THE CURIOUS MOLECULES OF NATURE

BY

OYIN SOMORIN

UNIVERSITY OF LAGOS PRESS - 1991
INAUGURAL LECTURE SERIES

University of Lagos Press Tel. 825048

THE CURIOUS MOLECULES OF NATURE

An Inaugural Lecture delivered at the
University of Lagos on Wednesday, May 2, 1990.

By

Oyin Somorin
Professor of Chemistry
University of Lagos

University of Lagos Press

1991

First Published 1991

By

University of Lagos Press
Unilag P. O. Box 132,
Akoka, Yaba,
Lagos.

ISBN 978–017–025–1

INTRODUCTION

IN ACCORDANCE with the traditional purpose of Inaugural Lectures as given by University Professors, I intend to present to you in this lecture the highlights of what I profess in the realm of Chemistry. Chemistry is the science which studies matter in terms of its composition, properties, its structure and the ways it can be transformed from one form to another. Chemistry has many applied branches and it is uniquely related to Engineering and Industry hence the terms Chemical Engineering and Industrial Chemistry. Chemistry is involved in almost everything around us and even inside us and it underlies a great deal of modern technology in the manufacture of numerous basic commodities.

The title of my lecture is *Curious Molecules of Nature.* Many people will wonder why I have chosen such a cryptic title. In another few minutes, you will agree with me that the title is not so cryptic afterall. The title requires the definition of two dominant words: *Curious and Molecules*. *The American College Dictionary* defines *Curious as:* exciting interest because of novelty. *Molecules* are defined as the smallest neutral particles of a substance capable of independent existence. Therefore, the curious molecules of nature can be interpreted simply as naturally occurring molecules that have exciting and interesting properties. Examples of such molecules include alkaloids, hormones, enzymes and other physiologically active compounds. Let us consider some examples.

ALKALOIDS

Alkaloids are nitrogenous organic compounds occurring as the active principles of many plants. There about 2,000 alkaloids, yet phytochemists claim that only 5 percent of flowering plants have been examined for possible alkaloid content. Alkaloids constitute an indispensable and most potent group of substances for the treatment and mitigation of functional disturbances and relief from suffering. This is the main reason why large multinational firms continue programs for the pharmacologic screening of alkaloids both new and old. Reserpine, a very valuable drug for antihypertensive and pyschotherapeutic action emerged from such a program in the 50s.

In addition to the basic nitrogen moiety, alkaloids contain one or more functional groups as in the case of cocaine with two ester functions as shown in Figure 1.

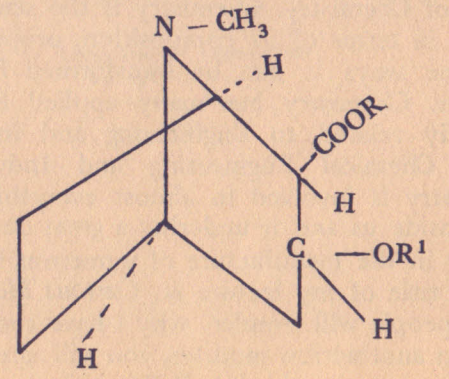


Fig 1

where:

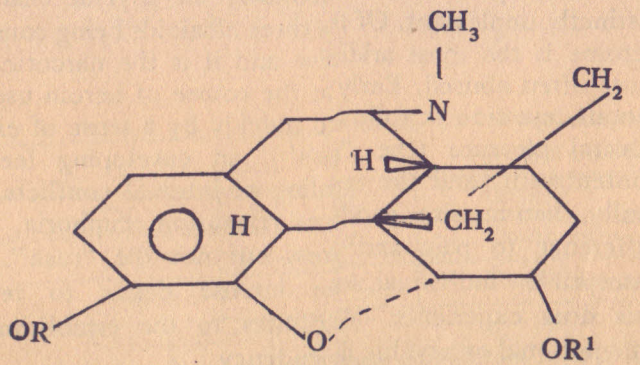
	R	R_1	Name of alkaloid
1	H	H	Ecgonine
2.	CH_3	$C_6H_5C_o$ (benzoyl)	Methylbenzoylecgonine (cocaine)
3.	H	CH_3	Methylecgonine
4.	H	$C_6H_5CH{=}CHCO$ (Cinnamoyl)	Cinnamoyl ecgonine
5.	H	$C_6H_5C_o$	Benzoyl ecogonine.

