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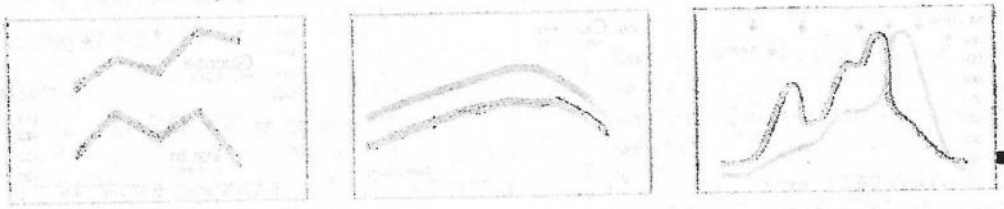

The Ghana Pharmaceutical Journal

THE GHANA PHARMACEUTICAL JOURNAL

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K. A. Ohene-Manu

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VOL. 3 No. 1 MARCH, 1975

CONTENTS

NOTICE

The Pharmaceutical Society of Ghana

announces for the information of all its members that the

33rd Ghana Pharmaceutical Conference and Exhibition

which coincides with the 40th Anniversary of the founding of the Society will be held at the

Conference Hall of the STATE HOUSE, ACCRA

from Thursday, 28th August, 1975 to Saturday, 30th August, 1975.

Members are asked to keep the dates OPEN!

D. Anim-Addo
Hon. General Secretary.

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1973—1975

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A SYMPOSIUM*

Is The Present Course Structure In Pharmacy Suitable For Ghana?

(i) A Student's viewpoint

—Miss Josephine S. Adusu, (B.Pharm. IV)
Faculty of Pharmacy, University of Science and Technology, Kumasi

I would not say the course structure in Pharmacy is or is not suitable for Ghana.

As professional men, Pharmacists in Ghana and in fact all over the world are supposed to have a wide knowledge of every aspect of the profession. Thus the knowledge of Pharmacology, Pharmacognosy, Pharmaceutical Chemistry and Pharmaceutics is very essential. To be able to talk fully about any particular drug one must know the source of the drug, its pharmacological actions, the chemistry of the active constituents and hence the best way to formulate it. Pharmacists in Ghana must be competent professional men and must have the necessary qualifications as all Pharmacists in any part of the world.

But Ghana is a developing country and cannot therefore schedule the Pharmacy course as it is in Britain or the United States which are more advanced. In my opinion the Pharmacy profession is not going to develop in Ghana as it is in Britain or the U.S.A. within the next fifty years or so. In fact, most people both literate and illiterate do not even understand the term Pharmacist. Pharmacists are considered to be dispensing assistants here in Ghana and somebody who is a professional man himself is known to have said that it does not require a degree to dispense. Most people think Pharmacy is simply dispensing. This shows how poorly developed the profession is in Ghana.

As a result of this, I feel its high time the structure of the course is reviewed and the necessary changes made.

The course structure is such that the student just tries to cram as much as possible in order to pass his examinations. Passing examinations is more important to him than sitting down and correllating what he is taught in the classroom with the outside world. And in fact, some lecturers make students feel that examinations are the most important part of the whole course.

The vacation training done during the long vacations is very helpful to students but it will be more helpful if at the beginning of the first term few lecture periods are allocated for exchange of ideas and experiences acquired by students instead of the individual reports we are made to write. I do not know exactly what happens to these reports but we never see them again and they are never discussed with us in class either. No one student can get the opportunity to work in all the various places concerned with the different aspects of the Pharmacy profession during the holidays. Thus I feel these discussions and exchange of ideas are very essential and should be introduced. For example during such periods articles like the report on A.P.C. which appeared in the dailies could be discussed. I can tell you that some of the 1st year students do not even know what the Pharmacy course is all about. I would therefore like to suggest that at the beginning of each year one or two lecturers should give a few talks or lectures to first year students and enlighten them on the various aspects of the course.

Ethics and Forensic Pharmacy are very important to the Practice of Pharmacy. It is wished therefore that these can be treated over longer period of time say during the second and third years of the course and should not necessarily be examinable. Knowing and understanding the laws governing the profession is more important than just spending a few weeks or days reading through and putting it on paper in the examination room. I wonder how many final year students can remember the constitution of the Disciplinary Committee of the Pharmacy Board and their duties. In fact, I do not remember myself.

The posology we are made to learn in the first and second years has not been useful in anyway to me personally. I am sure it has

* The Symposium was organised jointly by the Ashanti/Brong Ahafo Regional Branch of the Pharmaceutical Society of Ghana and the Ghana Pharmaceutical Students' Association, at the University of Science and Technology, Kumasi, in November, 1974.

contributed to the failure of several students in Pharmaceutics because some of us have very poor memories. After all, during practice one is free to check up on whatever dosage one is not sure of in the B.P. or Extra Pharmacopoeia. Why students should be bothered with it therefore I do not understand. Pharmaceutical Industry like many other industries is poorly developed in Ghana due to our economic position. As a matter of fact I do not know if there is a proper drug manufacturing firm in Ghana at the moment. The type of drug manufacturing done in Ghana is that where all the components of the drug are imported and then mixed together and labelled "Made in Ghana." I was surprised to hear from a prospective manufacturer of tablets that all the granules for the tablets are going to be imported and compressed here in Ghana when there are Pharmacists in Ghana who are supposed to know how to prepare granules. At this point I would like to ask why this has to happen since we are taught how to prepare granules in the laboratory. Does it mean then that, we are not taught how to prepare them properly? This question is directed to my Pharmaceutics lecturers and I hope to get a reply at the end of the symposium.

I do not know the sort of preliminary experiments performed in our manufacturing laboratories prior to manufacture of any particular drug because I have never been to any Pharmaceutical Industry myself but I have always wondered of what use experiments like determination of Upper and Lower consolute temperatures of certain substances and determination of phenol coefficients are to us when we could be taught practically how to coat tablets and and perhaps develop some modifications for coating in the tropics. Presently most people prefer coated tablets to uncoated ones and modern medicine requires that pharmaceutical formulations of new drugs appeal to the patient. We learn about coating of tablets in theory but we never get the opportunity to try it practically. Here I would like to point out that there are too many practical classes most of which are not useful to us after we leave school. For example it is rare to find a Pharmacist preparing a vaccine in a hospital. Most of these vaccines are usually imported so I do not really see the need for all these elaborate practicals in the laboratories. I do not mean we should not know how to prepare vaccines. As Pharmacists we have to know all these things but to have a practical examinations of preparation of such Pharmaceuticals is a bit nerve-racking. I feel personally that practical examinations are unnecessary and should be cancelled. This is because during such examinations the student is made to work under pressure and thus produces the worst results ever. I do not see why a student should fail a whole examination because of one practical examination which was done under pressure anyway. In fact, in the hospitals or even in industry, one takes his time to do any piece of practical work to ensure that it is properly done. More attention should be paid to the practical classes and there should be orals at the end of each term instead of the practical examinations.

I would like to suggest that trips to Pharmaceutical Industries would help the students very much in their studies. These trips are very important because as I have said earlier not all students get the opportunity to work in industries during the long vacation. Students must see some of the plants like dryers, filter units, evaporaters, etc. in order to understand how they actually operate. It is very difficult to understand how some of these instruments work without seeing them. The syllabus has been constructed in such a way that certain topics are treated of much as three times or more in the course. For example enzymes are treated in 1st year Biochemistry, 2nd year microbiology and 3rd year Pharmacognosy. Enzymes are very important and we should know as much as possible about them but I feel it is sheer waste of time to treat them over and over again while there are other equally important things to study. Why can't the syllabus be made in such a way that all aspects of any particular topic is treated at one go instead of stretching it over a long period. Here I appeal to the authorities responsible for construction of the syllabus to avoid this overlapping of topics.

I understand the Pharmaceutical Division of GIHOC is anticipating export of some of its Pharmaceuticals to neighbouring African countries. This is fair enough but we should not forget that most of these neighbouring countries are French speaking and its not going to be easy communicating with them. I feel that if some of the numerous practicals are cancelled and French lectures introduced for interested students it would help us a great deal. This should not necessarily be examinable.

Much of the work done in the hospitals is dispensing of drugs. This can be easily done by dispensing assistants and not necessarily Pharmacists. In fact, in our hospitals most of the work is done by dispensing assistants under the supervision of Pharmacists. Sometimes the Pharmacists do not even supervise and mixing of drugs is done in any manner, sometimes without accurate weighing.

Hospital Pharmacy requires dispensing knowledge and Pharmacology of drugs mostly. All the Pharmacognosy and analytical chemistry done is not applied in any way in our hospitals. Therefore I feel it is too much for anybody who wants to practise in the hospital to waste so much time learning things like determination of molecular weights by mass spectrometry and U.V. radiation, assay of certain compounds and determination of diagnostic features of crude drugs. I would like to suggest the introduction of clinical or ward pharmacy in Ghana where students can visit the wards in various hospitals and study any adverse effects produced in patients given certain particular drugs, or incompatibilities produced by administration of various drugs in any particular patient. This will be very helpful in future for practice in the hospitals. For instance a doctor may prescribe two drugs for a patient, which are pharmacologically incompatible, and in such a case the Pharmacist will have to apply his knowledge of both Pharmacology and the experience acquired during his studies in Ward Pharmacy. I hope the authorities will think about this suggestion seriously because I assure you it will be very useful indeed.

I am very glad that Pharmaceutical Management has been introduced

into the course this year. In fact it should have been introduced a long time ago because it is very important in Retail Pharmacy, Hospital Administration and Industrial Management. I have realised that Ghanaian Pharmacists are becoming more interested in the business sector these days and I bet you Pharmaceutical Management is more involved than anybody can imagine. I was working in a retail shop last long vacation and I realised this fact. I also realised that we are only acquainted with the theoretical aspects of Pharmacy in the University.

I found that one cannot practise Pharmacy in Ghana and be completely ethical. In fact, sometimes one has to behave like a Doctor in order to let your patients have confidence in you. This is against the laws of the profession but with a society like ours this cannot be helped. I think therefore that the ethics in the Pharmacy profession and the laws of Forensic Pharmacy in Ghana should be reviewed and made more suitable for Ghana.

In my opinion Pharmacognosy is the backbone of Pharmacy since most drugs are obtained from plants. I can assure you that Pharmacognosy is the headache of most students in the Faculty at the moment. I find it to be a very interesting subject but from interviews of several students I can tell you that about 80 per cent of the students find it most uninteresting. This is because of the way the practical syllabus has been constructed.

Instead of the usual examination of the numerous official crude grugs I think it will be better if local plants of medicinal importance are examined in the laboratory. In fact, most of the diagnostic features of these official crude drugs are in books and students are therefore compelled to copy or take "APO" as we commonly say. The course structure is such that we cannot help taking this "apo." I can tell you that there is no student in the Faculty who can survive without "apo." Take the Pharmaceutics course-work for example. When a student struggles with an experiment and obtains a set of results or graph which is not quite the ideal his work is considered to be poor and he is even considered to be lazy. I feel that as undergraduates we should be able to suggest reasons why our experimental results are not ideal, but if this is not acceptable to our lecturers then the next best thing to do is to copy results from somewhere and in so doing we in fact put less effort in our practical work.

Pharmacognosy practicals could be made more interesting if students could start cultivation of some local herbs on a small scale and collect samples to examine in the laboratory during practical classes alongside with the examination of the official drugs (if we are supposed to know the diagnostic features of all these by all means). It should also be borne in mind that there is an exponential increase in the knowledge of drugs in general. People are discovering more new plants of medicinal importance everyday and therefore I think it is high time we started exploiting our plant world more seriously. Work on projects in Pharmacognosy and Pharmaceutical Chemistry aims at achieving this objective but I feel this sort of work should be started earlier on in the course.

Students have been complaining about repetition of the same kind of experiments in Pharmaceutical Chemistry, like determination of Chloride, Sulphate, Chromate ions, etc. These determinations follow the same procedure so why can't some of these practicals be cut off and the time used for something else like tutorials.

To conclude I would like to suggest that talks and symposia of this nature should be organised from time to time not only by the Pharmaceutical Society but also by the Faculty to give students an insight to what problems they are likely to face after they leave school.

I hope a big fullstop will not be put at the end of my suggestions and nothing done about them. Students actually want to see changes. In fact, everybody wants to see changes within the next year or two.

(ii) A Professor's viewpoint

—D. K. Santra, M. Pharm., Ph.D.

Faculty of Pharmacy, University of Science and Technology, Kumasi

In order to answer this question, we may have to find the answer to another question. What *are* the needs of Ghana with respect to the functions that a pharmacist graduating from this University is required to fulfil?

As far as I am aware, the large majority of our graduates are employed in hospital or retail pharmacies—both in the public and the private sectors. In such establishments, they fulfil the major function of a professionally registered pharmacist, namely, the *dispensing* of the physician's prescription. He may also be called upon, in the line of duty, to carry out some limited *formulation* operations—from stock solutions to perfusion fluids. Occasionally, a senior hospital pharmacist's *technical advice* may be sought by his physician colleague.

A further number—usually small—amongst those who leave the Faculty of Pharmacy after completing the under-graduate programme, are recruited into the sales force of pharmaceutical companies — largely foreign-owned—for the task of *marketing* their proprietary products. In these establishments, a few may also be offered to share *management* responsibilities with their expatriate colleagues.

A still fewer number of graduating pharmacists find their fortunes in a variety of organisations, such as the C.S.I.R. Laboratories, National Standards Board, Government Chemical Laboratory, etc., where they are generally required to carry out the functions of:

(1) **qualitity control** — both establishment and/or enforcement of standards of quality and of storage conditions, etc. — and

(2) **research** into medicinal, pharmaceutical and other industrial potential of indigenous natural products.

Thus, it would appear that the identifiable functions currently fulfilled by a graduate pharmacist in Ghana are:

(*i*) Dispensing
(*ii*) Formulation
(*iii*) Quality Control
(*iv*) Research
(*v*) Marketing
(*vi*) Management and
(*vii*) Consultancy

The course structure comprised, as it is right now, of the four major areas of Pharmaceutical Sciences and an elementary course in Pharmaceutical Management, would seem to be on the whole, adequate to serve the major needs of Ghana, as they exist today. But needs and functions are not static entities nor are the areas of studies themselves. Not only new functions and needs will arise for the future pharmacists to fulfil, but also the relative importance of the individual functions in relation to one another will vary and thus warrant a commensurate change in the emphasis placed on and the treatment given to individual areas of study.

For instance, the number of prescriptions the present day pharmacist is required to actually compound is becoming smaller and smaller until a time will come when all that he has to do is to transfer a container from his shelf to the hand of the customer and his competence may be judged—on the surface, only by the speed with which he can count the pills! Thus, it may be necessary to drastically cut the time spent by the student pharmacist in the dispensing laboratory. Theoretical understanding of the principles and hazards of dispensing and a few representative practical exercises would perhaps be adequate.

