A. U. B.

APOTHECARY

VOL. 9
1954

The Apothecary

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1954

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by the faculty and students of the
School of Pharmacy of the
American University of Beirut, Beirut
Republic of Lebanon
JUNE 1954

This Number
of The Apothecary is respectfully
dedicated to

JOSEPH J. McDONALD B. S., M. S., M. D., MED. SC. D.

Dean of the Medical Faculty

JOSEPH J. McDONALD

Born in Seattle, Washington, February 25, 1913.

B. S. in Bacteriology 1935, University of Washington.

M. S. in Anatomy 1939, Northwestern University Medical School.

M. D. 1940, Northwestern University Medical School, Chicago, Ill.

Med. Sc. D. in Surgery 1946, Columbia University College of Physicians and Surgeons.

Internship at the Passavant Memorial Hospital in Chicago 1940-41.

Residency training in Surgery and Plastic Surgery at the Columbia-Presbyterian Medical Center in New York 1941-45.

Assistant Surgeon at the Presbyterian Hospital and Instructor in Surgery at Columbia University in New York 1945-46.

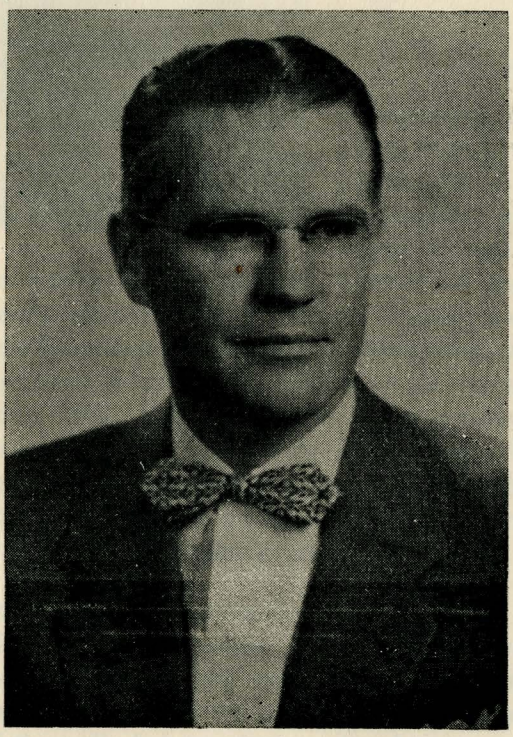
Associate Professor and Chairman of the Department of Surgery, American University of Beirut, 1946-48, Professor of Surgery 1948-51.

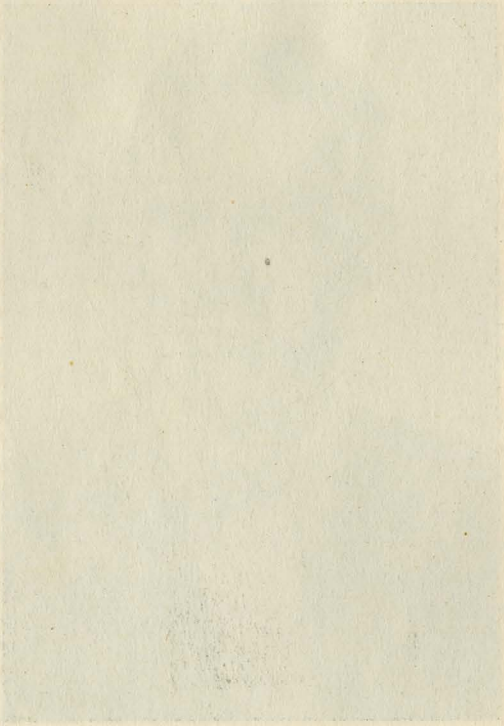
Professor of Surgery, Columbia University College of Physicians and Surgeons, 1951-53. Director of the Surgical Service Francis Delafield Hospital, New York, 1951-53. Chief of the Head-and-Neck Tumor Service, Presbyterian Hospital, New York, 1952-53.

Author: Correlative Neuroanatomy 1938-54, and a number of articles in scientific journals.

Producer: Of medical teaching films in the fields of anatomy, embryology and surgery

Present Position: Dean of the Medical Faculty 1953 —





FOREWORD

In the United States a pharmacy is usually known as a «drug store» and the pharmacist is a «druggist». Frequently a «drug store» seems to sell everything but drugs, from books and magazines to costume jewelry and picnic supplies. Nearly always there is a lunch counter and almost invariably a «soda fountain» or milk-bar. In small towns the «corner drug store» is very much a center of community life, particularly for teenage boys and girls. The druggist is a well-known and respected citizen whose part in the community life extends far beyond the normal functions of compounding prescriptions or selling pharmaceuticals. On occasion he may be called upon to give advice to the love-lorn or to render emergency first aid.

All this may seem to take the pharmacist far away from the professional dignity of his calling. It certainly renders him liable to service above and beyond the call of simple duty. The point I would make, however, is that it is his willingness to render service above and beyond the call of duty which makes him a personage who is so genuinely respected by his fellow men. A true professional man is far more concerned with his opportunities for service than with the narrower limits of his profession.

Graduates of the AUB School of Pharmacy may never become «druggists» in the broad American sense. But I hope that they will respond equally to the opportunities for service which may come their way or which they may create. Only thus will they be true representatives of a profession which is primarily honored for its unselfish devotion to the welfare of man.

Stephen B. L. Penrose
President

..... only by adhering to the moral and scientific principles ...

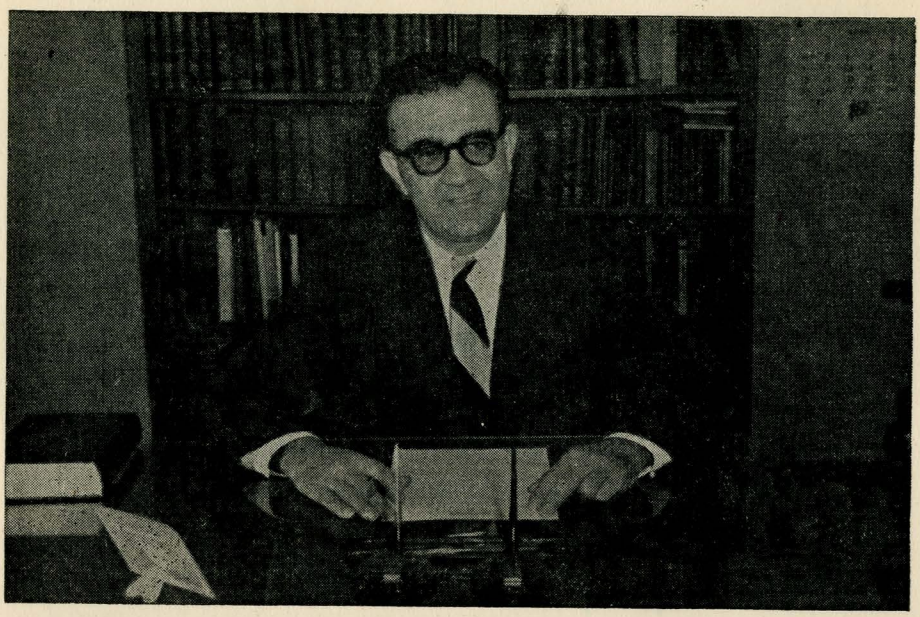
It is with great pleasure that I avail myself of this occasion to greet the graduating class of the School of Pharmacy, and to convey to them the greetings and sincere congratulations of the Medical Faculty.

You are not the first group of representatives to be sent out by this institution to the various parts of the world. Many were sent before you and many more will be sent after you. You are not going to be alone in this world but you will be a link between the past and the future. Your attitude and behavior will reflect not only upon you but upon your senior colleagues as well as upon those who will come after you.

You have spent time, effort and money to earn membership in this honorable profession. Let me draw your attention to the fact that the margin between performing your work as a profession or as a trade is very narrow, and the temptations may be very trying. There is a great need for you in your communities, and in the medical profession. Only by adhering to the moral and scientific principles impressed upon you by your professors can you keep the privilege of belonging to a respectable profession.

The various fields of knowledge have grown fast, and are continuing to expand so rapidly that it has become impossible for the graduates of any profession to learn all the facts about their specialty before graduation. Hence the modern trend in professional education is not to overburden the minds of students with factual knowledge but to train them in the scientific method, and to make them develop the habit of working regularly, and methodically. The primary duty of a good teacher is to guide and assist the student in his search for knowledge, and to straighten out what he may conceive wrongly. Unless the student acquires the habit of study and regular work and maintains this habit after graduation he will soon lose ground and find himself falling behind the caravan of his profession.

Joseph J. McDonald, M. D.
Dean of the Medical Faculty



CLASS OF 1954 !