Cocaine and Related Alkaloids

Cocaine (methylbenzoylecgonine) has been isolated from coca leaves. It is one of the early anaesthetics to be discovered although it is no longer used for that purpose because of its toxic side effect. Its effect on the central nervous system includes euphoria and cortical stimulation manifested by excitement, increased wakefulness, greater power of endurance of hunger and fatigue. Cocaine poisoning causes weight loss, tremors, confusion, convulsion unconsciousness and heart failure. The structure activity relationship is clearly manifested in cocaine and related alkaloids It is remarkable to note that ecogonine itself is inactive so also are the methyl and benzoyl derivatives. Clearly it seems that both the methyl and benzoyl groups must be present before the characteristic activity is manifested. Demethylation of the nitrogen gives norcocaine which has been found to be more active but also more toxic than cocaine.

Alkaloids can be classified according to source, chemical structure or pharmacological action. For instance the opium alkaloids, are the alkaloids obtained from opium poppy, *Papaver somniferum.*

Some of these are shown in Fig. 2.



where:

	R	R_1	Name of alkaloid
1.	H	H	Morphine
2.	CH_3	H	Codeine
3.	CH_3 O // C	CH_3 O // C –	Heroin

Opium Alkaloids

There is structural resemblance between the much dreaded heroin and codeine. Morphine, codeine and heroin are analgesics, the analgesic activity of codeine is only about 1/10th that of morphine whereas heroin is about 5 times as active as morphine as an analgesic. These three drugs are also narcotics. The term narcotic refers to a drug that diminishes sensibility, relieves pain and induces lethargy drowsiness or sleep. Narcotics produce indifference both to physical discomfort and to mental anguish and they suppress basic biological drives such as hunger, anxiety, fears, dissapointments, frustrations; all cease to be of concern to a narcotic addict;; For certain types of personalities this altered mental state is extremely pleasant but for many physically healthy and mentally balanced individuals the psychic changes are distinctly unpleasant. Of the three alkaloids being considered, heroine is the most addictive and it is the narcotic that is most often abused. Early in the course of heroin use, intravenous injection is followed quickly by a sense of exquisite visceral pleasure (the "rush"), an enveloping feeling of contentment, and the receding of internal conflicts. Taken orally, heroin also produces relaxation, euphoria, and indifference to pain and stress but not the "rush". In the susceptible individual, the intense desire to recapture this drug experience contributes to the establishment of an emotional or psychic dependency.

With frequently repeated administration the individual becomes progressively less responsive to the drug, thus ever–increasing doses are sought in an attempt to duplicate the characteristic effects. Chronic suppression of central nervous

system function results in a dependent state in which the drug must be taken on a regular basis to maintain a reasonable semblance of well-being and equilibrium and to prevent the anguish of the abstinence syndrome. Thus narcotic addicts soon find themselves taking heroin not for the pleasurable effects but primarily to prevent withdrawal.

The withdrawal symptoms usually reach maximum intensity between 36 – 72 hours after the last dose of heroin. The severity of obstinence syndrome is determined by the degree of acquired physical dependence. Signs and symptoms of narcotic withdrawal includes yawning, sneezing, lacrimation, restlessness, anxiety, insomnia, nausea, vomiting, sweating, gooseflesh, generalised body ache, tremors and jerking movements, Occasionally cardiovascular collapse occurs.

Xanthine Alkaloids

The important medicinal alkaloids of this group are caffeine, theobromine and theopphylline which are all structurally similar as shown in Fig. 3.

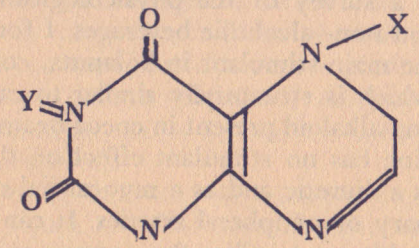


Fig. 3.