At the moment, there is in this country, hardly any large scale production of drugs involving organic synthesis and pharmaceutical technology. Therefore, inclusion of the study of a whole range of synthetic processes for individual drugs under pharmaceutical chemistry would appear to be a waste of effort. Treatment of this aspect may well be limited, for the time being, to a general study of reactions used in organic synthesis. But obviously, as basic chemical industries and infrastructure is established in this country—what with all the brilliant chemical engineers being turned out by the University—large scale pharmaceutical manufacturing operations are most likely to follow, which in turn, would require a category of pharmaceutical personnel who are well versed in the theory and practice of pharmaceutical technology. Thus, in such an event, specially designed courses incorporating unit processes and unit operations of pharmaceutical engineering for the production of drugs and dosage forms would have to be included in the course structure. Moreover, since production of any commodity on a commercial scale is or must be an economic proposition, the recently introduced elementary course in pharmaceutical management may have to be upgraded to a fairly advanced and comprehensive level.

One function, namely, *quality control*, would always remain a vital one for a pharmacist to fulfil, whether a drug is imported or locally manufactured. I would personally like to see the study of quality control methods and techniques strengthened in our chemistry and pharmaceutics syllabus.

In view of the vast wealth in natural products, the foreseeable future of pharmacy in this country, must depend largely upon our willingness and ability to investigate and exploit indigenous species for their medicinal, pharmaceutical and industrial potential. Thus, it is gratifying to note that most of the research effort at the Faculty of Pharmacy is at present being directed, and rightly so, towards this objective. Recent innovations in the course structure would seem to suggest this very important function —research into indigenous natural products—has been taken into consideration in making a course in pharmacognosy compulsory for all final year students. Previously, final year students could skip Pharmacognosy even though they might choose to work on a project involving a local herb.

Generally speaking, a professional course of studies is prescribed by the statutory body or professional society which regulates the profession. As provided in the proposed Pharmacy Decree, this provision is stipulated to be effected through a new Pharmacy Council advised by its Education and Science Committee —a function previously carried out, perhaps only on paper, by the Pharmacy Board. Over the past eight years, many changes have been introduced into the Pharmacy curriculum at the University, largely without consultations with or approval of the Board. Perhaps the nature of the composition of the Board discouraged the academics at the University to maintain a link with the Board as far as academic matters were concerned. Perhaps this lack of rapport between the University and the Board may have culminated in the fact that a question is being asked today as to whether the course structure is suitable for Ghana.

It is possible that in the process of imparting an academic respectability to a necessarily utilitarian professional curriculum, the academic may have introduced over the years such specialised courses and recent advances as may bear little relevance to Ghana's needs as they obtain today, thus perhaps dissipating the limited time at the disposal of a professional student. If such specialised courses have the effect of crowding out other professionally functional areas of study, there is a positive danger that the graduating pharmacist may be leaving the University inadequately equipped for the professional tasks that await him. Therefore, I believe that the communication links between the Faculty and the 'Pharmacy Council' should no longer be left to exist on paper but must be revived to become a 'hot line' with constant feedback of information regarding developments and changes both in the professional unctions and needs as well as in the pharmaceutical and management sciences.

In the event of such changes in these functions and needs, it is incumbent that relevant courses and innovations be introduced to meet the demands made by these changes. Since, however, the length of the programme of studies is limited in time, it is quite obvious that pruning of existing courses must be done to

give way to the new courses. Honest heart-searching on the part of the profession as well as the academics would reveal the extent of dead-weight that has accumulated in our syllabus over the years, and which must be discarded.

At the moment, apart from some specialization at the project level and additional papers in the same field, the organisation of the programme of studies is such that *all* the courses have to be taken by *all* the students. Little imagination is required to perceive that temperamentally, aptitude-wise and intellectually, not all students are suited for *all* the courses. Besides, not every graduating pharmacist is called upon to perform *all* the functions enumerated earlier. Therefore, it appears to be irrational to make all the courses compulsory for all students. This undesirable situation can be remedied by what is known as the 'Electives System.' In this system, there is a

(1) *Core curriculum*

consisting of courses prescribed by the Pharmacy Council as minimum requirements for a professional training programme and

(2) *'Elective' courses,*

a variety of courses being offered.

Each student chooses those courses in which he/she wishes to specialise or has aptitude for. The University prescribes a minimum number of such courses that must be taken to satisfy academic requirements for a degree. Thus, *all* students are not required to take *all* courses and therefore have time and aptitude to go into some depth in their chosen area of elective courses.

This system of electives should, in my opinion be integrated into the entire duration of the degree programme. An elective course in pharmaceutical management, for example, cannot be adequately handled in a lone paper in the final year. Management of a business or organisation requires an understanding of human nature as well as the principles of economics and organisational, commercial and technical operations. Therefore, a graded series of courses distributed throughout the degree programme is always better than a hotch-potch crammed into a single paper placed in the final year.

Finally, a professional course of training must incorporate into its structure, a built-in mechanism which permits the practising pharmacist to return to the University for a short period of refresher courses at regular intervals, of say, every seventh year. So many advances are being made in the field of chemotherapy so rapidly that a pharmacist wishing to maintain a consultant's position with his medical colleagues must be given an opportunity of keeping abreast of recent developments in pharmacy.

I had purposely omitted to mention teaching as one of the functions that a pharmacist may be required to fulfil because both aptitude and gift for teaching *and* further academic work are necessary before an undergraduate can be developed into a teacher. However, in designing a course structure in pharmacy as a University undergraduate programme of studies this possibility must not be overlooked.

Post-graduate work can only be built up if the foundation at the undergraduate level has a solid base in science and is not merely professional. A harmonious blend of courses catering to both academic and professional interests can be achieved through this system of electives more readily than any other system I am aware of.

Before a verdict can be passed as to whether the present course structure in pharmacy is suitable for Ghana, we have to examine in greater depth what each major area of study aims to achieve and place it along side of the existing needs and functions of a professional pharmacist. In speaking about the general principles which should guide the establishment or redesigning of the course structure, I shall end by saying I hope I have been able to stimulate discussion, so that we not only take a critical look at the present course structure, but also at course content and course organisation vis-a-vis future development of pharmacy in Ghana.

Two other viewpoints will appear in the next issue of the Journal.

— Editor

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BY

31ST JULY 1975

The Pharmaceutical Society of Ghana

The National Council of the Society

announces that in commemoration of the

40th Anniversary of the founding of the Society,

the week in which the

33rd Ghana Pharmaceutical Conference and Exhibition

will take place, i.e., Sunday, 24th August, 1975 to Saturday, 30th August, 1975, has been declared

"PHARMACY WEEK"

In addition to the Conference and Exhibition, Regional Branches of the Society will organise various activities at the Regional Centres during the week.

D. Anim-Addo
Hon. General Secretary.

INTERNATIONAL RECOMMENDATIONS OF THE FEDERATION INTERNATIONALE PHARMACEUTIQUE FOR THE DESIGNATION, PACKAGING AND LABELLING OF PHARMACEUTICAL SPECIALITIES

1. Considering the fact that the pharmaceutical speciality plays an important part in the field of medical treatment and.

2. Considering that problems may arise in the course of the distribution of a pharmaceutical speciality from the manufacturer through wholesale dealers and community pharmacists to the consumer, and

3. Bearing in mind that national regulations and practical difficulties may influence the adoption of these recommendations.

4. With the understanding that these recommendations cannot be interpreted as interfering with the rights and responsibilities of the manufacturers and distributors of pharmaceutical specialities or the rights and professional prerogatives of the practising pharmacist.

5. In the interest of a harmonious co-operation between physician and pharmacist in drug prescribing and in dispensing pharmaceutical specialities.

6. The following statement of principles regarding the designation, packaging and labelling of drugs is recommended by the General Assembly of the Federation Internationale Pharmaceutique:

Designation

7. It is desirable that the trade mark and internationally uniform non-proprietary names used for pharmaceutical specialities should be, whenever possible, the same in all countries.

8. If adjectives are used to differentiate between products (e.g. "Compositum", "Retard", "Sedative", "Depot", etc.) these descriptions should, if possible, be close to the main designation of the pharmaceutical speciality.

9. The substitution of single letters for additional words for the purpose of differentiating pharmaceutical specialities should, if possible, be avoided (e.g. "S" for "Sedative", "Sulfonamid", "Special" and "Simplex", "p" for "Pediatrics" and "Penicillin" etc . . .), because such letters are liable to cause confusion.

10. If there are several dosages of the same formulation of a pharmaceutical speciality with only one active ingredient the difference in dosage, on the label should, if possible, be expressed in figures and not by adjectives.

11. If a trade mark has been given to a special pharmaceutical form and if this name is not generally known and understood then, if possible, the type of formulation should be explained.

If a chemical or pharmaceutical term or non-proprietary name is used to define a pharmaceutical speciality, the name of the manufacturing firm or the distributor (or the name of the person responsible for putting the product on the market) should be shown on the label.

13. If a pharmaceutical speciality is marketed in separate formulations for adult and children's use, the difference between these packs must be clearly marked to avoid mistakes.

Packaging

14. Having regard to storage difficulties in community pharmacies packs should be designed, where possible, so that the side which remains visible when stocked should show clearly the complete name of the pharmaceutical speciality. Unnecessarily large packs should be avoided. The recommendations does not exclude the use of push-through packs.

15. As far as the size of the pack allows this, the pack should be designed in such a way that the pharmacist can affix his label or his stamp to it and note the directions for use as prescribed by the doctor without obliterating important indications.

16. When the use of a housestyle package design is adopted, it is desirable that the different pharmaceutical specialities should be distinguishable from each other in order to avoid confusion.

17. All the details needed by the pharmacist when dispensing the product (name of pharmaceutical speciality, dosage form, strength, content or volume) should, if possible, be shown on the same side of the pack.

Labelling

18. The content and dosage of the product should be indicated in such a way as to eliminate any possibility of misunderstandings in use. Adequate information should be given as to the method of administration.

19. Where necessary instructions for the storage of a pharmaceutical speciality should be shown clearly and unambiguously (with due attention to the recommendations of the F.I.P. 1966 in Madrid (J. Mond. no. 2/1966) as long as national laws or regulations have no contradictory requirements.

20. An uncoded expiry date should be shown on pharmaceutical specialities with very short stable life or when such products have an established shelf life after which they should no longer be dispensed.

21. If a pharmaceutical speciality must be reconstituted by the pharmacist before supply this should be stated explicitly. The mode of preparation, indications for the storage and the stable life should also be stated.

22. The General Assembly of the Federation Internationale Pharmaceutique supports the above recommendations which should lead to increased safety in the dispensing of pharmaceutical specialities and to the health of the patient.

Adopted by the General Assembly of the International Pharmaceutical Federation (F.I.P.) in Rome, September 1974

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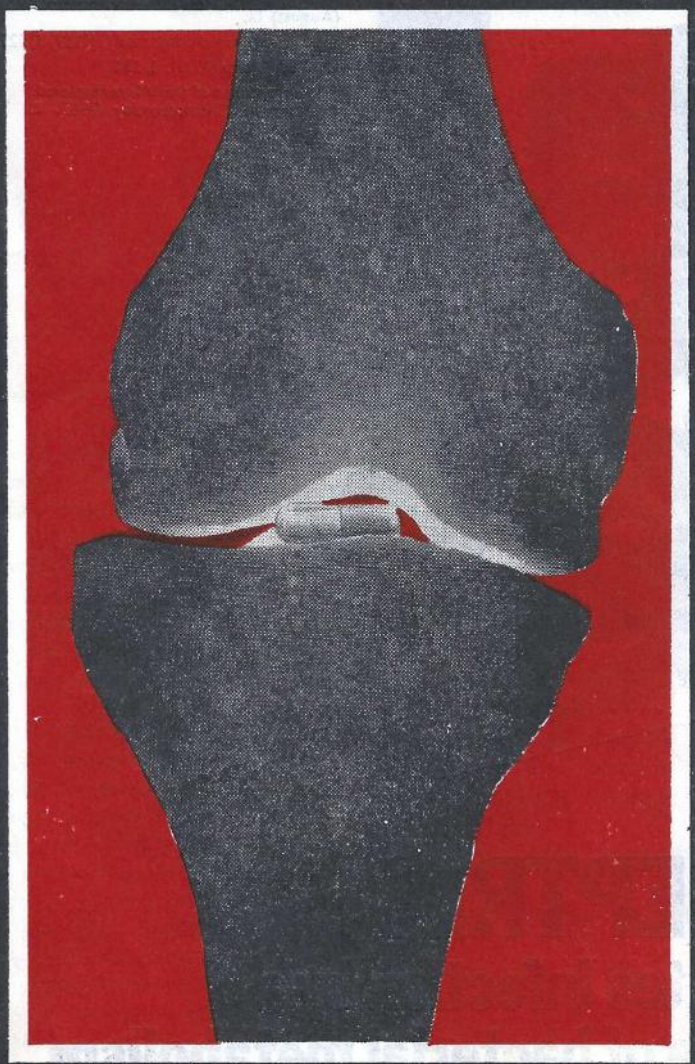

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SMA 1430

EFFECTIVENESS OF 0.25% v/v CHLOROFORM AS A PRESERVATIVE IN MIXTURES IN THE TROPICS

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Summary

The effectiveness of 0.25% v/v chloroform as a preservative against microbial growth in mixtures in the tropics has been examined. The author has also observed microbial growth in similar mixtures prepared with 0.5% w/w chloroform as a preservative and those prepared without chloroform, over a five-day period.

Introduction

Microbial contamination of pharmaceuticals has engaged the attention of pharmacists world wide. In the tropics the question of microbial contamination of pharmaceuticals needs serious study due to the more favourable environmental conditions for microbial growth. Recent work by Boakye-Yiadom and Buadu (1974) has shown a high incidence of bacterial contamination of mixtures collected from various hospitals in Ghana. One of the reasons offered for microbial growth in mixtures is inadequate preservation. In view of the volatility of chloroform and the normally high temperatures in the tropics the author decided to examine the suitability of the B.P. concentration of chloroform used in mixtures under conditions to which they are subjected during use in the tropics. The preservative activity of 0.5% w/w of chloroform was also examined since most pharmacopoeias use this concentration as the official preservative concentration (Matindale, 1973). Mixtures were prepared without chloroform as controls.

Materials and Methods

Five mixtures were used for the experiment and are listed below:

1. Potasium Citrate Mixture B.P.C. (1968)
2. Ferric Ammonium Citrate Mixture B.P.C. (1968)
3. Ferric Ammonium Citrate Mixture Paediatric B.P.C. (1968)
4. Chalk Mixture Paediatric B.P.C. (1968)
5. Kaolin Mixture, Paediatric B.P.C. (1968)

Three samples of each mixture were prepared as follows:
Sample A was prepared according to B.P.C. (1968) specifications and contained 0.25% v/v of chloroform.
Sample B was prepared as in A but contained 0.5% w/w of chloroform.
Sample C was prepared just as in A but without any chloroform. 250 millilitres of each sample were prepared.

Initial viable counts of the mixtures were made by plating 1 ml. portions of 1 in 10, 1 in 100 and 1 in 1000 dilutions of the samples made in quarter strength Ringer's solution, on nutrient agar (Oxoid). To evaluate the effect of the chloroform concentrations on the daily viable count of the mixtures under the conditions they were used, 15 millilitres of mixture were withdrawn from each sample three times daily (morning, noon and night) for five days. At the beginning of each day 10 millilitres of each sample were withdrawn, diluted as above and one millilitre portions plated on nutrient agar. All plates were incubated in the inverted position at 37°C for 48 hours, after which counts were performed. The mixtures were kept at room temperature during the period of the experiment (5 days). The average temperature recorded per day was 32°C and 26°C per night. (Day and night temperatures were recorded using a Zecol Wet and Dry Bulb Thermometer).