On the happy occasion of your graduation I take great pleasure in extending to you on behalf of the personnel of the School of Pharmacy and myself our sincere congratulations wishing you all prosperity in the practice of the honourable profession you have chosen for your life career.

On the eve of leaving your Alma Mater, to enter the greater school of life, may I ask you to stop and ask yourselves: « What are the objectives of the formal pharmaceutical program of study you have just completed ? » If you search, you will find that those interested in planning your courses have many other objectives, in addition to that of directing your ability so that you can practice your art in accordance with the highest possible professional standards and the generally accepted codes of ethics. These objectives aim at developing in the individual the eagerness for learning from personal experience as well as from the experiences of others, the spirit of cooperation with his fellowmen, the ability to integrate and to disseminate knowledge, the capacity to enjoy the beauties ot life, loyalty to his Alma Mater, devotion to duty unselfishness in service, and other traits so essential to a citizen who is to serve his community.

We trust that during your association with us for four years, you have attained these objectives, and that they will be your guiding principles later in life. While abiding by these principles may fortune, happiness, and the mercy of God smile on you always.

Amin F. Haddad
Director, School of Pharmacy

A Pharmacist's Prayer

O Lord of life and health and hope,
Help me, I pray,
To worthily fulfill my trust
Throughout this day.

Bless Thou each dram I am to mix,
Each grain to weigh,
That they may banish dread disease,
Dear Lord, I pray.

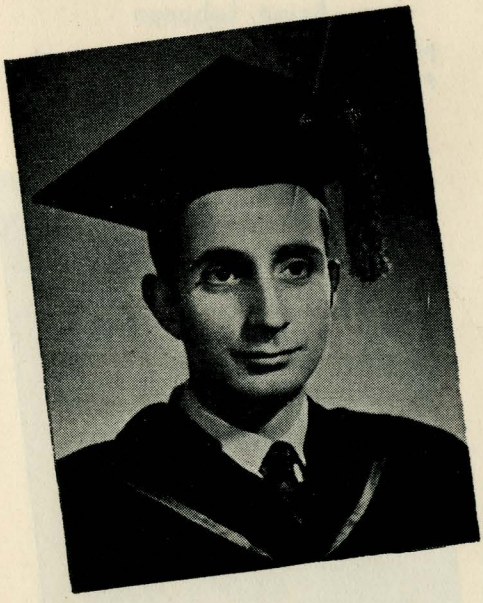
And bless each sufferer that comes
With pain or grief.
Oh ! Grant that I may use my art
To bring relief.

As health returns to those I serve,
Help me to be
A mighty force which draws them, Lord,
Closer to Thee.

Sister Barbara Marie, O. S. F.

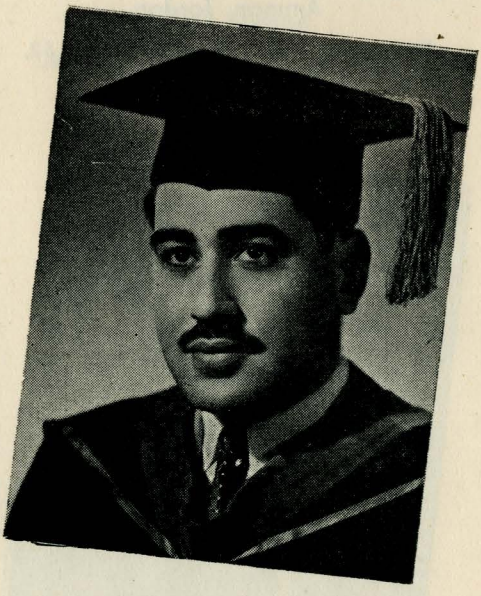
Graduating Class

Bachelors of Science in Pharmacy, B. Sc. (Pharm.).



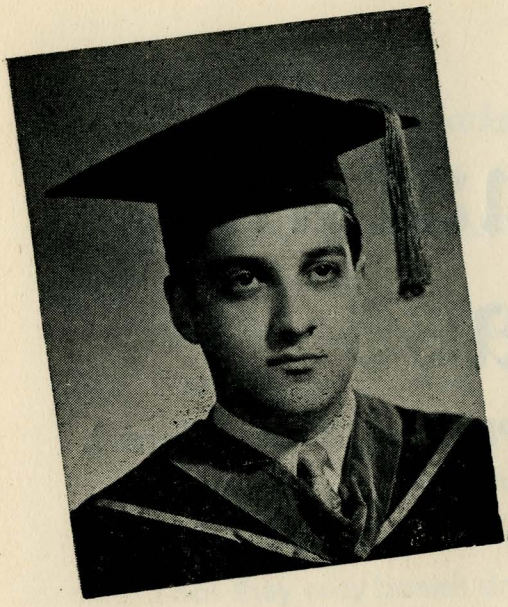
IBRAHIM FARID DURR
Beirut, Lebanon

CWL, Pharm. Representative 1951-52; Pharm. News, Sci. Editor 1951-52; Pharmaceut. Soc., Secretary 1952 - 53; *The Apothecary*, Board Secretary 1952-53.



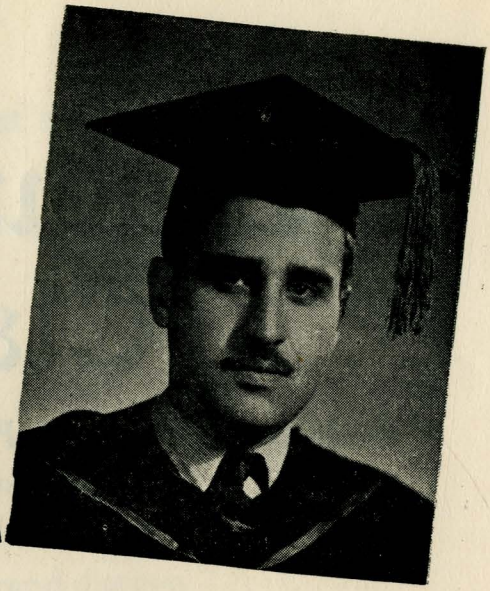
FADLU JALIL SHA'BAN
Amman, Jordan

The Apothecary, Assist. Advertising Manager 1950-51, Advertising Manager 1951 - 54; Pharmaceut. Soc., 1st Vice President 1953 - 54 (resigned), President 1953 - 54.



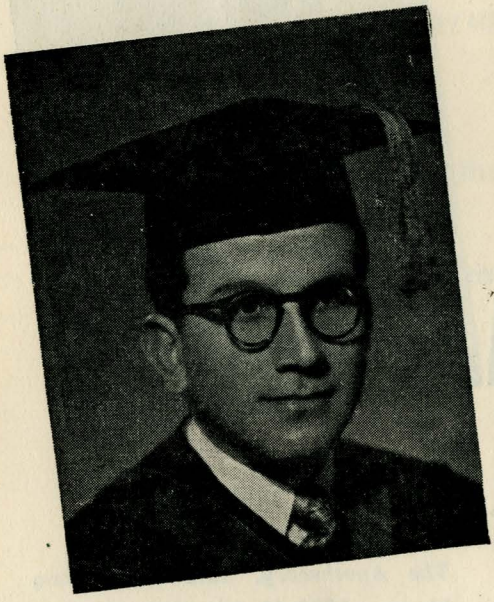
CHARLES JOSEPH NASSAR
Amman, Jordan

Pharmaceut. Soc., Treasurer 1951-52, 2nd Vice President 1952-53.



SULAYMAN HASHIM ABU KHADRA
Beirut, Lebanon

Pharm. News Reporter, 1950-51, Assist. Publisher 1951-52.



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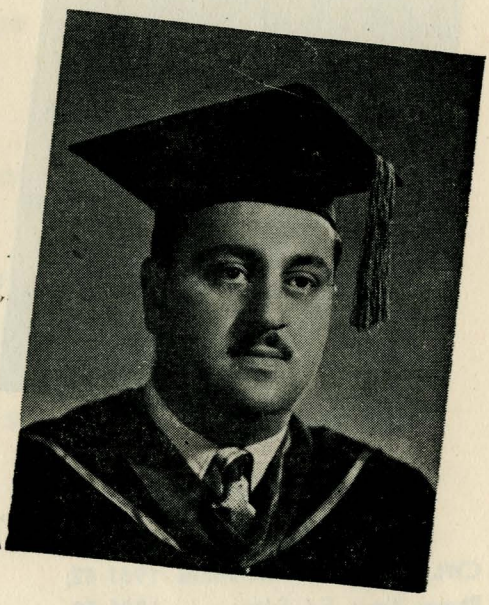
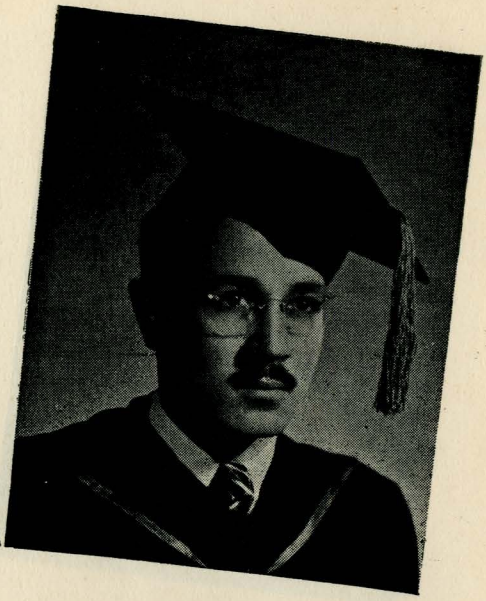