Where:

	X	Y	Name of alkaloid
1.	CH_3	CH_3	Caffeine
2.	CH_3	H	Theobromine
3.	H	CH_3	Theophylline

As I mentioned earlier I intend to use this forum to highlight my research findings and I will commence doing so with discussion on the Xanthine alkaloids.

It is known that Kolanuts affects the brain, the muscle including the cardiac muscle, and the kidneys. Kolanut is capable of producing a condition of wakefulness and increased mental activity. It is also known that the ability to interprete sensory impression is enhanced, thoughts become clearer and more rapid, mental fatigue is relieved and reaction time is shortened. Kolanut chewing also facilitates the performance of muscular work and increases the work load which can be performed by a muscle. It is also significant to note that kolanut stimulates the rate and depth of respiration and exerts a relatively mild diuretic effect.

All these pharmacological actions are attributable to the presence of caffeine in kolanuts. It is remarkable to note that the caffeine content varies with different species of kolanuts. Results of research that I carried out some 20 years ago show that *Cola acuminata* (Abata) contains a higher caffeine content that *Cola nitida* (Gbanja). It is remarkable to note that *Cola nitida rubra* (red kola) is physiologically more potent than *Cola nitida alba* (white kolanut) in terms of the caffeine content.

On carrying out a survey of the physicologically active stimulant in common non–alcoholic beverages I found that while caffeine is the main stimulant in kolanuts, coffee and tea; theobromine which is structurally similar to caffeine is the major stimulating alkaloid present in cocoa beans. Unlike caffeine, theobromine has no stimulant effect on the brain. It is used mainly as a diuretic and as a myocardial stimulant to dilate the coronary or peripheral arteries. It can be used along with phenobarbitone to allay the nervous excitement and insomnia associated with hypertension and arteriosclerosis. Theophylline is the most potent diuretic of the three alkaloids, although its effects is of shorter duration. It is a more powerful relaxant of involuntary muscle than either theobromine or caffeine. Like theobromine, it has no stimulating effect on the central nervous system.

ANZYMES AS DIAGNOSTIC AIDS IN CHEMISTRY

Enzymes are curious molecules of nature that have long been of special interest because of their nature being borderline between biology and chemistry. Undoubtedly, enzymes are of supreme importance since life depends on series of

complex network of chemical reactions catalyzed by enzymes and any modification of the anzyme may have far reaching effects on the living organisms. For instance, the ricim – thrombin interaction disrupts the homeostatic mechanism of the blood clotting system. Ricin is a potent and highly toxic protein from castor beans. This toxin is known to have haemorrhagic effect on animals by inducing multiple capillary haemorrhage around the liver, lymphatic tissue, occipital region and the eyes. I have reported that ricin can form a complex with thrombin. The ricin - thrombin complex so formed has a peptide bond hydrolytic activity different from that of thrombin and can therefore hydrolyse peptide bonds which are not normally hydrolysed by thrombin. The hydrolysis of such bonds within the delicate walls of the tiny capillaries causes blood to ooze out of the capillaries thereby creating haemorrhagic conditions characteristic of ricin poisoning.

Enzymes are known to be responsible for most of the chemical reactions of the body and are constituents of all tissues. Many are found in the blood to which they gain access from injured cells or intact cells. The use of serum enzymes as diagnostic aids in chemistry has been largely empirical but the values observed in clinical and experimental circumstances permit speculative analysis of the factors that lead to abnormal levels in diseased subjects. Table 1 shows such a correlation.

Increased rate of enzyme release is clearly responsible for the high serum levels of hepatic, pancreatic and myocardial enzymes in diseases that produce necrosis of the respective tissue. The pattern of abnormality of the specific serum enzyme values that results depends on the normal enzyme content of the tissue involved; on the extent and type of necrosis and other factors. Hence high serum levels of a number of digestive anzymes are found in acute hepatitis.