TABLE I

AVERAGE DAILY VIABLE COUNT PER ML OF MIXTURES CONTAINING 0.25% v/v CHLOROFORM

Name of Mixture	1st Day	2nd Day	3rd Day	4th Day	5th Day
Potassium Citrate	600	500	550	600	500
Ferric Ammonium Citrate	1,000	950	910	500	500
Ferric Ammonium Citrate (Paediatric) ...	1,050	910	950	900	400
Chalk Paediatric	2,000	2,000	1,800	1,200	1,000
Kaolin Paediatric	200	200	500	550	560

TABLE II

AVERAGE DAILY VIABLE COUNT PER ML OF MIXTURES CONTAINING 0.5% w/w CHLOROFORM

Name of Mixture	1st Day	2nd Day	3rd Day	4th Day	5th Day
Potassium Citrate	510	500	520	510	490
Ferric Ammonium Citrate	980	750	520	530	300
Ferric Ammonium Citrate (Paediatric) ...	1,200	1,020	1,050	1,100	750
Chalk (Paediatric)	2,000	1,200	1,100	1,000	950
Kaolin (Paediatric)	200	150	200	200	100

TABLE III

AVERAGE DAILY VIABLE COUNT PER ML OF MIXTURES CONTAINING NO CHLOROFORM

Name of Mixture	1st Day	2nd Day	3rd Day	4th Day	5th Day
Potassium Citrate	1,000	5,000	32,900	13,900	21,000
Ferric Ammonium Citrate	1,000	16,000	19,800	23,100	33,000
Ferric Ammonium Citrate (Paediatric) ...	1,100	16,800	29,900	28,900	35,300
Chalk (Paediatric)	3,000	19,300	35,400	39,700	24,500
Kaolin (Paediatric)	230	8,500	11,500	23,100	35,400

Results and Discussions

The results of the viable microbial counts over the five days of the different mixtures are summarised in tables I, II and III.

The daily average viable count for mixtures prepared using the two concentrations of chloroform showed very little variation over the five-day period. Mixtures preserved with 0.25% chloroform showed a decrease in viable count at the end of the five days, except for Kaolin Paediatric Mixture which showed a three-fold viable count increase from 200 organisms per millilitre of mixture to 560 organisms per millilitre. All the mixtures preserved with 0.5% chloroform showed a decrease in viable count at the end of the experiment. The mixtures prepared without the addition of chloroform showed significant increases in microbial population after the experimental period. The highest increase was observed in the Kaolin Mixture which had an initial microbial population of 230 organisms per millilitre increasing to 35,400 organisms per millilitre of mixture at the end of the experiment. The low count observed in the present work was most probably due to the fact that very clean conditions prevailed during the compounding of the mixtures and also the use of ingredients packed in small packages (500 grams) which had been stored in an air-conditioned room with a temperature of 20°C± 2°C having a percentage relative humidity of 50. Under these conditions bacterial growth in the raw materials would be minimal. The not-so-clean conditions of some of the dispensaries from which Boakye-Yiadom and Buadu collected their samples and the fact that the ingredients used in preparing those mixtures examined by them were packed in large containers of 5 kilograms or more and stored in highly humid stores without air conditioning might have been responsible for the very high viable count observed by them due probably to heavily contaminated raw materials used in the preparation of the mixtures. Initial high bacterial population in any mixture would adversely affect the action of any preservative present.

The experiment has shown that 0.25% v/v chloroform is an effective preservative for mixtures in the tropics. It also showed very little difference in the preservative action of 0.25% v/v and 0.5% w/w chloroform in mixtures. The high counts reported by Boakye-Yiadom and Buadu (1974) in hospital mixtures collected from some dispensaries in Ghana were due to other factors than the effectiveness of the chloroform concentration used as a preservative.

Acknowledgement

The author wishes to thank Messrs Charles Manful and Mike Pobee for technical assistance.

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NOTICE

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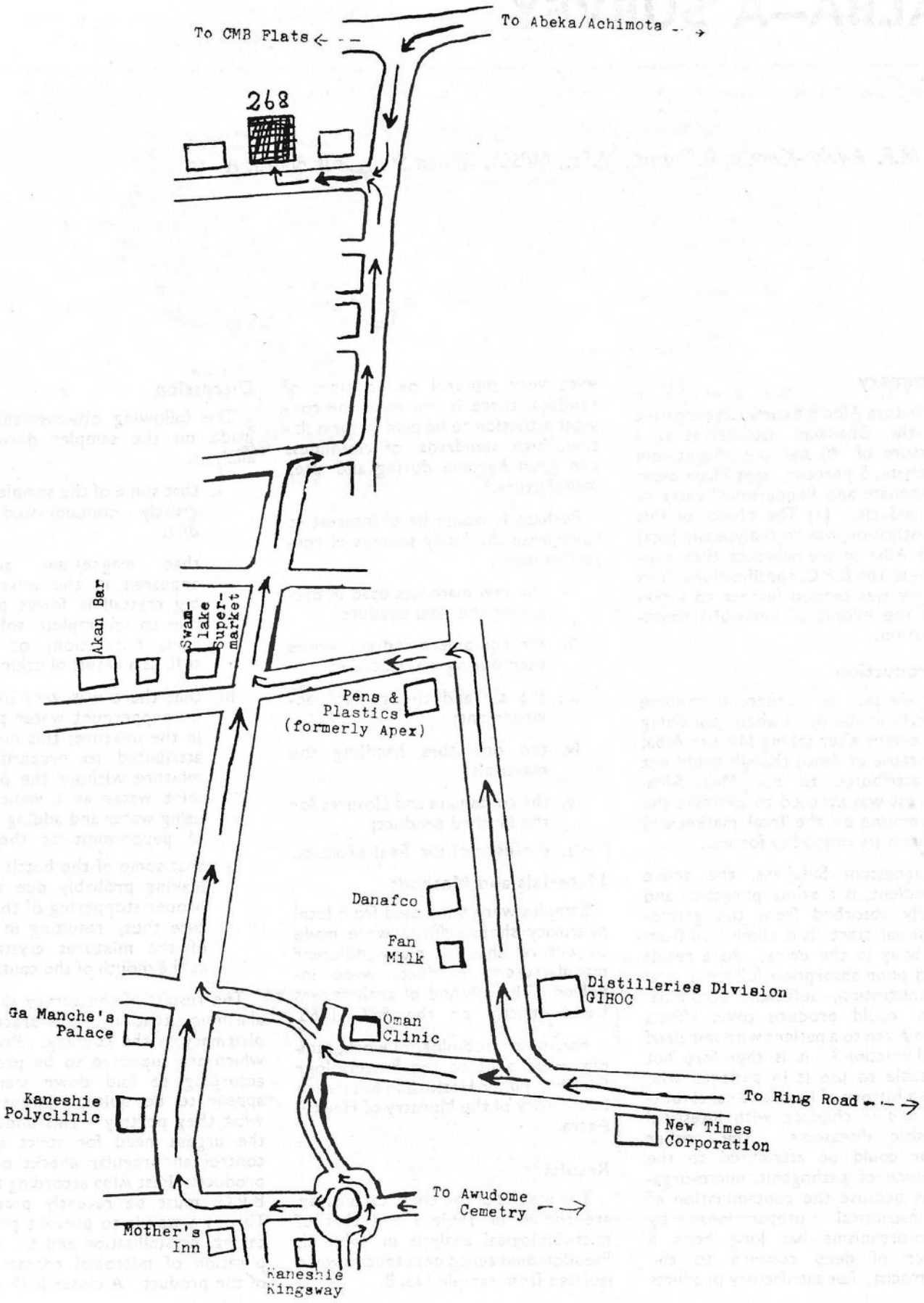

EVALUATION OF MISTURA ALBA—A SURVEY

by M.F. Awuku-Kwatia, B.Pharm., M.Sc., MPSG., Ghana Standards Board, Accra

Summary

Mistura Alba is a common purgative on the Ghanaian market; it is a mixture of 40 percent Magnesium Sulphate, 5 percent light Magnesium Carbonate and Peppermint Water as the vehicle. (1) The object of this investigation was to analyse the local Mist Alba to see whether they conform to the B.P.C. specifications. The survey was carried further to ascertain the extent of microbial contamination.

Introduction

In the late sixties there were some reports in the press about poisoning and deaths after taking Mistura Alba. The cause of death though could not be attributed to the Mist Alba, interest was aroused to examine the preparation on the local market and to assess its suitability for use.

Magnesium Sulphate, the active ingredient, is a saline purgative and poorly absorbed from the gastro-intestinal tract. It is eliminated from the body in the urine. As a result of its poor absorption following oral administration, sufficient accumulation could produce toxic effects when given to a patient with impaired renal function.[2] It is therefore not advisable to use it in patients who have a history of impaired renal function and in children with intestinal parasitic disease.[3,4] The other factor could be attributed to the presence of pathogenic micro-organisms because the contamination of pharmaceutical preparations by micro-organisms has long been a matter of deep concern to the pharmacist. For satisfactory products with very minimal or no signs of spoilage, there is the need for constant attention to be paid to formulation, high standards of cleanliness and good hygiene during and after manufacture.[5]

Perhaps it would be of interest to summarise the likely sources of contamination[6] ;

i. the raw materials used in preparing the final product;

ii. the equipment and containers used during manufacture;

iii. the air and the general environment;

iv. the operators handling the materials;

v. the containers and closures for the finished product;

vii. the user of the final product.

Materials and Methods

Samples were purchased from local pharmacy shops; efforts were made to ensure that as many different manufacturers' products were involved. The method of analysis was based strictly on the BPC 1968.

For the microbiological work, samples were sent to the Bacteriology Division, Public Health and Reference Laboratory of the Ministry of Health, Accra.

Results

The results of the chemical analysis are shown in Table I and that of microbiological analysis in Table II. Pseudomonas aeroginosa species were isolated from sample No. 8.

Discussion

The following observations were made on the samples during the analysis,

i. that some of the samples were grossly contaminated with dirt.

ii. that magnesium sulphate appeared in the mixture in big crystalline forms perhaps due to incomplete solubilisation, trituration, or worse still, as a result of caking;

iii. that there was very little or no peppermint water present in the mixture; this might be attributed to preparing the mixture without the peppermint water as a vehicle but using water and adding a drop of peppermint at the end;

iv. that some of the bottles were leaking probably due to improper stoppering of the mixture thus, resulting in some of the mixtures crystallising at the mouth of the containers.

The results of the survey show an alarming situation in the practice of pharmacy in the country. Products which are supposed to be prepared according to laid down standards appear to be quite different from what they portray. This underlines the urgent need for strict quality control and regular checks on our products. Mist Alba according to the B.P.C. must be recently prepared. This in a way is to prevent possible caking, crystallisation and the multiplication of microbial contaminants of the product. A closer look at the

TABLE I

Sample	% Content of $MgSO_4.7H_2O$	% Content of $MgCO_3$ as Mg	Remarks
1	33.8	1.30	Homogeneous Suspension. Does not settle readily. pH8.65
2	33.6	1.20	as above.
3	34.3	0.80	Slightly coloured with dirt. Does not settle readily. pH 8.10
4	34.0	0.81	Presence of dirt particles, does not settle readily. pH 8.60
5	39.2	0.50	Smooth to touch. Floating particles unidentified. pH 8.65
6	37.2	0.55	Fairly homogenous suspension. pH 8.65
7	39.8	0.87	Dirty suspension. Floating insect and particles. pH 8.60
8	39.0	0.82	Aggregate particles of crystals observed. pH 8.70
9	42.0	0.47	Crystals of Magnesium Sulphate observed. Very rough to touch. pH 8.20
10	21.9	0.35	Suspension not easily dispersed. pH 8.6
B.P.C. Limits	30.5 to 37.8	0.99 to 1.20	

TABLE II

Sample	Total Bacterial Count/ml	Pre. Coli Count / 100ml
1	30	0
2	50	0
3	6,830	0
4	5,430	1
5	255,000	0
6	17,550	0
7	69,500	9
9	10,700	1
9	280	0
10	220	0

products indicated that some of them might have stayed on the counter for long. It is rather unfortunate that most of the samples did not fall within the B.P.C. limits of content of $MgSO_4.7H_2O$ and $MgCO_3$ as Mg.

On the microbial contamination of the samples, this is a world-wide problem for non-sterile pharmaceuticals. The results showed high total bacteria count in samples No. 3–8 as indicated in Table II however these high values are not reflected in the presumptive coliform count. The isolation of Pseudomonas aeroginosa in sample 8 is a matter of deep concern. In the likely sources of microbial contamination, the most difficult to control microbiologically from the manufacturing point of view are the raw materials. In the case of Mist Alba it is likely that the water supply played a part in cases where instead of the Peppermint Water B.P., ordinary water might have been used in the formulation.

The presence of pathogenic bacteria in pharmaceutical formulations could be fatal. Boakye-Yiadom and Yaw Buadu[7] in their evaluation of microbial contamination of pharmaceuticals in Government hospital dispensaries in Ghana, established the presence of the following pathogens:—Staphylococcus aureus, Pseudomonas aeroginosa, Escherichia coli, Salmonellae and anaerobic bacteria. Out of the 50 samples they examined, 22 showed total viable bacterial count of less than 10,000 organisms/ml, 13 had between 10,000 and 100,000 organisms/ml and 15 more than 100,000 organisms/ml. Results for the presence of specific pathogens were quite alarming.

Perhaps it might be of interest to add that in another survey by Robinson[8] on contamination of liquid antacids, the author encountered a high level of bacterial contamination, with Pseudomonas aeroginosa being the predominant organism. The author submitted that with the high level of contamination with a potential pathogen in commercial preparations, there is the need for control of all raw materials notably those from natural sources; also the manufacturing processes of non-sterile drugs and finished product material must be controlled.

To attempt to eliminate microbial contamination completely from pharmaceutical products would be both unnecessary and expensive. The presence and dangers associated with this problem has led to the formation of many committees notably Kallings, et al,[9], Taylor et al[10] and Sykes et al[11]. Sadly Ghana has not undertaken such survey probably on a large scale. It would therefore be of interest to adopt the Swedish standard which suggests that the maximum permitted bacterial count in any preparation should not exceed 100/g of the medicament.

Conclusion

An attempt has been made by the survey to focus attention on some of the problems facing the pharmacist as the "medicine-man" in our society who has to protect the people from harm by administering the correct formulation, free from any hazards. The choice of Mist Alba was incidental but from the experience of the author in his contact with his small team of workers, the regular demand for purgative shows the extent to which people in this country are dosing themselves with a very poor quality and dangerous product. This situation may apply to other pharmaceuticals; thus the need for strict quality control of our products cannot be over-emphasised.