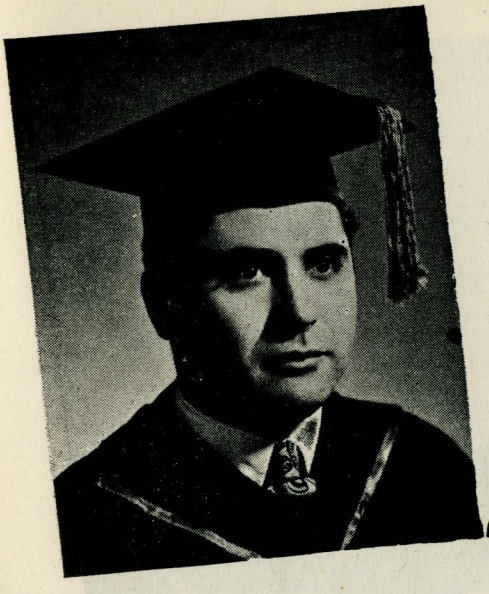
ARTHUR NASIR YOUHANA
Basrah, Iraq

Student Council Representative 1950-51; Lieut. Usher, Ushering Com. 1953-54.

SAMIH TALEB DARWAZAH
Amman, Jordan



BASHIR AHMED RASHID SAKKAL
Salt, Jordan
URWA Soc. Exec. Com. Secret. 1951-52.



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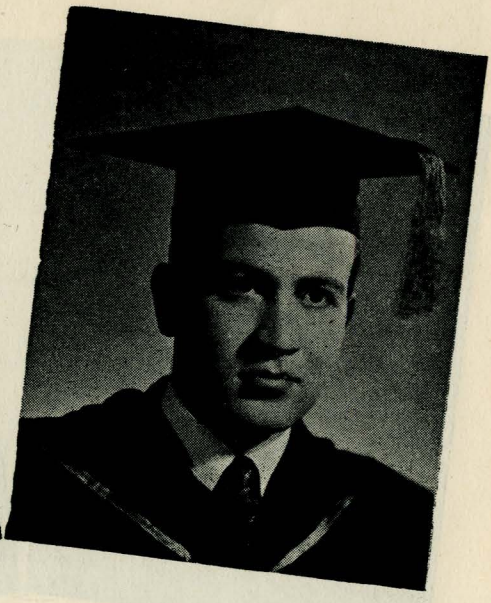
Saidnaya, Syria



GEORGE BISHARAH SLIM
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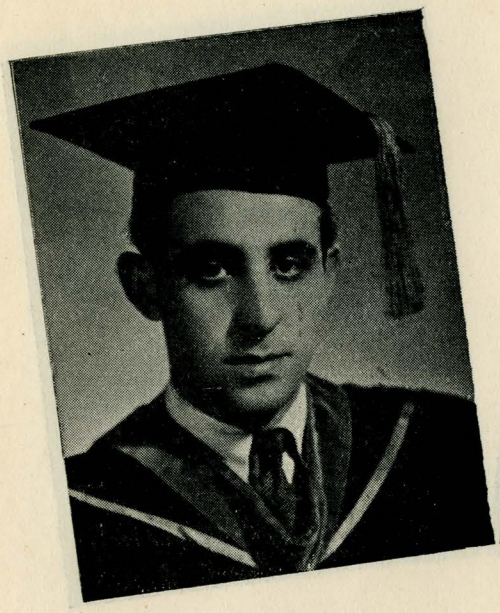
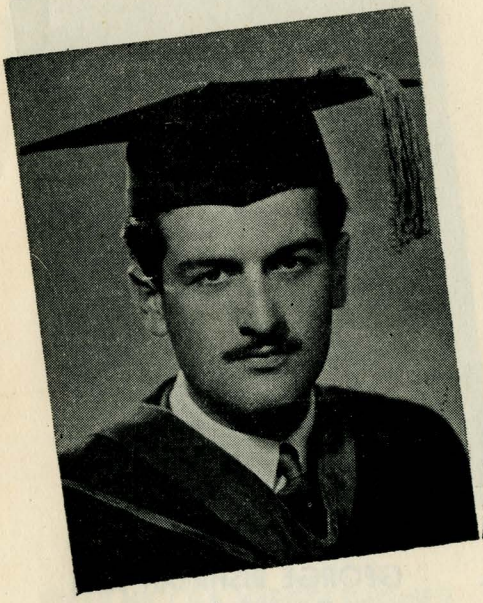


NAIM HANNA FARRAJ
Jerusalem, Jordan

ELIAS YOURGHAKI SARTAN
Tripoli, Lebanon
Pharmaceut. Soc. Vice Presid. 1953 - 54.



VARTKES MEGERDICH APELIAN
Beirut, Lebanon

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Port Said, Egypt
Pharm. Football Team, Capt. 1953 - 54.

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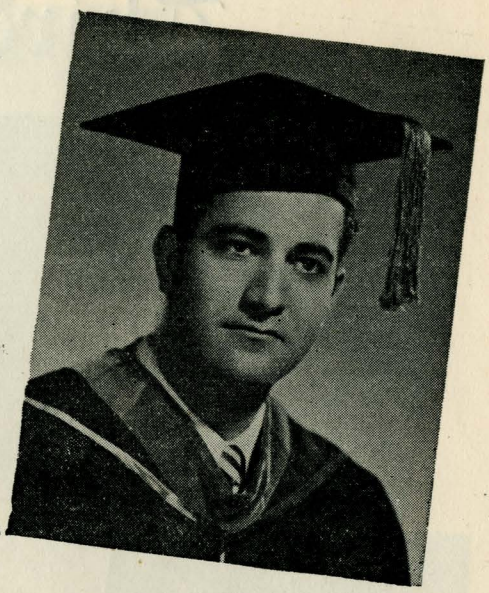
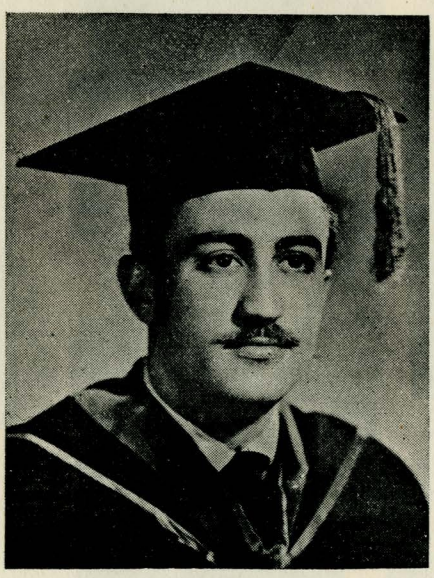
Dire-Dawa, Ethiopia

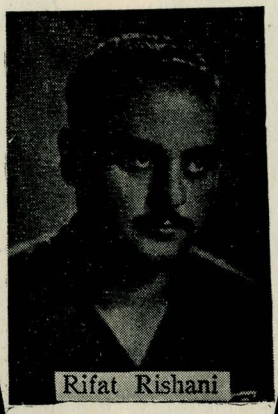


AGOP GARABED MARCARIAN
Jerusalem, Jordan
Pharmaceut. Soc. President 1953-54
(resigned).