An increase in the tissue source of anzymes because of increased rate of production per cell or increase in the number of cells may be responsible for the increased serum levels. This seems to be the mechanism for the increased levels of pepsinogen, alkaline phosphatase and acid phosphatase in patients with peptic ulcer, osteoblastic bone lesions and prostatic carcinoma respectively.

I will now focus attention on my own contribution in this field of application of chemistry to diagnosis of diseases.

TABLE 1

PATTERNS OF ABNORMAL SERUM ENZYME VALUES IN SEVERAL CLINICAL SETTINGS

		AST (GOT)	ALT (GPT)	ALS	ALP
Chest Pain and Related Circumstances	Myocardial infarction	↑↑	+	↑ ↑	N
	Pulmonary infarction	+	+	↑ ↑	N
	Heart failure	+	+	↑ ↑	N
	Shock	↑↑	↑	↑ ↑	N
Muscle Disease	Progressive muscular dystrophy				
	Trichnosis	↑↑	↑	↑↑ ↑	N
	Dermatomyositis				
	Polymyositis				
	Delirium tremens				
	Neurogenic muscle disease	N	N	N	N
Jaundice	Acute hepatitis	↑↑↑↑	↑↑↑↑	↑↑	↑
	Cirrhosis (Laennec's	↑	+	+	
	Obstructive jaundice	↑↑	↑↑	↑	↑↑↑
Neoplastic Disease	Localized carcinoma of small size	N	N	N	N
	Extensive carcinoma without hepatic or bone metastases	N	N	↑↑	N
	Carcinoma with metastases to liver or hepatoma	↑↑	↑	↑↑ ↑	↑↑ ↑
	Carcinoma with osteoblastic metastases to bone	N	N	↑↑	↑↑↑
	Leukemia (granulocytic or acute)	N	N	↑↑	N
	Leukemia (chronic lymphatic)	N	N	N	N
Anaemia	Megaloblastic	N	N	↑↑↑	N
	Iron deficiency	N	N	N	N
	Hemolytic	N	N	↑↑	N

*Number of arrows indicates magnitude of increase; N indicates no change
AST = Aspartate aminotransferase or Glutamate oxalacetate transferase (GOT)
ALT = Alanine aminotransferase or Glutamate pyruvate transaminase (GPT)
ALS = Aldolase
ALP = Alkaline Phosphatase

Firstly, I will discuss our research findings which show that aliphatic esterase (aliesterase) is a constituent of the human blood contrary to previous reports. Secondly, the use of chromogenic substrates for assaying small amounts of trypsin, an enzyme that has been implicated in the disease of the pancreas, pancreatitis.

Finding of Aliphatic Esterase, Aliesterase, in the Human Blood

Serum esterass are enzymes which hydrolyse esters into fatty acids and alcohol. It is known that the serum esterolytic activity decreases significantly under cancerous conditions, that is, if we compare the level of serum esterase present in a normal patient with that of a cancer patient, the esterase level in the blood of the cancer patient is remarkably lower.

After a thorough survey of all the methods in current use for determining esterase activity, we found that these methods either lack sensitivity, specificity or that the substrates (as in the flourometric methods which employs the use of acyl esters of 4–methylumbelliferone) are not readily available. Therefore, there is need for the development of a new sensitive and simple method with good accuracy and precision for measuring slight differences in serum esterase levels for purpose of detecting early stages of carcer. The technique reported by this lecturer along with some Czech scientists is based on Gas – Solid Chromatography (GSC) with a special synthetic support and detection by flame ionization. This technique is adequate for quantitatively determining slight differences in esterolytic activity of blood serum.

This technique involves the use of ethyl butyrate as substrate for the blood serum. The extent of hydrolysis by esterases in the serum and hence a measure of the serum esterase level is determined by efficiently extracting the butyric acid into ether in a single step extraction process followed by the injection of the extract into the gas chromatograph for quantitative estimation.

Accuracy and sensitivity of the GSC method are quit. high. The limit of butyric acid was about 1ug./ml. The speed of analysis permits this method to be proposed for routine clinical assay of esterolytic activity in blood serum.