ACKNOWLEDGEMENT

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STEROIDAL CONSTITUENTS OF SOLANUM WRIGHTII, BENTH

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Summary

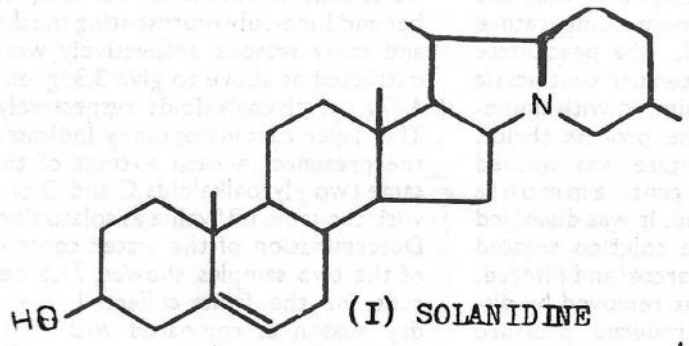
In view of the commercial importance of steroids of plant origin, used as intermediates for the synthesis of steroid drugs, and of the fact that the genus *SOLANUM* has been known to contain steroids, *Solanum wrightii*, a species widely occuring in West Africa was investigated. Chemical tests, physical constants and spectral data have been furnished to identify one of the two glycoalkaloids isolated as Solasonine (IV). The second glycoalkaloid had solasodine as its aglycone and the sugars rhamnose and glucose, thus indicating that it might be Solamargine (V).

The mature unripe fruits contain the highest amount of total glycoalkaloids. Stem and root barks contain only traces, while the leaf and flower do not contain any glycoalkaloids. Mature unripe fruit collected in the wet season show a somewhat higher total glycoalkaloid content.

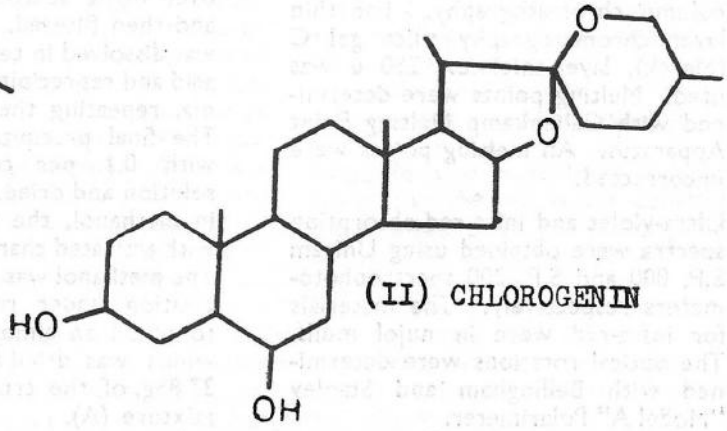
INTRODUCTION

Plants containing steroidal substances are of considerable economic importance because some of these organic natural products are particularly suitable as intermediates for conversion into corticosteroids and reproductive hormones. The genus *Solanum* is known to produce steroidal substances which offer such possibilities. Over a hundred species of this genus have been reported to contain steroidal compounds distributed in the various organs.[1]

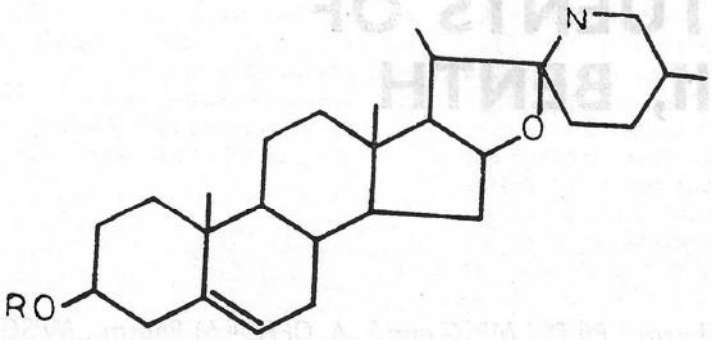
The West African flora include some twenty species of the genus *Solanum*. Many plants of this genus are indigenously used as sources of foods and drugs.[2] Alves, Prista and Ferreira[3] isolated from the leaves of *Solanum wrightii*, a glycoside which on hydrolysis yielded solanidine (I) and the sugars rhamnose, glucose and arabinose. This same species has been reported to contain chlorogenin (II) the free aglycone solasodine (III) and the glycosides solasonine (IV) and solamargine (V) by Fayez and Saleh [4] who examined the fruits from plants growing in Egypt. Since no work appears to have been done on the plant growing in Ghana, the local population of this species has been investigated for its steroidal constituents.



(I) SOLANIDINE



(II) CHLOROGENIN



R = H. (III): SOLASODINE

R = Rhamnose-galactose-glucose (IV): SOLASONINE

R = Rhamnose-glucose. (V): SOLAMARGINE

Materials and Methods

(*a*) Immature, mature unripe and ripe fruits were collected during the dry season (November-December) on separate days from plants growing in the University of Science and Technology campus, along Ridge and Asuogya roads. They were sliced immediately after collection and steeped in the extraction solvent (95% alcohol containing 5% acetic acid)

(*b*) Mature and immature leaves (leaves buds), and flowers were collected from the same plants on separate days. They were immediately dried in forced-air oven, controlled at 50°C. Collections were made during afternoons.

(*c*) Stem bark and root bark were collected from older plants and dried at 50°C.

(*d*) Another collection of mature unripe fruits were made in the wet season (June-July).

All collected specimens were authenticated by matching with a herbarium specimen of *Solanum wrightii* No. F.H. 6930 made kindly available by the curator of the Herbarium at the Forestry Division, Kumasi.

Alumina (BDH) was used for column chromatography. For thin layer chromatography silica gel G (Merck), layer-thickness 250 u was used. Melting points were determined with Gallenkamp Melting Point Apparatus. All melting points were uncorrected.

Ultra-violet and infra-red absorption spectra were obtained using Unicam S.P. 800 and S.P. 200 spectrophotometers respectively. The materials for infra-red were in nujol mulls. The optical rotations were determined with Bellingham and Stanley "Model A" Polarimeter.

Extraction and Isolation

Preliminary investigation of the various organs of *Solanum wrightii* showed that the fruits contain alkaloids, the stem and root bark only traces while the leaves and flowers were negative. No steroidal saponins were detected.

(*a*) 4 kg of mature unripe fruits were sliced immediately after collection and steeped in 95 per cent ethyl acohol containing five per cent acetic acid. The slices were minced in a blender with 5 litres of the solvent and kept for 48 hours at room temperature with occasional stirring. It was then filtered and the marc reblended with 3 litres of the solvent and macerated for 24 hours. It was again filtered and the two extracts bulked, and concentrated under reduced pressure to 1 litre. 1 litre of 10 per cent acetic acid was added to the concentrate and the precipitated non-glycoalkaloidal matter was filtered off. The filtrate was shaken with benzene—ether mixture (1:1) until the solution was clear, the benzene-ether mixture being rejected. It was then heated to about 70°C and ammonia solution (27%) added to bring the pH to 9. The crude glycoalkaloids which separated as a flocculent precipitate was left over night at room temperature and then filtered. The precipitate was dissolved in ten per cent acetic acid and reprecipitated with ammonia, repeating the process thrice. The final precipitate was washed with 0.1 per cent ammonia solution and dried. It was dissolved in methanol, the solution treated with activated charcoal and filtered. The methanol was removed by distillation under reduced pressure to obtain an almost white residue which was dried at 100°C to give 37.85g. of the crude glycoalkaloid mixture (A).

Thin layer chromatographic examination of A on silica gel using ethly acetate—pyridine—water (20:5:2) as solvent system indicated that the mixture contained two glycoalkaloids.

2g. of crude mixture (A) was dissolved in water-saturated n-butanol. The solution was chromatographed on a column of alumina. The chromatogram was eluted with 600ml. of water-saturated n-butanol, fractions being collected in 20 ml. portions. After monitoring by TLC, all fractions containing the same compound were bulked and shaken with five per cent acetic acid until exhausted. The combined acid layers were separately basified with ammonia solution and the precipitate filtered. It was washed with 0.1 per cent ammonia solution and then recrystallised from methanol to give two glycoalkaloids designated C and D.

Thin layer chromatography of the two separated glycoalkaloids on silica gel using ethyl acetate-pyridine-water (20:5:2) with authentic reference samples of solasonine and tomatine indicated that one of the glycoalkaloids (C) might be solasonine.

(b) 100g. each of mature unripe fruits collected in November–December and June–July representing the dry and rainy seasons respectively were extracted as above to give 3.33g. and 4.87g. of glycoalkaloids respectively. Thin layer chromatography indicated the presence in each extract of the same two glycoalkaloids C and D one with the same hRf value as solasonine. Determination of the water content of the two samples showed 71.6 per cent for the fruits collected in the dry season as compared with 84.15 per cent in the rainy season. 100g. each of the mature ripe and immature fruits gave 2.03g. and 2.67g. of total crude alkaloids respectively.

(c) Hydrolysis of the Glycosides:

20g. of the glycoalkaloidal mixture (A) was refluxed with five percent hydrochloric acid in ethanol (200 ml.) for five hours on a boiling water bath. 100 ml. of distilled water were added and the alcohol partially removed by boiling. A deposit of a brownish mass was obtained which was filtered off, dissolved in hot methanol (500ml ml.) and clarified with activated charcoal. The methanol was removed by distillation under reduced pressure giving a granular precipitate which was suspended in hot water and basified with ammonia solution (27%) while still hot. The mixture was cooled and filtered. The residue was crystallised from 80 percent aqueous methanol to give 10.2g. shining rod-like crystals (E).

Thin layer chromatography of the aglycone (E) and authentic solasodine, solanidine and tomatidine on silica gel using ethyl acetate and benzene (1:1) showed that the aglycone was a single compound and had similar hRf value to the reference solasodine. The two isolated glycoalkaloids (C and D) were separately hydrolysed as above and the hydrolytic products (F and G) subjected to thin layer chromatographic examination using the same reference compounds and system as for compound E above. It also gave a single-spot chromatogram with the same hRf value as reference solasodine.

(d) Detection of Sugars in the Hydrolytic Products

The filtrates resulting from the hydrolysis of the glycoalkaloid mixture A and the separated glycoalkaloids C and D indicated the presence of sugars when tested with Fehlings solution. The filtrates were therefore examined by both thin layer and paper chromatography for sugars using glucose, fructose, arabinose, rhamnose and galactose as references.

The solvent system for the paper chromatography was ethyl acetate-pyridine-water (50:25:20) while that for the thin layer on silica gel G impregnated with boric acid were (a) benzene-glacial acetic acid-methanol (20:20:60) and (b) methyl ethyl ketone-glacial acetic acid-methanol (60:20:20). The chromatographic examination showed that A and C contained rhamnose, galactose and glucose while D contained rhamnose and glucose.

RESULTS AND DISCUSSION

(a) *Melting Points:* (Uncorrected)

Solasonine, 285°C; Compound C 284–286°C
Compound D, 302°C
Solasodine, 198°C; Compound E, 196°C
Compound F, 196–198°C
Compound G, 197°C
Solasonine+Compound C 285°C
Solasodine+Compound E 196°C
Solasodine+Compound F 196°C
Solasodine+Compound G 196°C

(b) *hRf Values:*

i. Glycosides. Silca gel G/ethyl acetate-pyridine-water (20:5:2) Solasonine 29, Solanine 31, tomatine 34, Compound C 29 Compound D 54.

ii. Aglycones. Silica gel G/ethyl acetate-benzene (1:1) Solanidine 65, tomatidine 61, Solasodine 44, Compound E, F and G 44.

(c) *Ultra-violet absorption Spectrum (ethanol) of Solasodine:*

max 243 nm (log E=3.22), 235 nm (log E =3.36)
228 nm (log E=3.34).
min 231 nm (log E=3.33) 223 nm (log E=3.29)

(d) *Infrared Spectrum (Nujol)of Solasodine:*

840 cm^{-1} (double bond), 1060 cm^{-1} (ether)

3400 cm^{-1} (OH ; NH)

(e) *Specific Rotation:* Solasodine—94.1 (Methanol)

The compounds E, F and G obtained by hydrolysing the glycoalkaloids (C and D) are identical in hRf value, ultra-violet and infrared spectra and melting point with authentic solasodine. Mixed melting points of the isolated aglycones and solasodine showed no depression. Compounds E, F and G are therefore identified as *SOLASODINE* (III). By similar comparison, compound C is identified as SOLASONINE, the 3-rhamno-galacto-glucoside of solasodine. This was supported by the presence of glucose, galactose and rhamnose in the hydrolytic products of C. The aglycone of compound D was found to be solasodine and the sugars detected in the hydrolytic products were glucose and rhamnose. It would therefore appear that compound D is solamargine, reported to be present in the Egyptian species.

The fact that the leaves and flowers contain no glycoalkaloids and that there are only traces in the stem and root barks suggests that the glycoalkaloids are stored in the fruits, and probably synthesised in the root. It has in fact been proved that alkaloidal synthesis in some solanaceous plants occur at the root tips.[5] The mature unripe fruits was found to contain larger amount of total alkaloids than the mature ripe fruits. This may not necessarily be due to the possibility that during ripening a portion of the glycoalkaloids is broken down into simpler substances. It is probable that after maturity no more glycoalkaloids are stored whilst more non-alkaloidal materials like lignin and cellulose are added. This phenomenon would tend to increase the weight of the fruit without affecting the weight of the glycoalkaloids originally present, thus lowering the overall glycoalkaloid content of the fruit.

Different workers investigating samples collected from different habitats have variously reported on their steroidal constituents. Alves, Prista and Ferreira examined leaves of *S. wrightii* in South America—its original habitat—and found a glycoside solanidine and the sugars glucose, rhamnose and arabinose. Fayez and Saleh reported the presence in the fruits in Egypt of free solasodine, solasonine and solamargine, and chlorogenin.

In this paper we report the presence in the fruits in Ghana of solasodine in the glycosidal forms solasonine and most possibly solamargine thus confirming the findings of Fayez and Saleh but are unable to detect free solasodine in the fruit. The presence of free solasodine reported in Egypt may be the result of partial hydrolysis of the glycosides during the process of extraction. In addition solanidine and chlorogenin were not detected in any of our samples. The fact that two different types of nitrogenous steroids are found in specimens from the new world and the old world points to the occurrence of the phenomenon of chemical races in the species.

The method of extraction of solasodine is simple and the percentage content in the mature unripe fruit is high enough to merit its use as an economic source for solasodine.

Acknowledgements

Authentic reference samples of Solanine, Solasonine and Solasodine were kindly supplied by Prof. Dr. A. Hifuy Saber of Cairo University.

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PHARMACOGNOSTICAL INVESTIGATION OF *BLIGHIA SAPIDA* KöNIG (WITH SPECIAL REFERENCE TO ITS SEED-FAT COMPOSITION)

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Summary

Results of detailed investigations on the chemical (Table 1) and physical (Table 2) properties of the aril oil and the kernel fat are being reported. The seed fat, aril oil and kernel fat contents have also been reckoned on a dry weight basis (Table 3).

Three component fatty acids in the aril oil—palmitic (65.0), oleic (100.0) and stearic (21.4) acids; and five in the kernel fat—palmitic (4.9), oleic (25.9), stearic (7.4), eicos-11-enoic (100.0) and arachidic (53.4) acids—were identified by TLC (Fig. 2) and also in the form of their methyl esters by GLC, the above figures in parentheses—calculated from GLC analysis of the fatty acid methyl esters — indicating the relative amounts of the fatty acids in the aril oil and kernel fat, respectively.