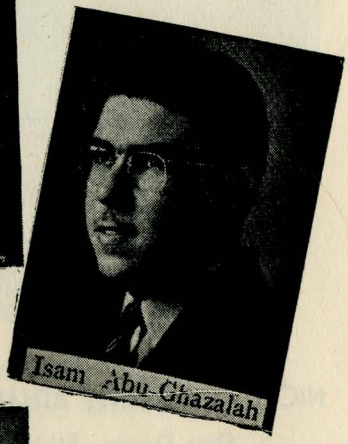


JERRY JACOB ZEROUNIAN
Jerusalem, Jordan
British Council Hostel, President 1953-54

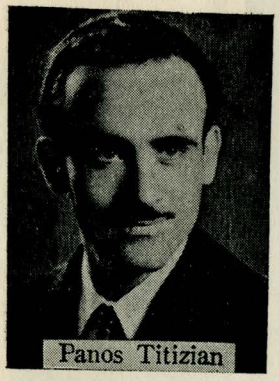
Third Year

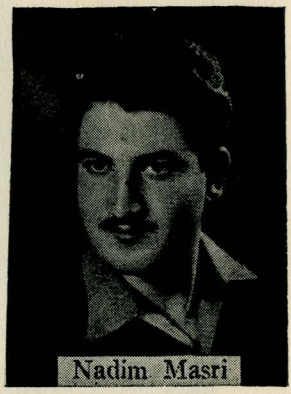

Rifat Rishani


Sami Khayyat


Isam Abu-Ghazalah

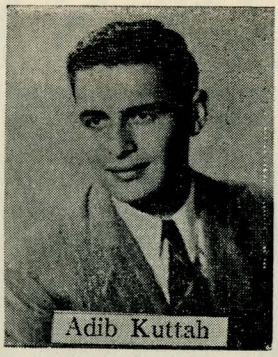

Nimat Huri


Panos Titizian


Nadim Masri


Iskandar Farkuh


Adnan al-Jabshah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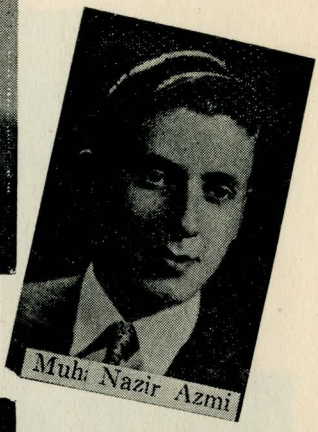
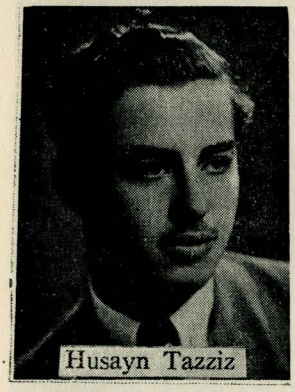
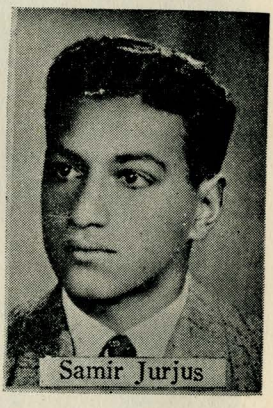
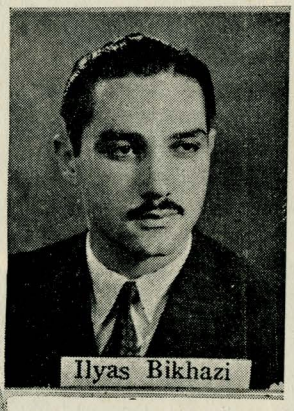

Muhi Nazir Azmi


Husayn Tazziz


Salfa Hamadah


Samir Jurjus


Khalil Samir Bishuti

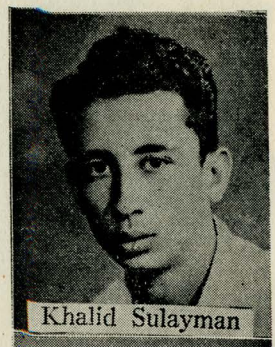

Ilyas Bikhazi


Varoujan Etyemezian

Second Year


Faysal Kanj


Haig Gourdikian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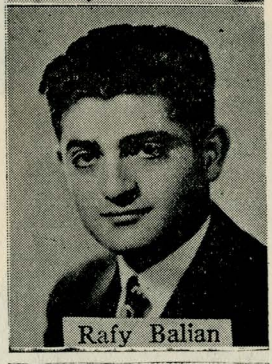
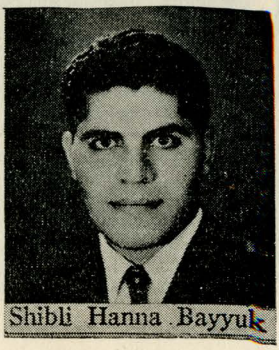
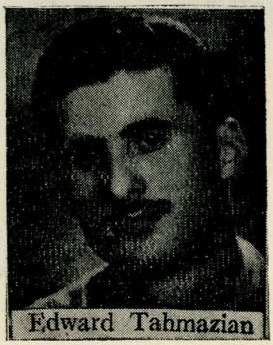

Rafy Balian

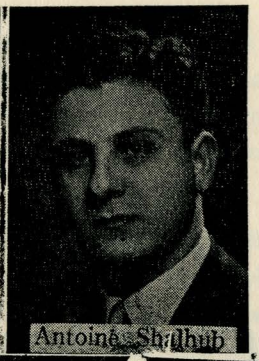

Badi Nuwayhid


Shibli Hanna Bayyuk


Edward Tahmazian

First Year

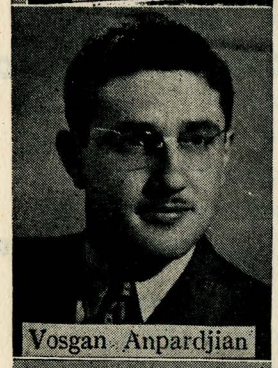

Ibtihaj Kazun


Antoine Shalhub

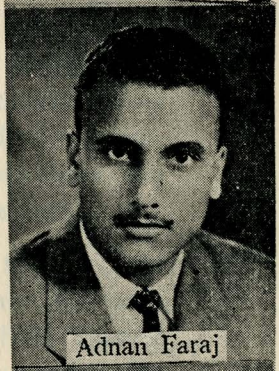

Rasul Jishshi

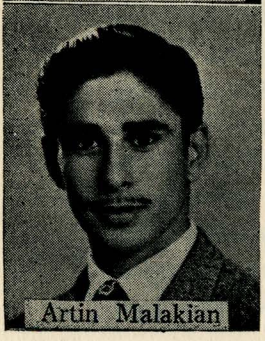

Muh Ziyad Habash

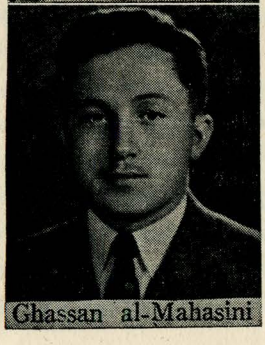

Barkev Mekhjian


Vosgan Anpardjian


Mary Pilikian


Adnan Faraj


Artin Malakian


Ghassan al-Mahasini


Tawfik Karam

I had six honest serving men,

They taught me all I knew.

Their names were Where and What
and When

And Why and How and Who.

Rudyard Kipling

Editorial

The editorial to this, the ninth volume of *The Apothecary*, will be longer than I usually make it. For there are few things on my mind which I want to pour out to you. And they concern the profession.

Alumni of this School never forget their second home or their second parents. And when they do not write, they often come to say hello. Shall we say they also take us, their professors, as father-confessors ?

We know a great deal about those who were once here under our immediate care. They graduated and they went away taking with them a part of ourselves. Is it surprising then that our hearts should vibrate to the different waves which they set and the pattern of life and work which they carry? Sometimes the vibrations are happy. Oftentimes, however, they set the heart into fibrillation, for the news is sad and the suffering great.

Fine capable young men graduate every year into life to commence their individual careers. Few Strong hearts survive the tumultous sea and with deep scars. All ask for a remedy.

What is the remedy?! Stand together, cooperate, do not enter into cheap senseless competition, do not attempt to build a false *success* on your *brother's* corpse. Protect his good name, he will protect yours; help him, he will help you; do not under-cut him, for there will be one who will under-cut you; and remember that unless you uphold the good name of Pharmacy, your good name will suffer with any disgrace that comes to the profession. Compete with your colleague in good service to your community and your community, no matter how inappreciative it

may seem to you at present, will place its trust in you. Only this will bring you lasting success and happiness.

Elating letters and reports, depressing letters and reports, set our days to different tunes Faith must be that salvation can only come if you stand together and in the right: support the creation and the existence of your professional societies, attend their meetings and never be disappointed whenever your suggestion is not adopted. Every single person counts, and if you dissent, never say *I am only one.* You are many. And the house that is divided will fall.

The Apothecary has found a permanent place in the life of many alumni, our School has become known to others through it, and a spiritual fraternity has grown among its readers.

May this very sincere and deep-felt plea be heeded; and may a real *esprit de corps* be reborn in the practitioners of the profession and may the ideals you learnt at A. U. B. and the oath you subscribed to guide your steps.

Charles Abou - Chaar

ORIGINAL ARTICLES

THE NEW PHARMACY LAW IN TURKEY

by **Hamdi Dürüst, Ph. C.** *

The advent of the year 1954 brought mixed feelings to Turkish pharmacists. The Turkish parliament had very recently, on December 18 , 1953, enacted and passed a new pharmacy law for Turkey. This law lifted the restrictions imposed by the old law of 1927, on the number of pharmacies to be opened in Turkey. To some pharmacists, the new year heralded a new era of hope and professional progress, while others feared that it may be the very beginning of pharmaceutical chaos.