Having devised a new technique which is a marked important advancement in the refinement of methods, we decided to re–examine the presence of esterases in the human blood. Generally esterases found in the sera of animal can be classified into three main types: the aromatic esterases (A–esterases) which hydrolyzed aromatic esters aliesterases (B–esterases) which hydrolyze aliphatic esters and choline esterases (C–esterases) which hydrolyze choline esters at higher rates than either aliphatic ester or aromatic esters. The A–esterases are resistant to both organophosphorus compounds and eserine, the B–esterases are inhibited by organophosphorus compounds but resistant to eserine and the C–esterases are inhibited by both organophosphorus compounds and eserine. Therefore on the basis of these inhibitor substance, we can easily distinguish between the three types of esterases. All the three types of esterases have been found in the sera of animals such as rabbit, mouse, rat and horse, but the human blood has been reported by several authors to contain A – and C–esterases. Evidence for the presence of aliesterase, that is, B–esterases, in normal (preheparin) and postheparin sera has been reported by this lecturer and his co-workers. Their partial purification on CM– and DEAE– Sephadex and some properties of these esterases have also been reported. We found that eserine completely inhibited the esterase activity of preheparin human blood serum against butyrylcholin chloride, a specific substrate for cholinesterase. Total inhibition of cholinesterase activity by eserine has also been reported previously. However, eserine did not completely inhibit the hydrolysis of ethyl butyrate thereby suggesting that enzyme (s) other than cholinesterase must be involved in the hydrolysis of ethyl butyrate. The total inhibition of esterolytic activity toward this substrate by organophosphate, E_{600}, suggests that aliphatic esterase rather than aromatic esterase was responsible for the residual esterolytic activity after eserine inhibition. Total inhibition of serum hydrolysis of ethyl butyrate by E_{600} also indicates that serum aromatic esterase is not involved in the hydrolysis since its activity is unaffected by E_{600}. Hence the hydrolysis is not due to only cholinesterase and an eserine-insensitive but organophosphate -sensitive esterase. A similar result, that the aromatic esterase of rabbit serum has no activity against ethyl butyrate, has been reported by others. The eserine – insensitive esterase

is different from serum aromatic esterase, which has been reported to be completely inhibited by EDTA (10^{-4}M) and magnesium chloride (0.1M), because this esterase was still very active at even higher concentrations of EDTA (2×10^{-3} M) and magnesium chloride (0.1M). In addition partially purified chromatographic fractions DE-3 and DE-4, which were active against ethyl butyrate showed no significant activity against p-nitrophenyl acetate, a specific substrate for serum aromatic esterase. On the basis of these results eserine - resistant but organophosphate - sensitive esterases which hydrolyzed ethyl butyrate are aliesterase. The results show that such enzymes are found in the preheparin (normal) serum and in the postheparin serum of human blood, and they may be refered to as preheparin aliesterase and postheparin aliesterase. Our finding of aliesterase in normal blood conflicts with previous reports by authors who observed the presence of only two types of esterases aromatic esterase and cholinesterase, in human blood, and suggested that aliesterase is not a constituent of human blood serum.

A very sensitive assay technique is essential for detecting the activity of aliesterase, which is very low in the preheparin blood serum, so a Gas - Solid Chromatographic technique which we recently developed, proved to be of significant assistance to us in detecting the aliesterase activity. Also, a study of substrate specificity and suitability for the assay of aliesterace activity in preheparin and postheparin sera indicated that ethyl butyrate was the most suitable substrate. The esterase showed no activity toward acetates and the activity on ethyl propionate was less than that toward ethyl butyrate, so the esterase appears to be a C-4 esterase. Although methyl butyrate has the advantage of higher solubility than ethyl butyrate, it was not suitable because of its higher volatility and higher rate of autolysis. Other alkyl esters of butyric acid and esters of aliphatic acids with more than four carbon atoms were also not suitable because of poor solubility in the aqueous buffer system.

