linoleic acid and á - linolenic acid. The essentiality of these fatty acids stems from the fact that they are constituents of phospholipids in cell membranes, and can be converted to more unsaturated fatty acids, which are also constituents of phospholipids in cell membranes and are precursors of prostaglandins and other eicosanoids.

The lack of adequate fat in the diet of the average Nigerian, is, to my mind, the cause of widespread deficiency in vitamin A in children these days. Vitamin A precursors (pro-vitamin A) are found in palm oil, tomatoes, pepper, carrot, sweet potatoes, etc. In the past, many Nigerian women, especially the so called "local women" cooked soup/stew in which excess palm oil floated

alluringly on top of other ingredients of the soup/stew. Although such excess oil is not to be recommended for other reasons, at least they and members of their family got enough provitamin A in their diet which the body could then convert to Vitamin A. These days, with the current inflation and the attendant poverty, the average Nigerian woman cannot afford to buy enough palmoil for her needs.

How Much Fat?

The saying "Excess of anything is bad" applies very much to fat intake. Fats, despite all the vital roles they play in the body, should be taken in moderation, as excess fat can lead to obesity, coronary heart disease, atherosclerosis and diabetes. Pardon me if I sound morbid, but for emphasis, I need to expatiate a bit on this by borrowing from some of the case notes of patients presented by Professor G. Shettler, as part of his Keynote address at the Second International Symposium on Atherosclerosis held in Chicago in 1969. He described his observation of severe degrees of Atherosclerosis and thrombosis in young people following a sudden change of nutritional and living habits. According to him, a particular young man came from one of the Mediterranean countries to work in West Germany. This fellow "almost doubled his body weight from 50kg to 95kg within two years. He died suddenly of a myocardial infarction (heart attack). At his funeral all the lean relatives stood around the grave of this prodigious man who paid a fatal tribute for his prosperous job". (Schettler, 1969). Gone are the days when an obese Nigerian woman is thought to demonstrate "African beauty" or pot-belly in a man is supposed to show "affluence".

What Type of Fats Is Desirable In the Diet?

Having said that fats are essential in the diet it is to be noted that there is need to be choosy about the type of fat we consume. It is common knowledge that fats rich in cholesterol such as the fats in egg yolk, butter, cheese, milk, meat and other animal fats are deleterious to health if taken in excess because they increase the blood level of cholesterol and the risk of coronary heart disease (CHD). What may not be so commonly known is that an excess intake of fats containing a high proportion of long chain saturated fatty acids (SFA) and a low proportion of polyunsaturated fatty acids (PUFA) is also not desirable because such fats also increase blood cholesterol level with the attendant increase in the risk of CHD.

On the other hand, fats containing a high percentage of PUFA such as in corn oil; soya been oil, sunflower oil and groundnut oil, help to lower blood cholesterol and are also richer in essential fatty acids. They are therefore more desirable in the diet. In general, plant fats have a higher ratio of PUFA to SFA than animal fats although there are exceptions. For example, palm oil, palm kernel oil, coconut oil and cocoa butter have a high ratio of SFA to PUFA;

they are therefore less desirable in the diet although it must be remembered that palmoil contains provitamin A. In this context, fish is also presumably better than meat in that fish is rich in the n-3 polyunsaturated fatty acids whose importance has been highlighted in recent times (Stansby, 1990). It should however be noted that fatty food (such as oils and food containing a lot of fat), especially those containing high PUFA content, should not be stored for too long before use as the fat may become peroxidized. Such oxidized fats, said to be rancid, are not conducive to health as they damage tissues, especially the gut, if not protected by sufficient artioxidants.

A further advantage of plant fats is that seed oils, which mostly constitute edible plant fats, contain very low levels of choleserol. For example, while 1kg (roughly 1 litre) of palmoil contains 20-26 mg of cholesterol (Gunstone, 1986) one egg contains an average of 300mg cholesterol (Gunstone and Norms, 1983). Plants contain other sterols (e.g sitosterol, stigmasterol) which are poorly absorbed by the intestine. Thus the label "cholesterol free" which we have on many commercial vegetable oils these days is more of a sales gimmick.

Another common knowledge is that margarine is preferable to butter since margarine is made from vegetable oil and butter is made from milk, which contains animal fat. One of the processes of converting vegetable oil to margarine is partial hydrogenation. In this process some unsaturated bonds in the fatty acids of the oil become saturated and others are converted from their natural *cis* to the *trans* form. The *trans* fatty acid content of margarine may vary considerably ranging from 0 to 50%. Trans unsaturated fatty acids normally occur in nature but usually at very low concentrations. Recent findings have linked *trans* fatty acids in margarine and some other processed fat such as vegetable shortening (used in baking) to high blood cholesterol, increase in low-density lipoprotein cholesterol, decrease in high density lipoprotein cholesterol and coronary heart diseases (Apllegate, 1994; Ascherio *et al*, 1994 Mensink *et al* 1992, Wahle and James 1993). They have these effects probably because they behave like saturated fatty acids in the cells. *Trans* fatty acids have also been shown to inhibit prostaglandin synthetase. Thus, margarine which was thought to be a healthy alternative to butter is now being "probed." So, is it to be butter or margarine? We seem to be caught between the devil and the deep blue sea. Various possible solutions to this dilemma have been proffered. Some investigators believe that occasional use of butter and/or lard will not have any important effect on health. Others have said that it should be possible to make margarine and shortenings without trans fatty acids. Maybe we should just play safe and go back to our grand-or-great grand-parents' diet in which neither butter nor margarine (or similar modified fat) features. However, I believe that moderation in the intake of either product should be the answer.

Recommendations

Mr. Vice-Chancellor, Sir, consequent upon the many important effects of FATS on LIFE which I have highlighted in this lecture, please permit me to make the following recommendations:

1. There is a need to create more public awareness about fats, that is, which fats are beneficial to health, which are not, and in what types of food these fats are found. To achieve such public awareness, there should be discussions on this topic on radio and television on a regular basis, especially as part of the Federal Ministry of Science and Technology sponsored "Science and Technology Digest". Some non-governmental organizations can also organize seminars on such enlightenment programme.
2. As a result of so many unresolved issues raised in this lecture, the government should fund research in Universities, particularly on lipids, much more than it is doing at present. On account of inadequate funding, many scientists, (including lipidologists) in Nigerian Universities have settled for what is termed "PROXIMATE Analysis" In order to carry out deeper, more fundamental research, a lot of funds are required to purchase the equipment and the necessary reagents. Otherwise fewer young Nigerian scientists will be trained, and there will be a dearth of young ones to take over from the older generation.
3. On account of the importance of lipids (FATS) to LIFE, and the need to further understand the effect of the lipid metabolites on health, a well equipped Lipid Research Institute should be established.

ACKNOWLEDGEMENT

I will like to acknowledge that a number of the figures (Figs 1, 2, 3, 6, 7 & 11) which illustrate well known biochemical concepts in this lecture, have been taken from the book *Principles of Biochemistry* by Lehninger, A.L., Nelson, D.L. and Cox, M.M, Worth Publishers, New York, 2nd edition. Figures 4 and 5 were taken from a 1988/89 *"Scholastic Calendar"* published by Carolina Biological Supply Company, U.S.A. Figure 9 was taken from the book *"Biochemistry"* by Stryer, L. 2nd edition.

Mr. Vice-Chancellor, distinguished ladies and gentlemen, I thank you all for your presence.

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