In a previous review of the history of pharmacy in Turkey (The Apothecary, 1950, p. 18) I had indicated that the Turkish pharmacy law, promulgated in 1927, limited the number of pharmacies to be opened in Turkey to the ratio of one pharmacy to every ten thousand inhabitants. When, in 1950, the Democratic Party won the national elections by an overwhelming majority over the Republican People's Party, it was decided to review all the laws enacted during the 27 - year term of government of the latter party, with the aim of determining which enactments were « anti-democratic » and modifying these in accordance with the Turkish constitution.

The article of the 1927 law restricting the number of pharmacies drew much interest and started off a series of academic discussions. Some considered the 1927 law

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* *Following his graduation from our School in June 1951, Mr. Dûrûst taught Qualitative Chemistry at the Engineering School of Robert College (Istanbul), his former alma mater. In June 1952 he was called for military service and joined the Medical Company of the Reserve Officers' Training College at Ankara. In late October of the same year, he was commissioned a pharmacy lieutenant of the Turkish Medical Corps Reserve, graduating from the Training College with « high distinction ». For nearly a year he was an officer in the medical supply section of the Ministry of National Defence in Ankara. In September 1953 he was transferred to Istanbul, where he has his home, to complete his military service as the pharmacist of a large military hospital there. Luck was with Mr. Dûrûst when, three weeks before his honorable discharge from the Army, the Turkish parliament passed the new pharmacy law which lifted restrictions on the opening of new pharmacies. He is now very busy establishing his «Modern Pharma cy» in the Sisli quarter of Istanbul only few blocks away from his home.*

totally anti-democratic, as it limited the opportunity of practicing one's profession freely and without hindrance; while others believed a limitation was necessarry so as to insure a homogeneous distribution of pharmacies throughout the country, much as it may seem anti - democratic. Pharmacists, physicians, members of parliament, health officials, the press and the whole public were divided on the issue, and throughout 1953 people were «pharmacy conscious» in Turkey as a result of the publicity the matter was getting in the press.

In opposition to the **Association of the Pharmacists of Turkey,** the organization which had advocated and supported the 1927 law with its restrictions, there came into existence a new group which called itself **The Society of Aid to the Pharmacists of Turkey.** This latter organization mostly comprised the young members of the profession who owned their own pharmacies as well as those who did not own pharmacies. It started a movement toward the abolishment of the restrictions on the opening of new pharmacies. For one whole year the Turkish press was full of articles in favor of or against the proposals of the two pharmaceutical societies, and one often read of curious incidents such as the one from Izmir, where a young pharmacist claiming to have no opportunity of establishing a pharmacy of his own under the 1927 law, decided to work as a mason in construction work until a new pharmacy law was enacted and the restrictions repealed.

The Association of the Pharmacists of Turkey, in existence since 1911, was in favor of keeping restrictions, with the following justification: first, that abolishing restrictions will start a rush of pharmacists to the bigger cities, thereby leaving the smaller towns and villages without an adequate number of pharmacies; and second, that the concentration of pharmacies in the bigger cities, as a result of the rush, will eventually end in a fierce commercial competition which will be deleterious not only to the members of the profession but also to the general public. The Society of Aid to the Pharmacists of Turkey, opposed, however, the above views, and countered with the following justifications for their own views: first, that the aim of the 1927 restrictions was to provide a homogeneous distribution of pharmacies throughout the country, which, statistically speaking, was not very successful; and second, that the expected competition will eventually force most pharmacists to become more attached to their profession and take more active interest in the professional aspects of their life-career.

The split of opinion also prevailed among members of parliament, some of whom favored reducing the ratio to one pharmacy per 5000 inhabitants instead of completely abolishing the older restrictions. Finally, however, the group favoring the full lifting of restrictions won.

Who can practice pharmacy in Turkey ?

The second article of the law allows the opening of a pharmacy in any locality provided the pharmacist is, a Turkish citizen, is a graduate of the Turkish School of Pharmacy, or if a graduate of a foreign institution abroad, must have «proved his professional identity» (see below), has had his diploma registered at the Ministry of Health and Social Aid and had not been convicted for offences mentioned in article 4 of the law. « Proof of professional identity» is the legal term for the colloquium examination where the candidate also submits all credentials identifying him with his profession i. e. diploma, certificates of apprenticeship, and full transcript of record at the foreign school where he studied pharmacy - all of which should have been previously authenticated by the Turkish consular representative nearest to the foreign school.

Article 3 deals with graduates of foreign schools of pharmacy, and divides them into three categories. Those of the first category come from schools which offer an identical

curriculum to that of the Turkish school both in content and duration. They are allowed to practice pharmacy after submitting a «proof of professionnal identity» as explained above. The second category includes those who come from institutions which offer curricula either of the same length of period or of content but not of both. They must pass additional examinations according to a schedule prescribed by the Turkish board of examiners to be able to practice the profession. Those candidates who come, however, from schools offering not only a different curriculum but a shorter one also form the third category. These are required to enroll at the Turkish School of Pharmacy to complete the requirements both as to course content and length of study, before they are allowed to take the examinations prescribed for the second category, to finally permit them to practice their profession. The Ministry of Health and Social Aid shall register the diplomas of candidates from foreign schools only after the establishment of professional identity and success in these examinations

Article 4 deals with those who cannot practice pharmacy. This includes those who were convicted of a degradatory crime, of heavy imprisonment of at least 3 years or ordinary imprisonment of 5 years, of fraud and misuse of professional authority in the preparation and / or sale of medicinals, and those prevented from practicing their profession abroad because of criminal professional offenses or because of ethical discrepancies. Those who are afflicted with an incurable disease as well as those who lost sight of both eyes are also not allowed to practice the profession.

Application to open a pharmacy.

This is dealt with in article 5 of the law. Those wishing to establish a new or buy an already existing pharmacy shall petition, in writing, the Ministry of Health and Social Aid in Ankara or shall apply in writing to the provincial Directorate of Health or the local Health Officer. The following documents should be attached to the petition : an approved copy of the identity card, a photocopy of the diploma, the biography of the pharmacist, the judicial papers establishing that the applicant has a clear record in respect of provisions of article 4 including the medical and eye specialist reports regarding his state of health and sight, and four photographs of the applicant. The pharmacist also sends in three copies of the approved plan of the interior of the pharmacy attached to the report of the Health Officer who had previously inspected the place. The law puts the Ministry under the obligation of issuing the permit wiithin 30 days of the date of application, provided that all the submitted credentials are in order.

Miscellaneous articles of interest.

Article 17 prescribes that pharmacists employed by the government or conscripted for military service cannot operate pharmacies of their own. A pharmacist, who is conscripted in the army or is elected to parliament or as mayor, must appoint a pharmacist as the responsible director to supervise his pharmacy.

Article 18 denies the right of a pharmacist to establish more than one pharmacy or be the responsible director of more than one pharmacy.

According to article 19 , it is stated that in as much as a pharmacist (owning a pharmacy) can not dispense prescriptions outside his pharmacy, he also cannot take up additional trades outside his profession nor can he accept jobs with the exception of teaching posts and posts won by public election.

Though restrictions on the number of pharmacies to be opened have been abolished, the requirements as to internal arrangement, surveillance and night-duty have by no means been relaxed. A pharmacist still cannot sell anything other than medicinals, perfumery and sanitary supplies. He cannot close down or move to another locality without the notification

of the proper authorities in advance. Again, physicians are not to be permitted to receive and examine patients in the pharmacy. This, however, excludes first aid given to people coming or brought to the pharmacy for immediate treatment after accidents.

As in the 1927 law, a minimum of two regular inspections per year are stipulated in addition to other unexpected inspections the local health authorities may find necessary.

As a prerequisite to the registration of the diploma with the Ministry of Health, the old law required certificates testifying to a total of two years of apprenticeship, three months of which must have been spent in an approved hospital pharmacy. The bill for the new law included the same requirement when it was brought before the legislature, but the House, arriving at the decision that apprenticeship was a part of the curriculum rather than a post-graduate requirement, excluded it from the law. It is now therefore, up to the faculty of the Turkish School of Pharmacy to give shape to the practice requirement which in its opinion would suite the profession best.

Another item, not required by the new law, is the «financial guarantee» previously required of every applicant wishing to buy or establish a new pharmacy. That requirement proved to be useless.

Effects of the new law.

What the nation-wide effects of the new law will be will only become evident after a number of years. So far there has been a tendency towards the opening of many new pharmacies. But the fear of a rush to the big cities, it seems, has been somewhat exagerated, for the establishment of new pharmacies in the already crowded cities, such as Ankara, Istanbul, Ismir, Adana and Bursa, requires a great outlay of capital. Proprietors wishing to rent premises in such cities must pay exorbitant prices.