The aliesterase in the preheparin serum appears to be different from that in the postheparin serum. The pH activity studies clearly suggest such a difference. The elution profile of postheparin serum on DEAE - Sephadex showed two distinct aliesterase activity peaks, DE–3 and DE–4, in

contrast to that of the preheparin serum, which showed only one activity peak identical with DE–3. These differences suggest that another aliesterase is released into the blood after intravenous administration of heparin. Several authors have reported that the administration of heparin causes the release of a variety of enzymes into the blood. The preheparin aliesterase was highly sensitive to fluoride ions, in contrast to the postheparin aliesterase. Sodium fluoride has been reported to be an inhibitor of liver esterase, so the strong fluoride inhibition of the preheparin aliesterase activity suggest that liver may be the source of the eserine resistant enzyme.

The finding of aliesterase in the human blood has introduced a possible new dimension into cancer research. Our findings show that the cholinesterase level and the level of aromatic esterase in the blood are unaffected by heparin whereas the blood level of aliesterase increases after heparin administration. Preliminary clinical reports have shown that the increase is very significant is cases of patients with liver cancer. Therefore, the possibility exists that the aliesterase levels in preheparin and postheparin blood may prove useful in the diagnosis of cancer, particularly cancer of the liver.

Trypsin and its Activity Determination using Chromogenic Substrates.

It has been reported that the serum level of trypsin may increase during pancreatic disorder. In order to monitor serum level of trypsin, substrates which are specific for tryptic activity are essential. Hence we designed and successfully synthesized new series of chromogenic substrates. These substrates have considerably simplified the determination of tryptic activity. At least twenty new chromogenic substrates have been synthesized as shown in Table 2. The most readily susceptible substrate to trypsin catalaysed hydrolysis is ZPVAPA N–benzyloxycarbonyl–L–phenylalanyl–L–valyl – L – arginine–p–nitroanilide hydrochloride which is comparable to the commercially available BPVAPA N–benzoyl –L –phenylalanyl –L ––valyl–L–arginine–p–nitroanilide hydrochloride.

TABLE 2

LIST OF NEW CHROMOGENIC ARGININE AND LYSINE SUBSTRATES

1. N^{α}– benzoyl–L–arginine–p–nitroanilide hydrochloride (L–BAPA. HCl)
2. N^{α}– acetyl–L–arginine–p–nitroanilide hydrochloride (L–AAPA.HCl)
3. N^{α}– arginine–p–nitroanilide dihydrochloride (L–APA. 2HCl)
4. N^{α}– benzyloxycarbonyl- L–arginine–p–nitroanilide hydrochloride (L–ZAPA.CHl)
5. N^{α}– benzyloxycaronyl– L –arginine 3, 5–dinitroanilide hydrochloride (L–ZADA. HCl)
6. N^{α}– benzyloxycarbonyl–L–arginine 3- nitroanilide hydrochloride (L–ZANA. HCl).
7. N^{α}– benzylocycarbony l–L–arginine 3–nitro–5 chloroanilide hydrochloride (L–ZANCA. HCl).
8. N^{α}– benzyloxycarbonyl – L – arginine 3 –nitro–5–bromoanilide hydrochloride (L–ZANBA. HCl).
9. N^{α}– benzyloxycarbonyl – L –arginine 3–nitro–5–fluoroanilide hydrochloride (L–ZANFA. HCl).
10. N^{α}– benzyloxycarbonyl–L–arginine 3–nitro–5–iodoanilide hydrochloride (L–ZANIA. HCl).
11. N^{α}– benzyloxycarbonyl–L–arginine 3–nitro–5–(methylsulfanyl) anilide hydrochloride (L–ZANMA. HCl).
12. N^{α}– benzyloxycarbonyl–L–arginine 3–nitro– 5 –(trifluoromethyl) anilide hydrochloride (L–ZANTA. HCl).
13. N^{α}– benzyloxycarbonyl–L–lysine 3, 5–dinitroanilide hydrochloride (L–ZLDA. HCl).