The fatty acids in both the aril oil and the kernel fat have been characterised, in the form of their methyl esters by hRf values from TLC (Fig. 3), by retention times (Rt) in GLC (Figs. 4a and 4b) and by GLC-mass spectrometric data (Figs. 5a; 5b and 6).

Examination of plant samples from the Coastal (Accra), Forest (Kumasi) and Wet-savanna (Tamale) Belts showed no marked variations in the oil/fat content, nor in the fatty acid composition.

Introduction

Blighia sapida Konig (Sapindaceae), commonly known as the Ackee (Akee) Apple, a West African species common in Ghana, has been studied with special reference to its seed fat composition. The edible walnut-like aril and seed kernel (Figs. 1a and 1b) are reported (Irvine, 1961 and Kerharo & Bouquet, 1950) to be rich in oil and fat respectively. However, the aril is poisonous if imperfectly ripe and when the fruits (Figs. 1a and 1c) have lain on the ground for some time. The poisonous properties are believed to reside in the raphe (Mackay, 1955; Feng & Kean, 1955, Hassal & Reyle, 1955; Chen *et al.*, 1957; Persaud, 1968a and 1968b; Yardley & Godfrey, 1967; Posner, 1967 and Brooks & Audretsch, 1970).

Materials and Methods

Extraction: Partially dried (50–60° C for 24 hrs.) powdered aril and kernel, respectively, were separately extracted with light petroleum (40–60°) in a Soxhlet. The extracts were concentrated to dryness under reduced pressure and desiccated in an oven (103°C) to produce a clear golden yellow oil (from the aril) and a pale yellow fat (from the kernel), on cooling to room temperature (29°C) (Table 3).

Fatty acid preparation: The oil and fat were separately refluxed (1hr) on a water bath with ethanolic KOH. The non-saponified matter was extracted in each case, with diethyl ether, and after adjusting the aqueous solution to a pH of 4.0 with 1N HCl, the liberated fatty acids were extracted with diethyl ether. The ether was distilled off, using a water bath, to obtain the fatty acids (fractions 1a and 1b).

Esterification: The methyl esters of the fatty acids were synthesized by refluxing the fatty acids (2 hrs) on a water bath in conc. H_2SO_4 (specific gravity, 1.84) in dry methanol. The esters were precipitated by the addition of water and extracted with ether. After washing the ethereal extract successively with water, dilute sodium carbonate solution and again with water, it was finally dried over anhydrous sodium sulphate. The ether was distilled off, on a water bath, to obtain the methyl esters (fractions 2a and 2b).

Chromatography: TLC was done on silica gel G plates (250u) impregnated with the following:— (*i*) saturated solution of silver nitrate in 95% methanol (solvent system:—hexane: diethyl ether (90:10); (*ii*) 5% w/v liquid paraffin (wt/ml, 0.88) in petroleum ether (60–80°) (solvent

system:— 90% v/v glacial acetic acid in water) and (*iii*) 5% w/v n-undecane in petroleum ether (60–80°) (solvent system:— glacial acetic acid:acetonitrile (1:1), 70% saturated with n-undecane).

GLC of the methyl esters, with 2.5% SE-30 on Chromosorb G (80–100 mesh), was by the use of a Perkin Elmer F 11 gas chromatograph (glass column—1 metre x 0.3 cm), fitted with a hydrogen flame ionization detector and a Hitachi 159 (0–2.5 mV) potentiometric recorder, at an oven temperature of 160°C, the carrier gas and column pressure being nitrogen and 20 psi, respectively.

For the GLC-mass spectroscopy,* the stationary phase used was 10.0% OV-101, and the flow rate of the carrier gas was 60 mls/min., at an oven temperature of 220°C, the glass coloumn being 5 ft x $\frac{1}{4}$ in. The mass spectra were determined on A.E.I., MS. 902 high resolution (1,000) mass spectrometer, the interphase and source temperature being 215° and 200°C, respectively.

The fatty mixtures examined were (1) the fatty acid mixtures obtained from the aril oil—designated as FAA; and those obtained from the kernel fat—designated as FAK (fractions 1a and 1b, respectively); and (2) the fatty acid methyl ester mixtures obtained from FAA—designated as BS-A; and those obtained from FAK —designated as BS-K (fractions 2a and 2b, respectively).

Discussion of Results

FAA (fraction 1a)

TLC (Fig. 2) indicated that this fraction consisted of: palmitic (hRf: I, 55.9; II, 42.5; III, 57.6), oleic (hRf: I, 56.7; II, 56.5; III, 56.2) and stearic (hRf: I, 40.1; II, 38.2; III, 45.3) acids.

FAK (fraction 1b)

TLC (Fig. 2) showed that this fraction was composed of: palmitic, oleic, stearic, eicos-11-enoic (hRf: I, 31.1; II, 29.2; III, 44.1) and arachidic (hRf: I, 20.2; II, 18.0; III, 34.1) acids.

BS-A (fraction 2a)

TLC (Fig. 3) and GLC (Figs. 4a and 5a) indicated the composition of BS-A to be methyl palmitate (hRf: I, 41.3; II, 35.2; III, 45.6 and Rt: SE-30, 5.0; OV-101, 14.2), methyl oleate (hRf: I, 53.1; II, 39.1; III, 49.7 and Rt: SE-30, 10.6; OV-101, 23.8) and methyl stearate (hRf: I, 34.2; II, 23.5; III, 31.3 and Rt: SE-30, 12.3; OV-101, 25.9). It was confirmed by the mass spectrum data (Fig. 6):—

Methyl palmitate:

M^+ m/e 270, fragment ions at m/e 255, 241, 239, 227, 213, 199, 185, 171, 157, 143, 129, 115, 111, 101, 97, 87, 83, 75, 74, 69, 57, 55, 43, 29 and 15, the ions, $CH_3O.CO.(CH_2)_n^+$, being responsible for the peaks at m/e 255, 241, 227, 213, 199, 185, 171, 157, 143, 129, 115, 101 and 87.

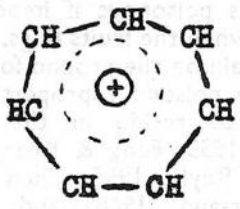
The fragmentation ion at m/e 239 corresponds to $(CH_3(CH_2)_{14}.CO)^+$ as a result of the loss of $-OCH_3$, and at m/e 74, the intense peak is due to $(CH_3O.C(OH)=CH_2)^+$, obtained as a result of the McLafferty rearrangement.

Methyl oleate:

M^+ m/e 296, fragment ions at m/e 265, 264, 248, 222, 207, 180, 166, 152, 151, 137, 123, 111, 110, 101, 97, 87, 83, 74, 69, 55, 43, 41, 29 and 15, the peak at m/e 265 being due to $(CH_3(CH_2)_7.CH=CH(CH_2)_7—CO)^+$, as a result of the loss of $-OCH_3$.

At m/e 264, the peak, corresponding to the loss of CH_3OH from the molecular ion, is a characteristic feature in mono-unsaturated fatty acid esters (Chapman 1965).

The peak at m/e 91 arises probably from the presence of the tropylium ion $(C_7H_7)^+$, due to rearrangement and cyclization (Rylander *et al.*, 1957).



The peak due to $(CH_3O.C(OH)=CH_2)^+$, obtained by the McLafferty rearrangement, occurs at m/e 74.

Methyl stearate:

M^+ m/e 298, fragment ions at m/e 283, 269, 267, 255, 241, 227, 213, 207, 199, 185, 171, 157, 143, 129, 115, 111, 101, 97, 87, 83, 74, 69, 57, 55, 43, 29 and 15, the ions, $(CH_3O.CO.(CH_2)_n^+$ being responsible for the peaks at m/e 283, 269, 255, 241, 227, 213, 199, 185, 171, 157, 143, 129, 115, 101, and 87.

The peak at m/e 267 is due to $(CH_3.(CH_2)_{16}.CO)^+$ as a result of the loss of $-OCH_3$, and the intense peak at m/e 74 is due to $(CH_3C.O(OH)=CH_2)^+$, obtained by the McLafferty rearrangement.

BS-K (fraction 2b)

TLC (Fig. 3) and GLC (Figs. 4b and 5b) indicated that this fraction was composed of methyl palmitate, methyl oleate, methyl stearate, methyl eicos-11-enoate (hRf: I, 47.0; II, 24.0; III, 33.0 and Rt: SE-30, 25.5; OV-101, 43.2) and methyl arachidate (hRf: I, 28.2; II, 12.2; III, 22.4 and Rt: SE-30, 29.9; OV-101, 46.9). It was confirmed by the mass spectrum data (Fig. 6):—

Methyl eicos-11-enoate:

M^+ m/e 324, fragment ions at m/e 293, 292, 250, 235, 221, 207, 193, 179, 164, 151, 139, 138, 123, 111, 110, 101, 97, 87, 83, 74, 69, 57, 55, 43, 41, 29 and 15, $(CH_3.(CH_2)_7.CH=CH.(CH_2)_9.CO)^+$ being responsible for the peak at m/e 293, obtained as a result of the loss of $-OCH_3$.

The peak at m/e 292, corresponding to the loss of CH_3OH from the molecular ion, is, as stated earlier, characteristic of mono-unsaturated fatty acid esters (Chapman, 1965).

The tropylium ion, as discussed earlier, is responsible for the peak at m/e 91, due to rearrangement and cyclization (Rylander *et al.*, 1957).

$(CH_3O.C(OH)=CH_2)^+$ obtained by the McLafferty rearrangement, is responsible for the peak at m/e 74.

Methyl arachidate:

M^+ m/e 326, fragment ions at m/e 297, 295, 283, 269, 255, 241, 227, 199, 185, 171, 156, 143, 129, 111, 101, 97, 87, 83, 75, 74, 69, 57, 55, 43, 29 and 15, $(CH_3O.CO.(CH_2)_n^+$ being responsible for the peaks at m/e 297, 283, 269, 255, 241, 227, 213, 199, 185, 171, 157, 143, 129, 115, 101, and 87, the peak at m/e 213, not being prominent.

At m/e 295, the peak is due to the presence of $(CH_3(CH_2)_{18}.CO)^+$, as a result of the loss of $-OCH_3$.

The base peak at m/e 75 is due to $(CH_3O.C(OH)=CH_2)^+$, which is obtained as a result of the McLafferty rearrangement.

Conclusion

Plant samples of *Blighia sapida* König from three different regions of Ghana (Greater Accra, Ashanti and Northern) were examined with a

* By the courtesy of the School of Pharmacy, University of London.

TABLE I

CHEMICAL PROPERTIES OF THE SEED FAT

Determinations	ARIL			KERNEL		
	Coastal Belt	*Forest Belt*	*Wet-Savanna Belt*	*Coastal Belt*	*Forest Belt*	*Wet-Savanna Belt*
Ash (% w/w)	0.3112	0.3098	0.3001	0.0110	0.0095	0.0121
Saponification Value	150.4	149.2	150.2	128.3	128.7	128.0
Unsaponifiable Matter (% w/w)	0.4626	0.4622	0.4640	0.5220	0.5235	0.5229
Acid Value	2.588	2.600	2.584	2.634	2.645	2.639
Free Fatty Acids	1.300	1.312	1.298	1.323	1.329	1.326
Iodine Value (wijs)	50.62	50.65	50.60	57.42	57.60	57.48
Ester Value	147.81	146.60	147.62	125.67	126.06	125.36
Phosphorus Content (% w/w) ...	5.56	5.57	5.57	8.20	8.21	8.22

TABLE II

PHYSICAL PROPERTIES OF THE SEED FAT

Determinations	ARIL			KERNEL		
	Coastal Belt	*Forest Belt*	*Wet-Savanna-Belt*	*Coastal Belt*	*Forest Belt*	*Wet-Savanna-Belt*
Specific Gravity	0.8802	0.8802	0.8802	0.8987	0.8987	0.8987
Apparent Density (gm/ml) ...	0.8758	0.8758	0.8758	0.8939	0.8939	0.8939
Refractive Index	1.4577[a]	1.4577[a]	1.4578[a]	1.4601[b]	1.4601[b]	1.4601[b]
Melting (Slip) Point (°C) ...	19.5–20.0	19.5–20.0	19.0–19.5	29.5–30.0	29.5–30.0	29.5–30.0
Titre (°C)	43.25	43.30	43.30	53.30	53.30	53.33
Volatile Matter [c] (% w/w) ...	1.05	1.08	1.09	0.79	0.78	0.80

a—at 29°C
b—at 30°C
c—at 105°C

Table III Seed Fat Extraction

Plant Material	*Region*	*Yield (% w/w)*
Seed Fat	Coastal Belt	21.6
	Forest Belt	21.5
	Wet-savanna Belt	21.6
Aril	Coastal Belt	52.9
	Forest Belt	52.8
	Wet-savanna Belt	53.0
Kernel	Coastal Belt	12.5
	Forest Belt	12.4
	Wet-savanna Belt	12.7

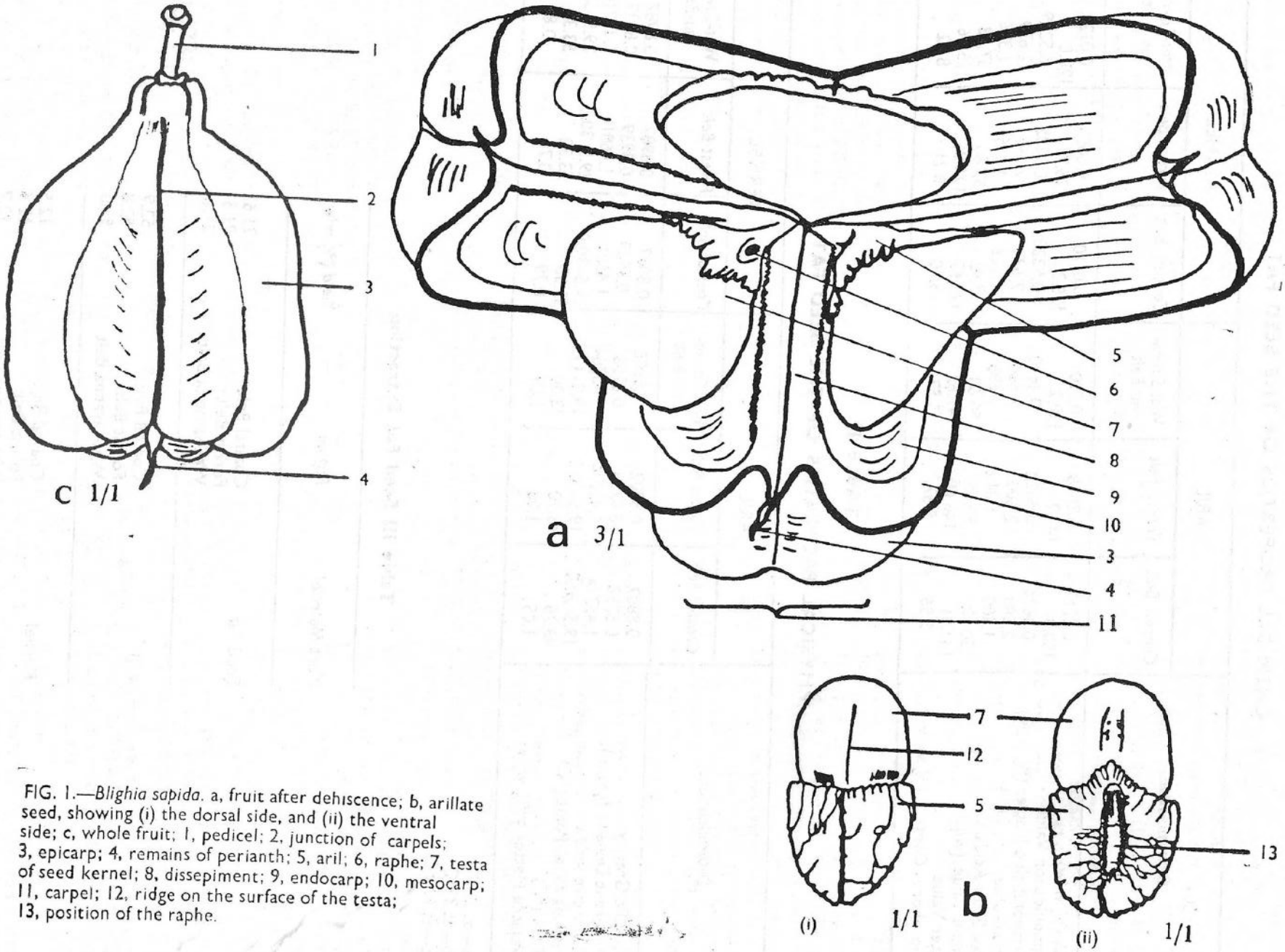


FIG. 1.—*Blighia sapida*. a, fruit after dehiscence; b, arillate seed, showing (*i*) the dorsal side, and (*ii*) the ventral side; c, whole fruit; 1, pedicel; 2, junction of carpels; 3, epicarp; 4, remains of perianth; 5, aril; 6, raphe; 7, testa of seed kernel; 8, dissepiment; 9, endocarp; 10, mesocarp; 11, carpel; 12, ridge on the surface of the testa; 13, position of the raphe.