An interesting news item which appeared in the papers early in March gave the following figures for the city of Istanbul : there were about 155 pharmacies in the beginning of January 1954. Of the 30 new applicants since the abolision of restrictions, only four are moving their pharmacies from other towns, while the remaining 26 pharmacists did not own pharmacies. We may not be hasty in saying that the new law has given the opportunity to many pharmacists to establish their own pharmacies in the town and locality of their choice.

Whether there will be fierce competition is something yet to be seen. The fact is that a great and bold step in pharmaceutical jurisprudence has been taken in Turkey, but it is too early to draw conclusions yet.

A Three-Hour Tour

by **Dr. Rudolph J. Pauly, Ph. D.** *

For the last three years I have promised to write an article for the Apothecary, yet, for some excuse or other kept postponing it until it was too late to meet a printing deadline. This year, Professor Abou-Chaar has reminded me of my promise early. In his letter he even quotes an old adage that I used to use on him in order to keep him hustling, i.e. «The busier a person is, the more work he is able to get done» thus eliminating any excuse on my part. As he is not asking for a scientific article, but rather implied that you are anxious to hear from and about me, I am pleased to comply with his request. This letter will not have a profound title but will, I hope, bring you up-to-date on what I have been doing for the last four years.

You all know that we made our home in Albany, New York and that I am connected with the Sterling-Winthrop Research Institute. Allow me to devote this message to telling you about the Institute and its work.

Sterling and **Winthrop,** joined in the name of Sterling-Winthrop Research Institute, identify two corporate entities which, although organized in this century, have histories trailing far back into the Nineteenth.

Sterling stands for Sterling Drug Inc., which started as a small business producing a single packaged medicine for a market within horse-and-buggy delivery range of Wheeling, West Virginia. The establishment occupied two rooms on the second floor of an old building, its two principals serving as office and sales force and as production staff. The business grew. In time, it acquired other business which had been established much earlier. Today, Sterling employs 11,500 men and women, operates more than 50 plants throughout the world and maintains 110 branch sales and service offices. The many products that carry the names of its divisions and subsidiaries include medicinal preparations available through physicians or on their prescription, packaged medicines directly available to the public, household and toilet articles like dentifrices, shaving cream and cleaning compounds, and bulk chemicals for process manufacturers and other industrial users. Among the more than 70 countries served by Sterling are the United States, all of the Republics

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* *The students of Dr. Pauly, and they are in hundreds, will welcome this article by their former teacher and director. Having taught for 25 years at the School and become its director during the last few years, he resigned his position at the University and left the country,which had become a second home to him, to be with his family in the States where his children had to complete their higher education. He is now director of the Pharmaceutical Division of the Sterling-Winthrop Research Institute at Rensselaer, N.Y. and lives at 147 South Pine Ave., Albany 8, N.Y., U.S.A.*

of Latin America, most of the Dominions and Colonies of the British Empire, as well as others whose initials run the range of the alphabet.

Winthrop stands for Winthrop-Stearns Inc., which was formed in 1947 to conduct the businesses hitherto carried on by two separate units of the Sterling organization. These were the Winthrop Chemical Company, Inc., organized at the end of World War I, and Frederick Stearns and Company, incorporated in 1855.

Winthrop-Stearns Inc. is the largest of the Sterling subsidiaries engaged in pharmaceutical manufacture, but it is not the only one in that field. Others serving the medical, dental and veterinary professions in the United States include: American Ferment Company, George A. Breon and Company, and Cook-Waite Laboratories, Inc. Similar service is provided abroad by Bayer Pharma (Proprietary) Limited, South Africa; Bayer Products Limited, England; Carter, Cummings and Company, Ltd., Canada; Frederick Stearns and Company Division (Australia); and Winthrop Products Inc., which operates in various foreign countries.

Most of the research work for these companies is done here at the Institute. Substantial sums are also allocated for grants and fellowships in universities, medical schools and hospitals; and our medical research staffs cooperate with many institutions in clinical investigation. The Institute is housed in a building completed in 1950 and located on a 70 acre tract of land on a hill overlooking the Winthrop-Stearns Plant and the city of Rensselaer. When completed, it was the largest building devoted exclusively to pharmaceutical research in the United States having 186,000 square feet floor space. The center section of the four-story building, devoted to administrative functions, houses the library with its thousands of books and bound journals. It currently subscribes to 200 scientific journals. Adjoining it on the fourth floor is the Patent Division, spending full time searching the patent literature in order to avoid infringement and drawing up applications for patents on any new drugs discovered. The next two floors of this section are devoted to offices, central files, accounting, purchasing, infirmary, a seminar room that looks just like a class room in Van Dyck Hall, photostating and mimeographing, mail and telephone exchange, five Executive offices, a display and a conference room. The lowest floor houses a modern cafeteria capable of serving and seating 250 people at a time.

The Pharmaceutical and Chemical Divisions of the Institute are housed in one wing of the building, while the Biological Division is in another. I think the best way to tell you about the place and the work is to take you on a tour exactly as if you were a very important visitor to the Institute. Let us begin on the top floor of the Chemistry wing, as the search for new medicinal agents begins in the Chemical Laboratories, where hundreds of new compounds will be synthesized each year. On this and the floor below are nine organic chemistry laboratories, each having three long double benches with reagent shelf, hoods, sinks, and apparatus cabinets. Between each two such laboratories is a large room which is used for special apparatus and office desks. A group of two to six chemists is assigned to each new project on synthetic compounds. More than a dozen such groups are continuously engaged in developing syntheses relating to families of compounds. At the start of a synthesis, only a few of the compounds comprising the family are made. If these prove interesting in biological tests, intensive studies are undertaken on other related compounds. Research has been inaugurated on the relationship of hormones to age in the expectation that some answers to a longer life may be found. Under study are radiopaques, x-ray agents used as diagnostic aids by physicians, Telepaque being the latest one commercialized; amebacides; anthelmintics, to combat such diseases as tapeworm, hookworm and pinworm; improved antimalarials like Aralen to fight one of the world's most prevalent diseases. In the sympathomimetic field, a new antiasthmatic drug has been deve-

loped at the Institute which holds promise for the asthma sufferer. New antispasmodics to aid patients suffering from ulcers and intestinal spasms have recently been introduced for physicians' use. Research studies also relate to the synthesis of drugs now derived from natural sources. From a method worked out at the Institute, Winthrop-Stearns has been able to make and deliver to the United States Government over 300 pounds of synthetic Atropine which constitutes a stock-pile of antinerve-gas drug sufficient for the entire population for several years. From a method of synthesis worked out at the Institute, Cortisone was manufactured by the Bayer Company in England in sufficient quantity to supply that country, its first British-made drug.

For the more common types of aches and pains, Sterling's Bayer Aspirin has no peer. But, the Institute's program calls for unceasing research to maintain the high quality of existing products, as well as to develop compounds which may lead to new products. Among sanitizing agents, the chemists are seeking new formulations which show greater activity against bacteria and which can be marketed at lower prices. Detergents for use in many ways are being studied. New, highly potent local anesthetics recently commercialized by Cook-Waite for use by the dental and medical professions have been discovered here; and studies are going forward in steroids looking to the development of improved antiarthritic compounds. Attention is directed to the synthesis of amino acids, and the Institute has succeeded in devising a practical synthesis of trytophan, an essential amino acid, occurring naturally, without which the human race could not survive.

Also on the two top floors of the Chemistry wing are the Physical Chemistry Suite of three laboratories and an office, the Micro-Analytical Laboratory and office, and the Central Analytical Laboratory in three rooms and an office. The physical Chemistry Laboratory serves an important function, for it is frequently able to provide new approaches to research problems by conducting measurements on a quantitative scale. Equipped with both a recording infra-red and a recording ultra-violet spectrophotometer, the two of which cost as much as five Cadillacs, they are able to «fingerprint» compounds. Since information obtained from spectra tells the chemist about the arrangement of atoms within the molecule, it is helpful in determining the structure of new compounds, and provides data on identity, purity and even on the stability of a compound. By measuring the electrical conductivity of unknown compounds, the physical chemist studies the strength of acids, dissociation constants, and whether or not such data correlate with the toxicity of the compound or with its pharmacological activity. He also has precision instruments such as the refractometer, tensimeter, polariscope, etc.

The Micro-Analytical Laboratory seldom uses more than five milligrams of a material for running a complete determination of the Carbon, Hydrogen and Nitrogen content of a compound. From these and determinations for certain radicals, the laboratory can tell the synthetic chemist whether he has prepared what he had planned. New compounds must be carefully analyzed for purity and identity before they are tested biologically, and the Chemical Analytical Laboratory is responsible for this phase of the Institute's operations. Here, too, are developed methods for the analysis and control of pharmaceutical combinations. It must also compile accurate data as to the constituents of new combinations for submission to governmental agencies prior to commercial manufacture. Divisions and subsidiaries of Sterling Drug seek advice as to the analytical problems encountered in manufacturing processes. For example, the Salvo Company, which manufactures a large portion of all the vanillin produced in the United States, wished to determine the amount of vanillin contained in certain by-product solutions to decide whether recovery would be economically feasible. Another unit producing colors and dyestuffs for industrial use, as well as pharmaceutical intermediates, needed a rapid method for determining

the three most important constituents in a mixture of aniline derivatives; an appropriate method to obtain this result was evolved.