14. N^{α}– benzylocycarbonyl–L–lysine 3 nitroanilide hydrochloride (L–ZLNA. HCl)

15. N^{α}– benzyloxycarbonyl–L–lysine 3- nitro- 5–chloroanilide hydrochloride (L–ZLNCA. HCl)

16. N^{α}– benzyloxycarbonyl–L –lysine 3- nitro 5 bromoanilide hydrochloride (L–ZLMBA. HCl).

17. N^{α}– benzyloxycarbonyl–L–lysine 3–nitro- 5–fluoroanilide hydrochloride (L–ZLNFA. HCl).

18. N^{α}– benzyloxycarbonyl–L–lysine 3- nitro–5- iodoanilide hydrochloride (L–ZLNIA. HCl).

19. N^{α}– benzyloxycarbonyl–L–lysine 3–nitro- 5- methylsulfonyl) anilide hydrochloride (L–ZLNMA. HCl).

20. N^{α}– benzyloxycarbonyl–L–lysine 3–nitro- 5- (trifluoromethyl) anilide hydrochloride)ZLNTA. HCl).

21. N^{α}– benzyloxycarbonyl–L–phenylalanide- L–valyl –L–arginine – p– nitroanilide hydrochloride (L–ZPVAPA. HCl).

Remarkably we should have taken a patent on this interesting substrate rather than merely reporting the full synthetic scheme in an internationally reputable journal because the patented BPVAPA costs about $2,000.000 per kg. We missed the million but generated a lot of publicity as evident from the large number of requests for reprints all over the world.

These new chromogenic substrates have also been found useful in the quantitative estimation of other enzymes such as plasmin and thrombin.

CHITIN : A NATURAL RESOURCE FROM CRABS SHRIMPS, PRAWNS E.T.C.

Chitin, a biopolymer consisting N–acetylglucosamine units occurs in large quantities in crustaceans such as crabs shrimps, prawns, lobsters and in insects. From the processing of crustaceans, billions of tons of chitin are produced

as waste material and are usually discarded. The waste disposal of chitin has always been a problem hence there is need to recycle this waste material into a new useful raw material. How can chemistry help in solving this problem of chemical modification of this vast quantities of industrial/ domestic waste?

Chemical Modification of Chitin

The poor solubility of chitin and chitin derivatives in common solvents has been the main drawback in its utilization. Although chitin is structurally similar to cellulose but it is more resistant toward chemical regents because of the strong micelle structure of the acetamide groups. For instance, cellulose acetate which is soluble in many organic solvents has many practical uses as fibres, films paint constituents but chitin acetate is insoluble in all solvents except acids which tend to decompose it on standing.

Chemically modified chitin derivatives with good solubility in organic solvents are highly desirable in order to promote the usefulness of chitin and widen the scope of its industrial application. It is with this aim in view that I was invited to Japan in 1977 to work along with some Japanese scientists to crack the problem. In tackling this problem we had to introduce hydrophobic groups into the chitin molecule because it is known that hydrophobic groups have affinity for organic solvents. We successfully introduced benzoyl and benzyl groups and attained the desirable solubility. The success in preparing these derivatives led in rapid succession to the preparation of other acylated chitin derivatives such as formyl, propionyl, butyryl and p–substituted benzoyl chitins. It seems that was the turning point for our research team. Since then we have prepared several derivatives including water soluble derivatives most of which have very useful industrial and medical applications.

Industrial/Medical Applications.

Fibre and Paper from Crabs.

Chitin and chitin derivatives have been spun into fibres. Also paper has been made from chitin derivatives, mostly alkyl chitin. Chitin derivatives have also been reported to be useful as binders in paper manufacture.

Antitumor, Antibacterial and Antiparasitic effects from Crabs,

Mice fed with chitin and chitosan were found to show immunoadjuvant effect when the test animals were either transplanted with tumor cells or challenged with *Staphylo coccus aureus*. For the antiparasitic effect, finely ground sterile chitin powder in physiological saline was injected subcutaneously into dogs infested with ticks and mites. After a few days they were found to be free of such infections. Observations on live fleas and ticks demonstrated that blood taken from such injected dogs has lethal effects on the ticks and mites. The serum of warm blooded animals containing such antibodies developed by chitin, is useful for immunization of other animals against parasitic attack and associated diseases.