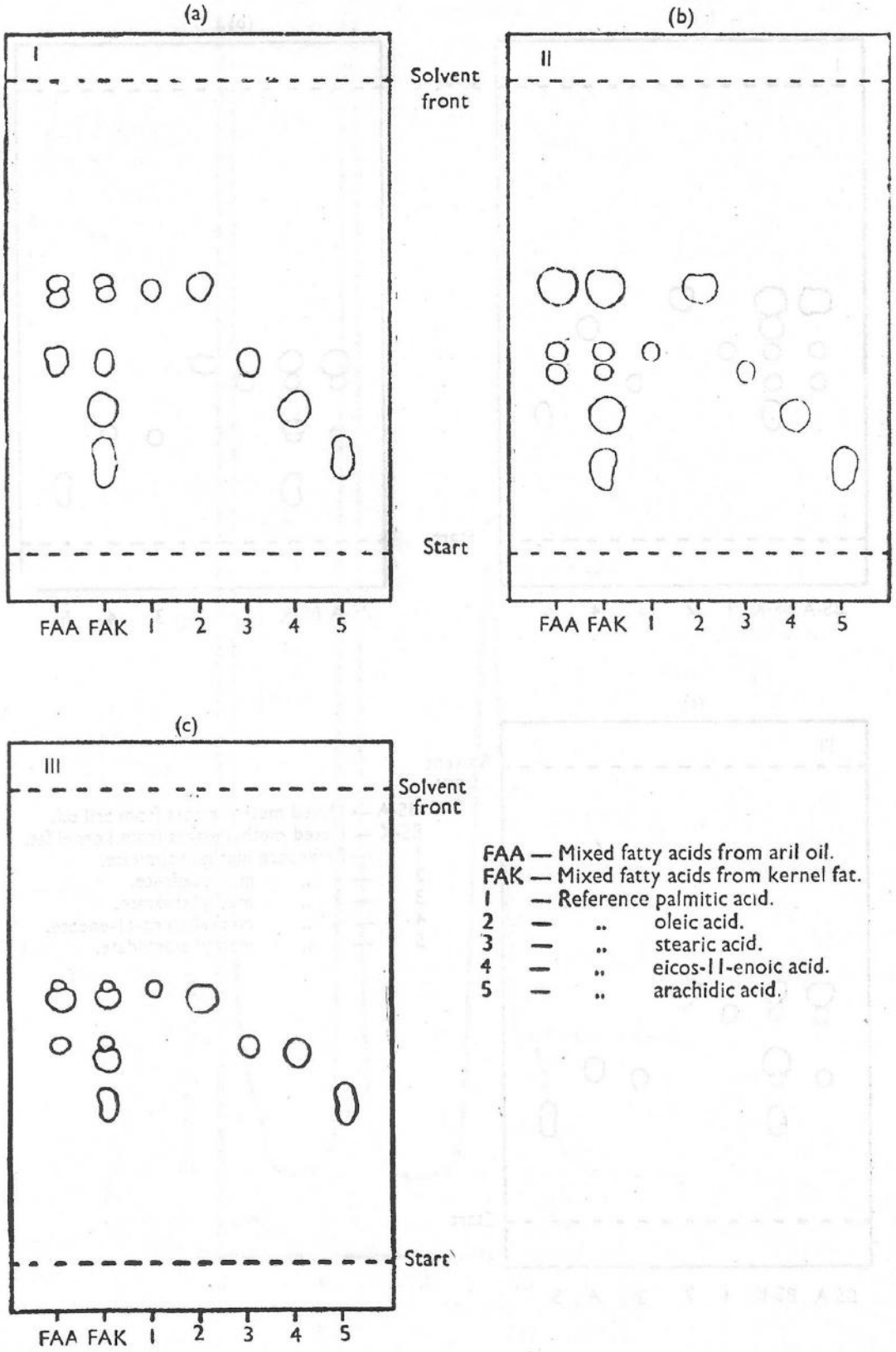


FIG. 2. - TLC of the mixed fatty acids from the seed fat of *Blighia sapida*.

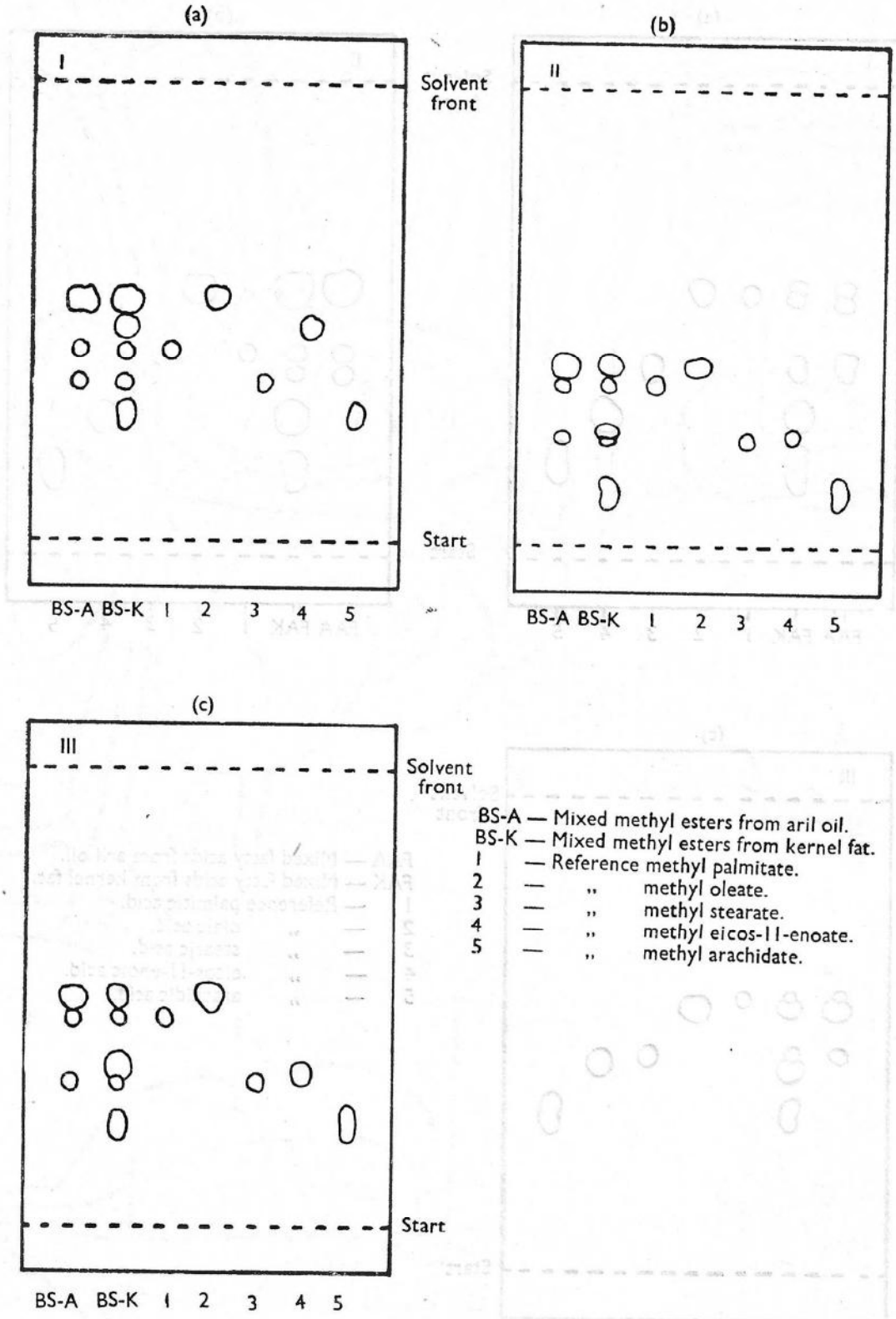


FIG. 3. - TLC of the mixed fatty acid methyl esters from the seed fat of *Blighia sapida*.

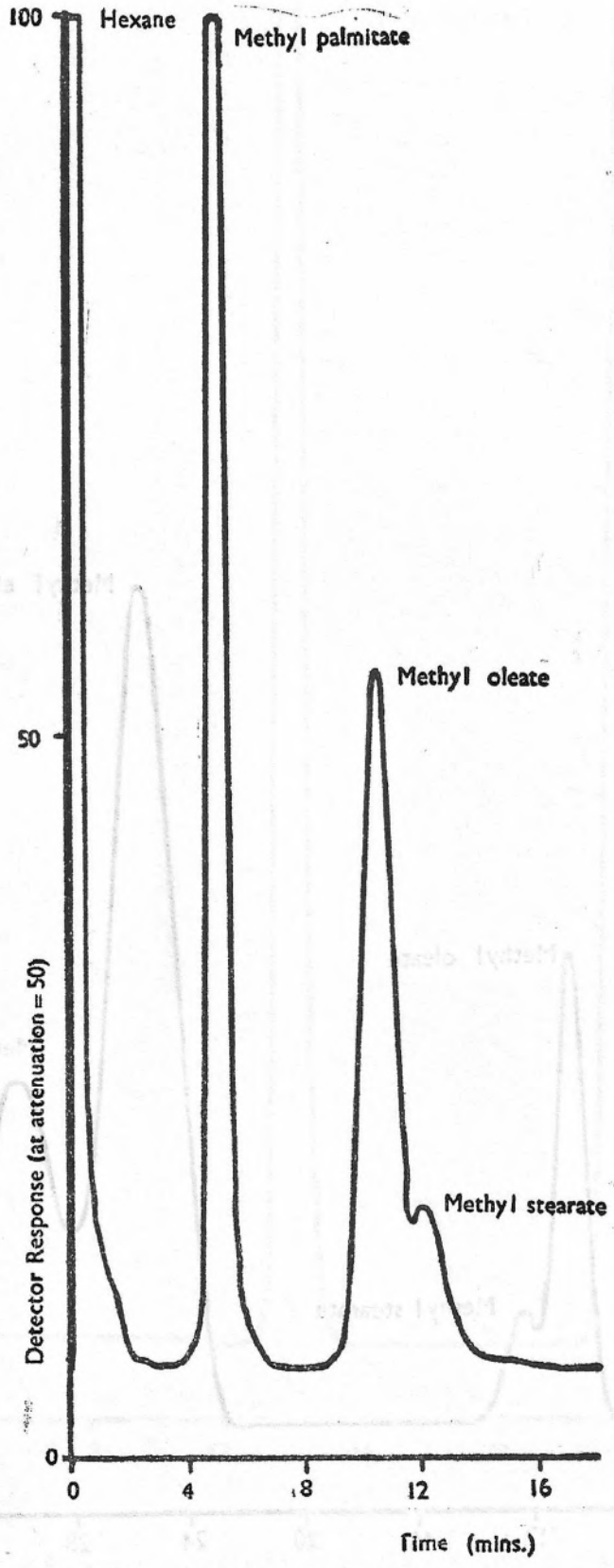


FIG. 4a.—GLC of fatty acid methyl esters from the aril oil of *Blighia sapida* on 2.5% SE-30.

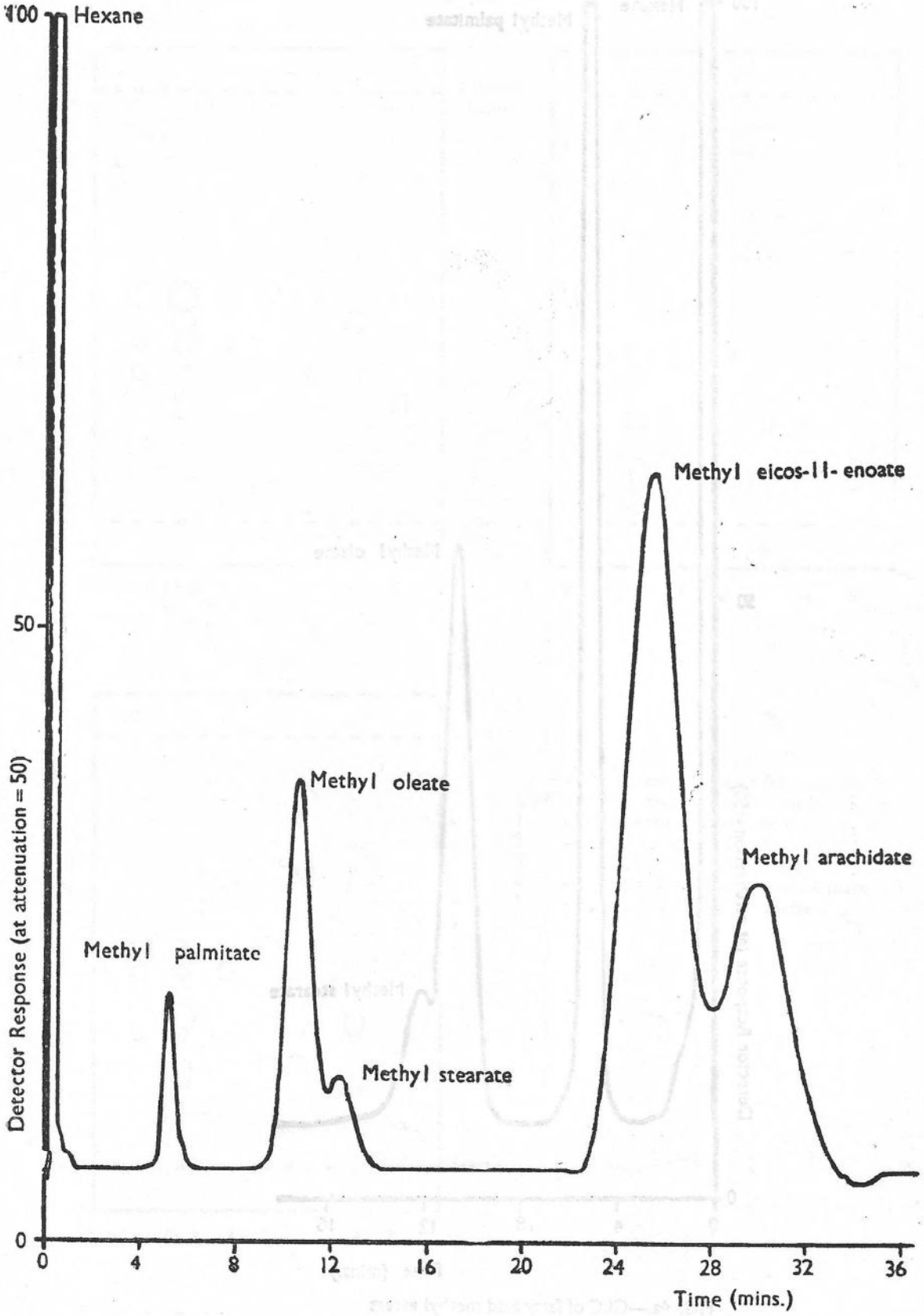


FIG. 4b—GLC of fatty acid methyl esters from the kernel fat of *Blighia sapida*, on 2.5% SE-30.