From the Chemical Analytical Laboratory, new compounds are sent to the so-called **Win** room for storage and distribution. More than 8,000 compounds which have been synthesized in the Chemical Laboratories (most of which are not listed in Beilstein as yet) comprise the Institue's reservoir. These compounds either have been tested are in the process of being tested, or will be tested by laboratory or clinical means, or both. Usually the Chemical Laboratories provide a clue to the possible uses of a new compound, and under standard practice, it is normally tested for many uses at a time. Sometimes tests of a compound reveal an application which had not originally been anticipated in its synthesis; thus, a discovery is made leading to exploration along a new line.

When a compound has been found to have sufficient pharmacological action that a full-blown study of it is to be made, the chemist who first synthesized it in an amount of only 5 or 10 grams will be asked to provide 100 to 200 grams of the material. This means that he will have the chance to improve his method of synthesis so as to give larger yields. The chemical will go through the control laboratories for identity and purity another time and then will be sent to the Biology Division where it will not only be given a thorough pharmacodynamic study, but acute, sub-acute and chronic toxicity studies will be made.

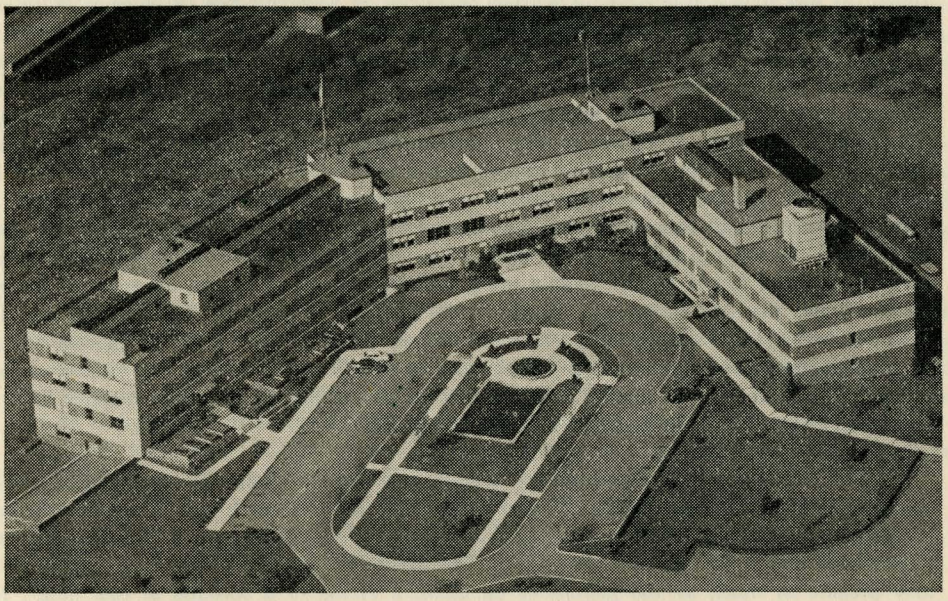
The Biology Division has fully-equipped laboratories on Pharmacology, Bacteriology, Parasitology, Pathology, Histology, Biochemistry, Endocrinology, Nutrition and Metabolism for such investigations. It also houses a Virus Suite where mice or hamsters infected with virulent virus diseases for testing purposes are housed in specially designed stainless steel drawers which prevent accidental infection of research workers. All injections are made in closed hoods provided with negative draft so that all the air leaving the hood is passed between ultraviolet lamps thus destroying any living virus in the air to be discharged into the outer atmosphere. Only workers assigned to these projects are permitted entrance, which is through an air chamber operated by electric locks. Dressing and shower rooms are provided where complete change of clothes is made upon entering and leaving the working rooms. Clothes worn in contact with infectious material are sterilized before being sent to another part of the building for further washing and sterilization. The Biology wing also houses an Insectorium protected not only with double screen doors, but also double electrically charged screens to insure that no infected insects leave a certain area. New drugs on clinical trial in Egypt and the Philippines have been developed at the Institute to combat schistosomiasis. Dr. Dennis, formerly professor of Bacteriology at the A.U.B. and now director of the Bilogical Division here, has named one of these **Felladin** in recollection of the millions of peasant workers in Egypt, Persia and Iraq who are afflicted with the disease. After the new compounds were synthesized, they were tested in the Institute's snail colony. The parasite which causes schistosomiasis has a complicated life cycle, undergoing part of its development in a species of snail from which it escapes and burrows into the skins of the victim while bathing or wading.

The other Beirutians connected with the Institute are : Dr. Dicran Berberian, in charge of Parasitology and Tropical Diseases and Director of the Medical Department; Manuel Hadidian, research assistant in the Virus Laboratory; and Dr. Alfred Farah, Professor of Pharmacology at the Syracuse University Medical School, who acts as consultant to the Institute for diuretic drugs.

Much of the space of the Biology Division is devoted to animals. Spacious, immaculate, air-conditioned quarters have been set aside for animals used in biological test-

ing, and the finest type of laboratory apparatus has been provided to record the effects of drugs under test. The animal patients receive the best of care, and food is prepared for them under the same sanitary conditions that prevail for humans.

In the Pharmacodynamics Laboratory tests are made on drugs for the treatment of functional disease to determine their potential value. Such new therapeutic agents may be useful in prolonging life and contributing to its enjoyment. Their safety is measured by means of short and long term toxicity tests as well as irritation studies. The Biochemistry Development Laboratory is well equipped with 100 gallon kettles and centrifuges of large capacity for the processing of natural products on a pilot plant scale. Products from natural sources are extracted here : cholinesterase from blood cells, histaminase from kidneys, and active materials from plants. Analyses are made on blood, urine and other body excretions in order to determine the metabolism of drugs and thus determine their assimilation and stability. A large laboratory for Bacteriology and Parasitology is equipped with walk-in incubators, one kept at a constant temperature of 25°C. for molds, and another at 37°C. for bacteria. Also, large walk-in refrigerated rooms are available for the cold storage of materials.



After a compound has successfully and successively passed the tests to which it has been subjected in the various laboratories, it is ready for manufacture in quantities sufficient for clinical testing. This is done by the Chemical Development Laboratory in large-scale, glass-lined equipment which is a replica of factory apparatus. Methods for commercial manufacture are developed here by taking the method used by the chemist first synthesizing the drug, adapting it to larger equipment and adjusting each step to give the highest possible yield. Versatility in design of this manufacturing equipment permits of innumerable intricate operations such as stirring, heating and gassing all at the same time in one kettle, and when a reaction is finished, shifting the stopcocks so that distillation can be made direct from the same apparatus. The space allotted to this manufacturing unit is two stories in height in order to accomodate four complete distillation assemblies.

In the high-pressure laboratory, located in a detached room below ground level, ex-

traordinary precautions have been taken to guard against danger. Built of heavily reinforced concrete, it is separated from the main building by concrete walls and six feet of sand. It houses a wide range of hydrogenating equipment, as well as a number of specially designed autoclaves for reactions requiring high temperatures and pressure up to 5,000 lbs. per square inch. Operation is by remote control, with the operator protected by a 12 inch concrete barrier backed by armor plate.

If a new compound succeeds in meeting chemical and biological tests, proving it to have valuable physiological activity and possibility of manufacture, the PHARMACY DIVISION takes over in order to put the new drug into a form appropriate for use by physicians in clinical trial and have it in an appealing form for the patient. Will it be a tablet or a solution ? Will it be an injectable and, if so, will it be stable over a definite period of time—will it withstand sterilization or must it be aseptically filled into ampuls or vials ? Such decisions rest with the Pharmacy Division. Not only does it deal with new compounds, but it seeks constantly to improve existing products. To carry out such operations, its equipment is a counterpart of that found in large-scale manufacturing.

The Pharmacy Division occupies the second floor of the chemical wing of the Institute. It has sixteen rooms and a walk-in incubator to accommodate its sections of Pharmaceutical Research, Pharmaceutical Development, and Proprietary Pharmacy. The Pharmaceutical Research Section takes on the task of developing the basic formulation, determining the compatibility of proposed ingredients, performing accelerated tests of aging at elevated temperatures or under specific conditions of light or humidity so as to determine the probable shelf-life of the formulation, conducting flavor panel tests in order to present the product of optimum palatability, assembling specifications for all the ingredients of a formulation so that this may be transmitted to the factory should the preparation become a commercial item, and even supplying personnel to assist with the preparation of the first commercial factory production. This section has all the equipment of a dispensing pharmacy in addition to pH meters, colloid mills, vacuum ovens and pumps, all types of motorized stirrers, an «Aire-Regulator» which cycles between 12 hours at 25°C. and a similar period at 37°C. while maintaining relative humidities ranging from 70 to 95 percent so as to simulate tropical climates, and a walk-in incubator kept at 37°C. with one section maintained at 45°C. for the storage of hundreds of samples which are sent for chemical analysis checks every month in order to determine their stability.