Crab as a source of Biodegradable Pharmaceutical Carriers

Chitin in form of membrances has been used as enzymically decomposable pharmaceutical carriers. Chitin and its derivatives are appealing substances as carriers since they are biodegradable by lysozyme, an enzyme present in the human body and the degradation products do not introduce any disturbance to the system.

Chitin from Crabs as Wound Healing Accelerators

Improvement in the healing of wounds is one of the aims of medicine, particularly for patients suffering from diabetes or undergoing cortisone treatment because of their slow rate of wound healing. Rapid healing of wounds have been effected by chitin derivatives such as hydroxyethyl chitin and carboxymethyl chitin.

Blood Anticoagulants from Crabs

Heparin, an expensive anticoagulant polysaccharide, inhibits thrombin activity. Thrombin plays a very prominent role in blood clotting. In order to understand the exact mechanism of heparin action, the stepwise preparation of heparin-like materials should be investigated with a view to studying the inhibition mechanism. Chitin has a similar sugar skeleton as that of heparin. We have succeeded in

preparing new chitin derivatives such as sulphated chitin, carboxymethyl-chitin and sulphated carboxymethyl-chitin. These chitin derivatiives exhibit heparin-like activity. Their clinical use as potential heparinoids will depend on the out come of the toxicity studies.

CONCLUSION

Mr Vice–Chancellor Sir, permit me to comment briefly on one curious thing that disturbs me very much. This is in connection with the colossal waste of funds in terms of non-functional equipments which abound in large numbers in all our institutions of higher learning, research institutes and government laboratories. The current values of these broken down equipments run into billions of naira, ofcourse it cannot be less if Chemistry Department at University of Lagos alone has well over ₦ 1,000,000 worth of broken down equipments. Many of you may wonder why we don't rectify the situation by effecting immediate repairs. Firstly, it will cost about half a million naira to do so in the Department but the funds are not available. Even if the funds are available it will not be resonable to repair all such equipments as most of them are old modelled. We should repair the repairable at minimal cost.

A wiser approach to solving this national problem will be to set up a central committee that will collate data on the billion naira equipments arrange to salvage as many of such equipments by swapping parts since minor spare parts that is bad in one equipment may be good in another one, and then redistribute the equipments after the repairs. Surely, I am aware that this may not be as easy as it sounds because most of these equipments are not necessarily of the same brand since they were purchased from different vendors all over the globe. This is a terrible national mistake which must be corrected immediately. There must be a National Policy on the purchase of scientific equipments. The purchase should be restricted to only 2 vendors who are internationally reputable for efficient services and who are prepared to establish functional regional Workshops in Nigeria. They should be made to sign contractual agreement to:

i) train Nigerians, including the technical staff of the patronising institutions;
ii) give a reasonable period of guarantee on new equipments; and

iii) supply spare parts and effect any repairs within a stipulated period of not more than 4 weeks.

This arrangement has the advantage of effective maintenance of expensive equipments throughout the country besides the opportunity of trading in the old equipments at a future date for new ones. Structural Adjustment Programme (SAP) is an integral part of Chemical Economics and this calls for more prudent management of our dwindling financial resources.

I wish to conclude this lecture by thanking all those who have contributed to my academic achievement. Firsly, I thank my parents: my late father Chief Somorin for the financial support and encouragement and my mother for her encouragement particularly for her compulsory early morning tutorials at the early stages. I am grateful to Profe ssors Mathieson, Corwin and Seligman for their boundless encouragement during my early research days. I am indebted to my research collaborators: Professor Skorepa and Dr. Mares in Czechoslovakia; Professor Tokura and Dr. Nishi in Japan and my research students for carryig out the bench work. I am most grateful to my wife, Mrs. Olaseni Somorin for her numerous contributions including the effective management of the homefront. I am particularly grateful to my children: Lola, Ladun, Seun and Bunmi.

University of Lagos Press Tel. 825048