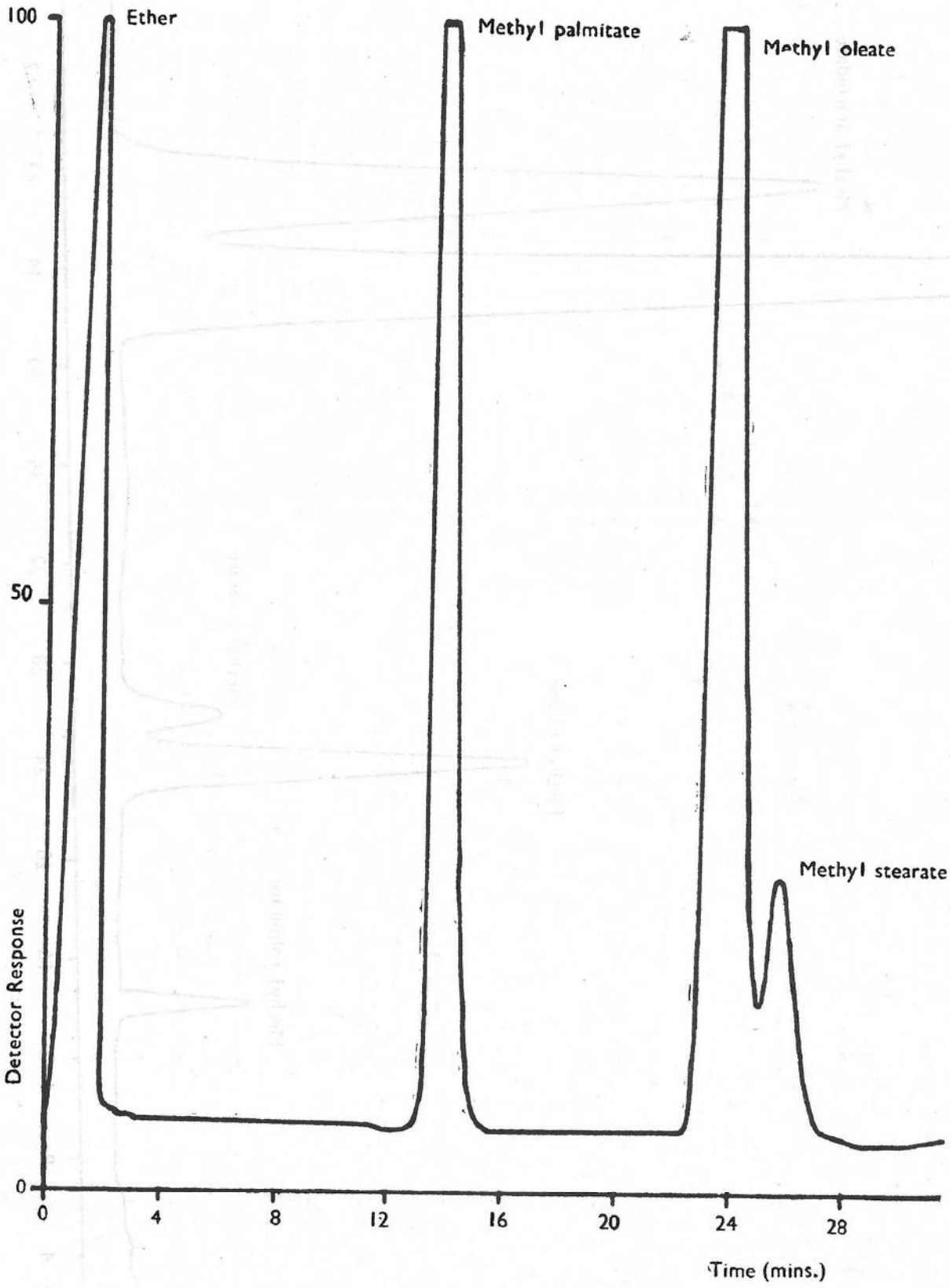


FIG. 5a.—GLC of fatty acid methyl esters from the aril oil of *Blighia sapida*, on 10.0% OV-101

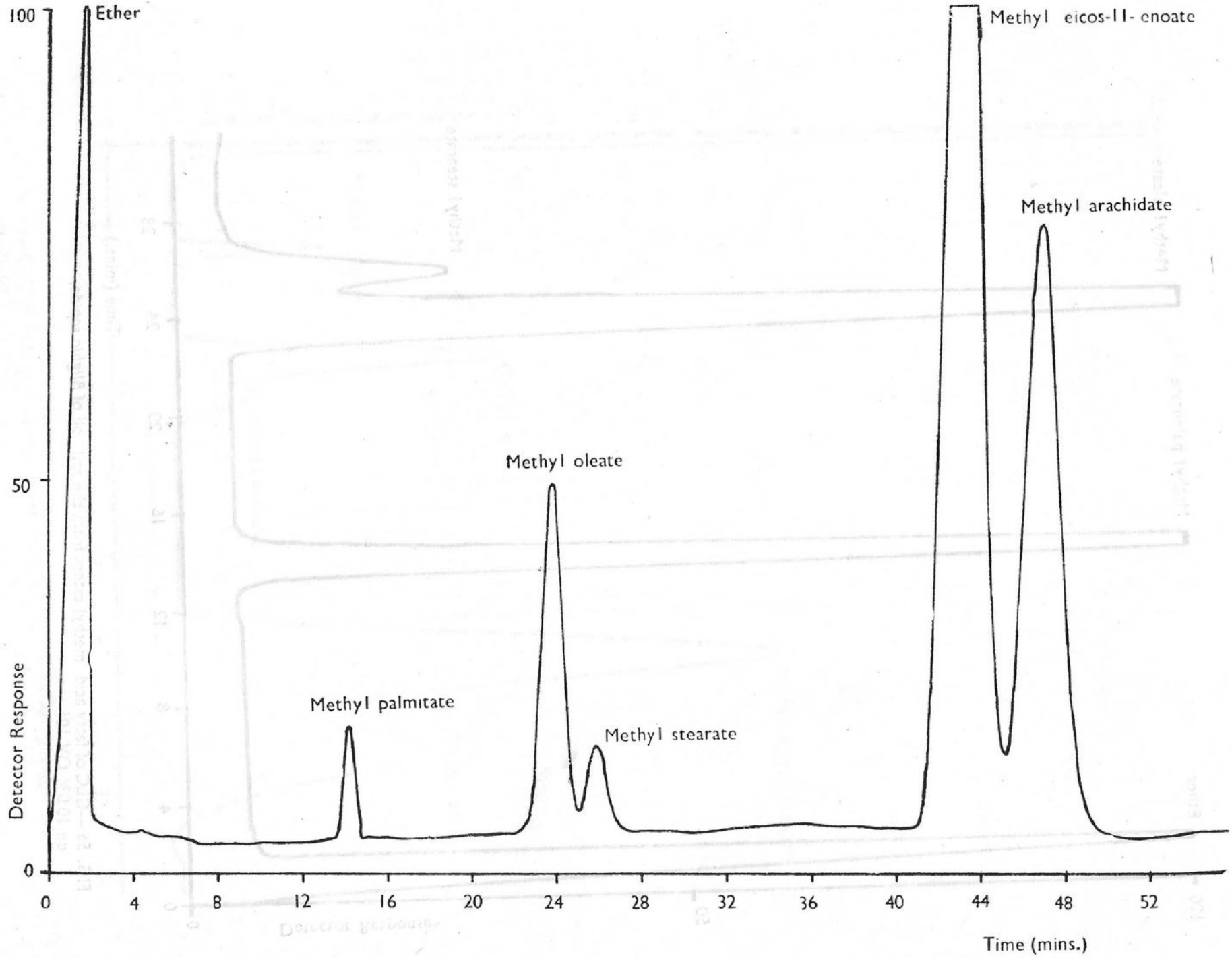


FIG. 5b.—GLC of fatty acid methyl esters from the kernel fat of *Blighia*

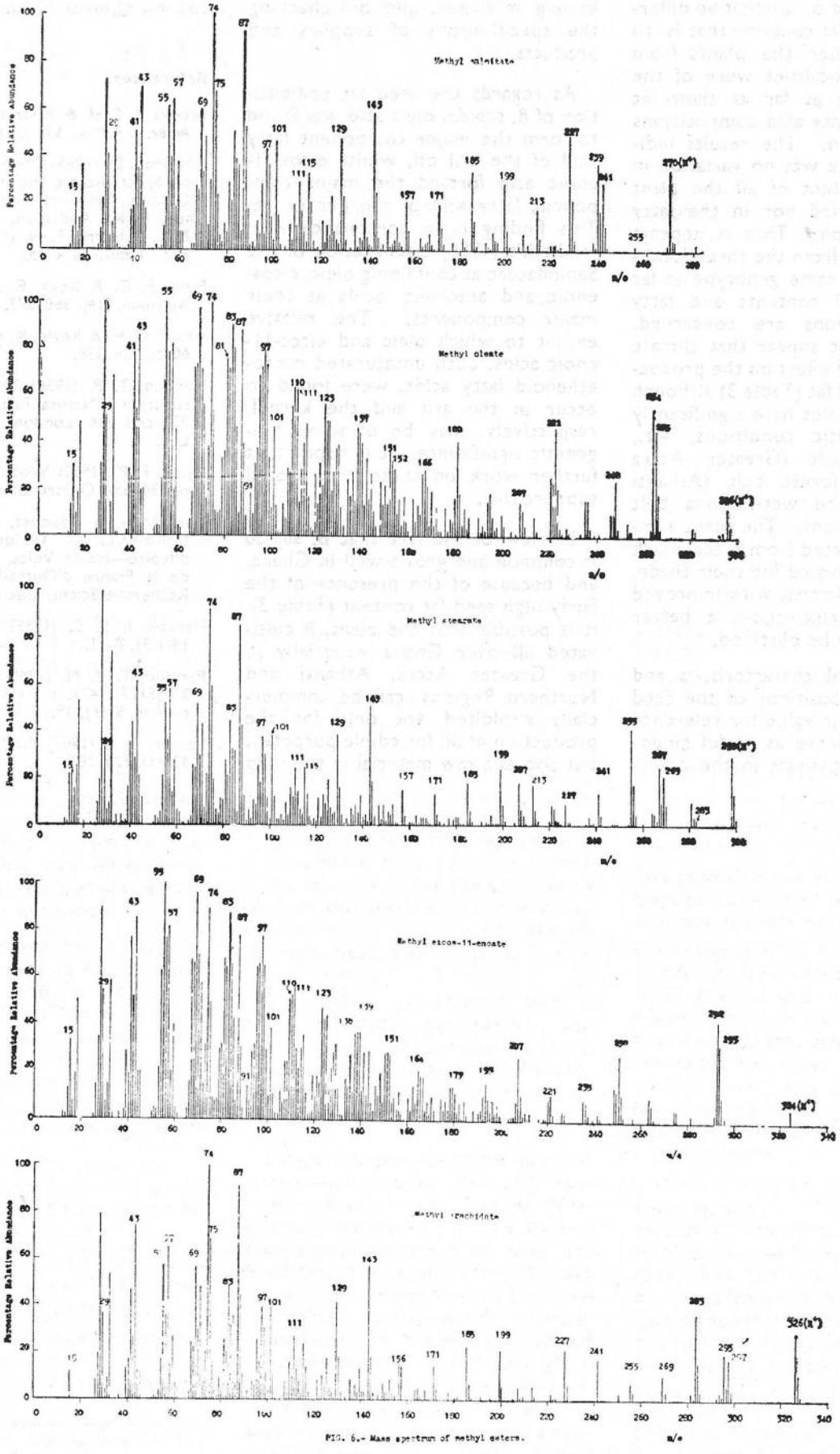


FIG. 6.- Mass spectrum of methyl esters.

view to finding out if there were any quantitative and/or qualitative differences in their fat content; that is, to find out whether the plants from the different localities were of the same genotype as far as their fat contents and fatty acid compositions were concerned. The results indicated that there was no variation in the fat/oil content of all the plant samples examined nor in the fatty acid composition. Thus it appears that the plants from the three localities are of the same genotype as far as their fat/oil contents and fatty acid compositions are concerned. Also, it did not appear that climate had any marked effect on the production of the seed fat (Table 3) although the three localities have significantly different climatic conditions, viz., the coastal belt (Greater Accra Region), the forest belt (Ashanti Region) and the wet-savanna belt (Northern Region). The plant samples were collected from trees which have been cultivated for their shade, and it is possible that with improved conditions of cultivation, a better yield of fat may be obtained.

The analytical characteristics and fatty acid compositions of the seed fat, besides their value for reference purposes will serve as useful guides to oil and fat analysts in the determination of the components of unknown mixtures, and or checking the specifications of supplies and products.

As regards the seed fat composition of *B. sapida*, oleic acid was found to form the major component fatty acid of the aril oil, whilst eicos-11-enoic acid formed the major component fatty acid of the kernel fat. This finding is in consonance with Hilditch's (1956) classification of the Sapindaceae as containing oleic, eicosenoic and arachidic acids as their major components. The relative extent to which oleic and eicos-11-enoic acids, both unsaturated monoethenoid fatty acids, were found to occur in the aril and the kernel, respectively, may be of some biogenetic significance. It is hoped that further work on these lines would support this.

In view of the fact that *B. sapida* is common and grows well in Ghana, and because of the presence of the fairly high seed fat content (Table 3), it is possible that the plant, if cultivated all over Ghana, especially in the Greater Accra, Ashanti and Northern Regions, can be commercially exploited not only for the production of oil for edible purposes, but also as a raw material in the soap and allied industries and in the production of eicos-11-enoic acid.

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EXCRETION OF DRUGS IN HUMAN MILK

By Miss Bright E. Takyi, B. Pharm., MPSG., Princess Marie Louise Hospital, Accra

Introduction

The excretion of drugs in human milk is not an easy subject for study, since it is difficult to get a nursing mother to lend herself willingly for such experimental observations. Available information on this subject has been sought by looking through the medical literature and through information received from the different pharmaceutical manufacturing firms concerning their specific products. There has been a general lack of information, but some of the firms have been able to supply information on some of their products.

Nearly all drugs taken by the nursing mother will be found in her milk. In some instances the amount excreted is considerable and may have adverse effects on the infant, eg. phenobarbitone. In other cases minute or negligible quantities are found in the milk and have very little or no effect on the infant, eg. chlordiazepoxide.

The drugs which are likely to be taken by the nursing mother can be grouped as follows:—

(*a*) Drugs about which no information is available on their excretion in human milk.

(*b*) Drugs which are excreted, but the concentrations of which in milk are not known or are negligible.

(*c*) Drugs which are excreted in minute amounts, the concentrations of which are known.

(*d*) Drugs which are excreted in known significant concentrations.

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Drugs about which no information is available on their excretion in human milk

Antimicrobial agents including griseofulvin (Fulcin Forte), sodium cephalothin (Keflin) cephalexin monohydrate (Keflex), chloroquine and erythromycin have not been traced in human milk. It is not possible to confirm the absence of excretion of erythromycin, and as it diffuses through most bodily tissues it may appear in milk.

Diuretics — frusemide[9] (Lasix), cyclopenthiazide (Navidrex) and spironolactone (Aldactone) have not been traced in human milk. Bendrofluazide[5] also has not been traced, though it has been found to suppress lactation.

Drugs acting on the central nervous system—pentazocine (Fortral), ibuprofen (Brufen), amitriptyline (Tryptizole), imipramine (Tofranil) and tranylcypromine (Parnate) have not been traced in human milk. Minute traces of tranylcypromine have however been found in dog's milk. Phenylbutazone has not been traced in maternal milk. It has been given together with hydroxyphenylbutazone (Tanderil) to mothers for the treatment of superficial thrombophlebitis, but their infants showed no adverse effects.

Cardiac reactants — methyldopa (Aldomet) has been traced in cow's milk but not in human milk. Propranolol (Inderal) has not been traced.

Other drugs — thyroid, corticosteroids[3], tolbutamide (Rastinon) orciprenaline (Alupent) and propantheline could not be traced in human milk. However, litters of lactating rats receiving 20 mg of cortisone daily were retarded and some died.

Drugs which are excreted but the concentrations of which in milk are not known or are negligible

Antimicrobial agents — the amount of oxacillin[3], excreted in human milk is very small and not measurable. Rolitetracycline[3], is excreted in milk, but insignificant amounts are received by the infant. When nalidixic acid (Negram) was administered to lactating women no significant quantities of it or of its metabolites were excreted in milk.

Drugs acting on the central nervous system — alcohol[2] taken in moderate amounts, and chloral hydrate, are not excreted in amounts harmful to the infant. There is an assurance from unpublished literature that although the benzodiazepines, chlordiazepoxide (Librium) diazepam (Valium) and nitrazepam (Mogadon) are excreted in milk, the amounts excreted have no effect on the breast-fed baby. Phenytoin[7] has been given to epileptic mothers and its concentration determined in their milk. No

apparent deleterious reactions have been observed in breast-fed babies (but see case recorded under barbiturates). Indomethacin (Indocid) and mefenamic acid[6] (Ponstan) have been traced in negligible amounts which had no effects on the baby.

Hyoscine and atropine are excreted in insignificant amounts. Nicotine[1] reduces the milk yield in nursing mothers who smoke. It is excreted in small amounts in milk and can be demonstrated there one to two hours after smoking, but the main excretion occurs four to five hours later. Babies nursed by smoking mothers are apparently unaffected by the quantity of nicotine in the milk.

Purgatives—most of the commonly used domestic purgatives are excreted in breast milk and are thought to lead to increased bowel activity in infants. However a trial with senna[3] administration showed no difference between the stools of infants of treated or control mothers. Cascara[2], rhubarb, aloes and phenolphthalein are excreted in milk, but the amounts are too small to affect the baby.

Other drugs—information about the excretion of folic acid and vitamin B-12 in milk appears to be uncertain, but these vitamins are probably only excreted in small amounts. Vitamin K[3] excretion occurs at a low level.

Antihistamines may be excreted in negligible amounts. Caffeine and guanethidine (Ismelin) are also excreted but in negligible quantities, and no hypotensive effect was observed in a child after the mother took guanethidine in theaepeutic doses.

Drugs which are excreted in minute amounts, the concentrations of which are known.

There has not been much information about drugs in this group. Only a little information was obtained on metronidazole, chlorpromazine, sodium fusidate, and ampicillin.

A dose of 200 mg metronidazole[8] was given to nursing mothers and milk samples taken at intervals. Concentrations of metronidazole in breast milk were comparable with those in the serum. The maximum amount of metronidazole ingested by an infant was 0.41 mg. None of the babies developed oral or gastrointestinal upset.

Chlorpromazine[4] 1200 mg was given to a nursing mother and milk samples were taken at intervals and the concentration of chlorpromazine determined. It was found that the total amount of chlorpromazine ingested by the infant was 3 mcg per kg. The paediatric dose of chlorpromazine is 250 mcg per kg every four to six hours; therefore the infant ingested an insignificant amount.

Sodium fusidate 1000 mg was given orally to normal lactating women. This dose produced a concentration of 0.2 mcg per ml in their milk (unpublished data). Since the dose of sodium fusidate is 20 to 30 mg per kg for infants, it can be seen that the quantity excreted is insignificant.

Ampicillin 500 mg was given orally to a nursing mother. After two hours the concentration in the milk sample taken was found to be 0.07 mcg per ml. The paediatric dose of ampicillin is 125 to 250 mg four times a day so the amount excreted as above is insignificant.

A woman suffering from recurrent depression was given 900 mg lithium carbonate daily during pregnancy and after delivery. The concentration in her milk one week after delivery was 0.3 mEq lithium per litre and the level in the child's serum was the same.

Drugs which are excreted in known significant concentrations

Iodides—as much as 27 per cent of a tracer dose of radioactive iodine[3] can be found in milk 24 hours after the mother has taken the drug. This could have a significant suppressive effect on the activity of the infants' thyroid.

Bromide[3] 2 mg to 8 mg per 100 ml. has been recovered in milk of mothers receiving 5 g daily. Ingestion of bromide may lead to rashes and drowsiness in the infant.

Thiouracil[3] is excreted into milk in a concentration higher than that in the blood or urine, after an oral dose of the drug. This may cause serious side-effects such as goitre or agranulocytosis in the infant. Carbimazole is also excreted in milk, so care must be taken when giving it to a nursing mother.

Antimicrobial agents — penicillin, novobiocin and streptomycin[3] are excreted in the mother's milk in quite large amounts. Following an injection of 1,000,000 units of penicillin to a nursing mother, the concentrating of penicillin in her milk was found to be 0.015 to 0.06 units per ml. Penicillin is therefore liable to cause sensitivity symptoms in the baby.

In the case of novobiocin,[3] an oral dose of 500 mg followed by 250 mg every six hours was given to some nursing mothers and milk samples were taken six to 30 hours later. The concentrations of novobiocin in milk were found to range from 0.36 to 0.54 mg per 100 ml.

A trial with tetracycline hydrochloride[3] showed that an average of 70 per cent of the concentration in the serum was found in the milk; but the concentration in the infant's serum was negligible. Tetracycline may however cause discolouration of the infant's teeth, and should be avoided during breast feeding.

The concentration of chloramphenicol[3] in milk has been found to be 50 per cent of that in the serum.

Sulphanilamide[3] and sulphapyridine in doses of 2 g and 3 g per day respectively produced concentrations in milk of 3 to 13 mg per 100ml. The levels in milk were approximately equal to those in the maternal serum. Sulphonamides may be responsible for certain rashes in the baby.

Isoniazid[3] appears in breast milk in approximately the same concentration as it does in the maternal serum.

Anticoagulants — anticoagulants[10] like phenindione and warfarin pass into the mother's milk and may produce a prothrombin deficiency in nursing infants. The concentration in milk was found to be appreciably higher than in serum. It is therefore advisable to give a breast-fed baby 1 mg of synthetic vitamin K daily while the mother is receiving an anticoagulant drug; or alternatively, and preferably, the baby should not be breast-fed during this period.

Vitamins — mothers with vitamin B_1 avitaminosis[3] produce milk toxic to the infants because a reduction in certain co-enzymes leads to the accumulation of the intermediary products of incomplete carbohydrate oxidation in the tissues and body fluids, including milk. These intermediary metabolites consist of lactic acid, acetoacetic acid, glycuronic acid, methylglyoxal and pyruvic acid

or sodium pyruvate. Of these methylglyoxal is toxic, and has caused deaths of babies who were breast-fed.

Miscellaneous

Diamorphine (heroin) in maternal narcotic addicts, the drugs especially diamorphine, are excreted in milk.

Barbiturates[3]. The amount of barbiturates excreted in breast milk does not normally affect the nursing infant. A case is recorded however of methaemoglobinaemia in an infant breast-fed by an epileptic mother taking 390 mg phenobarbitone and 400 mg phenytoin daily. Feeding by a donor led to recovery.

Lead acetate[3]. Application of lead acetate ointment to the breast led to ingestion of quantities of lead by the infant, sufficient to cause encephalitis.

Hexachlorobenzene[3]. The ingestion by nursing mothers of seed treated with hexachlorobenzene led to severe skin disease and death in many breast-fed children. It was assumed that hexachlorobenzene or one of its metabolites was excreted in the mother's milk.

Ergot Alkaloids[3]. Ergot alkaloids have been reported to be excreted in the milk of nursing mothers. The infant had symptoms of ergotism, such as vomitting, diarrhoea, weak pulse and unstable blood pressure. Large amounts of ergot can cause convulsions. Since many of the preparations intended for the treatment of migraine contain ergot alkaloids, care must be taken when giving them to nursing mothers.

Fluorides[2]. Small quantities have been found in milk. As excess of fluoride affects bone and tooth enamel, care should be taken when giving it to nursing mothers.

Carotene[2]. Consumption of several carrots daily caused carotenoderma (carotenaemia) in a nursing mother and her suckling of six months. The yellowness of the infant's skin disappeared when the breast feeding was stopped.

Allergens[3]: Protein substances sometimes pass into the milk and may cause allergic responses in a sensitive child. Lactating mothers should therefore avoid over-indulgence of any particular food, especially eggs, milk, cereals, nuts and fish.

Staphylococci & antibodies[3]. These may be ingested by an infant, but the former are usually derived by external contamination from cracked nipples.

Pyrimethamine[3] *(Daraprim)*: Can be detected by chemical methods in the milk of nursing mothers, with their peak concentration at six hours after ingestion of the drug.

Discussion

Knowledge about the excretion of drugs in human milk is limited and mostly inconclusive. It will be seen from this review that there is no information at all on many drugs used in therapeutics and information about others, even when obtained from the manufacturing firms, is not detailed. Thus the general conclusion that can be drawn is that nearly all drugs taken by the nursing mother are excreted in her milk; but that the amounts excreted vary for different compounds. In view of the increased use of a wide variety of medication, the risk to the infant from drugs administered to the mother may be considerable; but that is not a reason for discouraging breast feeding. Rather, this possibility should stimulate an interest in the subject so that a more thorough study of drugs presently available, as well as new products as they become available, can be made.

Acknowlegement is made of information provided by the following pharmaceutical companies concerning the substances named: Abbott Laboratories (erythromycin), Beecham Research Laboratories (ampicillin), CIBA Laboratories (guanethidine), Leo Laboratories (sodium fusidate), Merck, Sharp and Dohme (methyldopa, indomethacin, amitriptyline), Roche Products (chlordiazepoxide, diazepam, nitrazepam), Winthrop Laboratories (nalidixic acid, pentazocine).

This paper was prepared by the author while gaining experience at St. George's Hospital, London who would like to acknowledge the help given by R. W. Horne and G. Raine.

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Useful information may also be found in Practitioner (1970), **204**, 14-19; Transmission of drugs by the placenta and the breasts.

SOCIETY NEWS

1. The Proposed Pharmacy Instrument 1975.

Consequent to the deliberations of the 1974 Annual General Meeting held at Cape Coast, a Committee headed by Mr K.A. Ohene-Manu, was appointed by Council to prepare a Draft on the above subject for submission to the Commissioner for Health.

On the 9th of January, 1975, the final Draft was presented to the Commissioner by a delegation made up of the following members:—

Prof. A.N. Tackie (leader),
Mr K.A. Ohene-Manu
Mr D. Anim-Addo and
Mr R.Q. Lamptey.

As a follow-up, a second interview was held with the Commissioner on the 7th of March by another delegation composed of Capt. I. Buabeng, Messrs K.A. Ohene-Manu, D. Anim-Addo and Ago-Simmonds.

On a third visit to the Commissioner he referred the delegation to his Technical Adviser, the Chief Pharmacist. The delegation is yet to meet the Chief Pharmacist for discussion.

2. 33rd Ghana Pharmaceutical Conference and Exhibition

This year's Conference and Exhibition will take place at the State House from 28th to 30th August. The Conference will commemorate the 40th Anniversary of the Society. The 40th milestone in the history of the Society is of great significance to us all and we pray that as many members as possible will make it their duty to attend the Conference. The Theme of the Conference is "The Pharmaceutical Industry and the National Economy."

Conference Fee: ₵10.00 per every member.

Dinner/Dance Fee: ₵15.00 per single and ₵25.00 per couple.

ALL DRINKS ARE FREE.

3. Congratulations to Dr A. N. Tackie.

We announce with pride that Dr A.N. Tackie, Fellow of the Society and formerly the Dean of the Faculty of Pharmacy, UST, Kumasi, and now the Executive Chairman of the Council for Scientific and Industrial Research, has been elected a Fellow of the Royal Institute of Chemistry. Congratulations, Dr Tackie.

4. The National Headquarters

The Society will as from 1st April, move its Headquarters to House No. 268, North Kaneshie Estate, Accra. A diagram giving the directions to the new offices appear elsewhere in the Journal.

5. Obituary

We regret to announce the death of the following members:—

1 K. Agyeman-Dua Regn. No. 335
2 S.K. Konadu Regn. No. 174
3 C.S.T. Caesar Regn. No. 113
4 J.A. Koranteng Regn. No. 167

May they rest in peace.

by Hon. General Secretary

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Salary: Negotiable, ~~but not less than ₵5,000 p.a. plus~~ fringe benefits.

Age: Not more than 45 years.

Applications should be addressed to:—

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Pharmaceutical Society of Ghana,
P.O. Box 2133,
Accra.

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