The Pharmaceutical Development Section has the responsibility of preparing the research orders for clinical trials. It also carries out some research and a certain amount of stability study. The Section is divided into a Solution Laboratory, a Dry Preparation Laboratory, and a Parenteral Laboratory. The Solution Laboratory has three rooms and may prepare as much as 100 gallons of an elixir, a syrup, or a solution at one time. It also may be called upon to make several hundred suppositories or large quantities of an ointment or cream and is equipped with proper filters, tanks, kettles, scales, mills and other apparatus for such work. The Dry Preparation Laboratory is housed in two rooms and an air-conditioned cubicle and is asked to prepare runs of tablets anywhere from 200 to one million in quantity. They also prepare capsules, granules and powders. They are equipped with grinding mills, small and large electric drying ovens, tumbling and pony mixer, wet and dry granulators, paste mill, two single punch and two rotary tablet machines and coating and polishing pans of all sizes. Those tablets which must be free of moisture are compressed in a specially dehumidified cubicle. In scheduling a product for use as a tablet, consideration must be given to speed of disintegration, taste, fragility, whether or not a coating is needed or desired and, if so, what type. The Parenteral Laboratory occupies two rooms and a cubicle. In one room, a triple-distillation still is fed with deionized

water to produce pyrogen-free water used in making parenteral solutions. Each still has a boiling chamber and condenser which turns water into steam three times before it enters a holding tank. Ampuls and vials are washed in a mechanical washer and autoclaved, both before and after filling, for sterilization by steam under pressure. This is done in an autoclave which is also in this room together with a large electric oven for the sterilization of dry glassware. In an adjoining room, the solutions are filtered and filled in measured amounts into the proper container and sealed. If aseptic filling is required, this is carried on in the cubicle which is air-filtered, dehumidified, dust-free, fitted with ultra violet lamps, and which is under positive pressure to prevent outside air from entering. Sealing apparatus for the preparation of ampuls of dry powders is also available as is also a small scale lyophile machine which freeze-dries solutions of chemicals too delicate to be sterilized with heat and not stable enough to be packaged in solution form.

These three Pharmaceutical Development sections are provided with a packaging room where several persons are kept busy filling and labeling the finished preparations that are packed and shipped out for clinical trial. After the product has proven itself a valuable drug on sometimes as many as 1,000 patients, then all data concerning it is gathered together and presented to the Food and Drug Administration which may permit its commercial manufacture. Even though some new drug may not have a large potential sale, Sterling Drug Inc feels honor bound to make it available if it mitigates a disease for which no other drug is known.

The Proprietary Pharmacy section has one room with three large laboratory benches and another room for special apparatus and office use. Here the various over-the-counter hair and skin preparations sold by various Sterling subsidiaries and the dental pastes and preparations are formulated or kept abreast of continual improvements as newer raw materials become available.

Now that I have taken you through the Institute on what we call the three hour tour, I trust that you have some idea as to what is keeping me so busy that I do not often get a chance to write to you. In the Pharmacy Division we have over one hundred and fifty projects continuously under way. These must be reported on or written up for the various companies that hold conferences here at least every two months. It is very interesting and stimulating work and provides a great deal of satisfaction whenever one feels that one has in part contributed to the birth of a new drug.

A PRESCRIPTION SURVEY

from London

by **Maria Widacka, Ph. C.** *

« This is the first prescription survey ever made in Beirut... Jaffa ... Amman... Nablus... Istanbul....»—that is how the introductions to all the prescription surveys published in the Apothecary begin. To follow the pattern and the already firmly established tradition, I have to start thus:

This is the first prescription survey ever carried out by a graduate of the School of Pharmacy of the American University of Beirut, for the Apothecary, in ....London, England.

I hear you humming the tune of «it is a long way to Tipperary » and smiling with some irony perhaps. It certainly is a long way from the Middle East to London, no doubt about that. And I do not expect you to take a very special interest in the dispensing that is being done in England.

Yet would it not be of some interest to take a glance at those tables or to compare the data of this survey with the ones of Beirut, Amman or Istanbul ?.

As I did not have any possibility of obtaining the data from any dispensary other than the one I am in charge of, the collected data represent the prescriptions dispensed in one pharmacy only. From my experience, however, I may safely say that dispensing in the different pharmacies, in the various districts of London, and even all over England, is more or less the same. My figures therefore will give you a general picture..

The 6000 prescriptions considered in my survey were all issued under the N.H.S. , (the National Health Service). There are so very few private prescriptions that to collect the same number of these I will have to work on them for years. Even then, I am not sure, I shall ever reach the figure 6000.

Names of official drugs and preparations were mostly written in the accepted

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* *Miss Widacka obtained her Ph. C. degree at A. U. B. in June 1950. Originally born in Poland, she had arrived in Beirut during the war not knowing a word of English. In a surprisingly short time she learned and perfected her knowledge of the language and became one of the best students in her class. In her own words she "fell in love with Lebanon and her Alma Mater". The year after her graduation was spent in Beirut and more correctly at the School where she attended regularly the seminar meetings of the senior class. Then she left to England, her adopted country, and arrived in London in the autumn of 1951. There she worked as an assistant dispenser at one of the branch pharmacies of Timothy, Whites and Taylors, Ltd. After the expiration of a six-months practice, she sat for the qualifying examination and passed it. She is now a member of the Pharmaceutical Society of Great Britain and is in charge of one of the branch pharmacies of J. T. Davy in London. She writes often to the School, regularly subscribes and contributes to THE APOTHECARY and believes that all alumni are morally bound to support it financially. She also subscribes to the AL-KULLIYAH MAGAZINE.*

Total number of prescriptions considered in the survey	6000

Official preparations (B. P., B. P. C., N. F.*)	79.10 %
Proprietaries	18.32 %
Doctor's own formulae	2.58 %

D.D.A. preparations (narcotics)	0.72 %
Antibiotics	4.05 %
Barbiturates	6.27 %

* British N. F.

Signa	Per cent
Latin	57.72
English	10.70
Mixed	7.93
None	23.65

Ratio of tablets and capsules containing *babiturates* to the total of tablets and capsules	24.05 %

Type of Preparation	Per cent
Appliances (cotton-wool, bandages, plasters, lint, hyp .needles, droppers, smog masks, etc.)	5.57
Dusting powders	0.35
Ear and nose drops and sprays	3.37
Emulsions	1.35
Eye drops	0.48
Gargles and mouth washes	1.20
Inhalations	0.98
Injections and vaccines	1.82
Linctuses	6.53
Liniments	2.05
Lotions	2.48
Lozenges and chewing gums	1.47
Mixtures	30.43
Oils	1.03
Ointments, creams and pastes	5.60
Paints and collodions	0.37
Pessaries	0.22
Poultices	1.00
Powders and granules	0.63
Suppositories	0.33
Syrups	3.10
Tablets, capsules and pills	26.05
Others	3.59

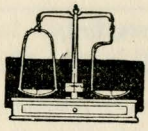
Latin abbreviations, the proprietaries' names as such. The quantities were stated in the Imperial System of weights and measures

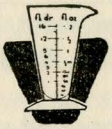
Going over the tables you will notice two types of preparations hardly ever prescribed in the Middle East: the linctuses and the poultices. Linctuses are preparations usually containing medicaments having a local action on the mucous membrane of the throat; the vehicle is some mucilaginous, syrupy, or viscous substance; and to ensure prolonged action, they are sipped or swallowed slowly in doses of small volume without dilution. They possess demulcent, expectorant or sedative properties. Poultices or cataplasms are soft, semiliquid, external applications which either stimulate a body surface or alleviate an inflamed area by supplying medicating substances in the presence of heat and moisture.

You will not come across any cachets in this survey. They are not used in England, something many of you, recalling to mind the charcoal cachets, will approve of.

But you will find a strange item, an appliance that you never had and will never dispense or sell in the Middle East: the smog mask. This is a special mask designed to be worne in the smoke-polluted fog (smog).

I shall end this prolonged introduction by a challenge to fellow alumni in Syria, Egypt, Sudan and elsewhere : what about a prescription survey of these countries ?





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A PROFESSION is an occupation that requires the combined practice of knowledge, skill, and art for the benefit of the community.

PROFESSIONAL men and women render service without being servile. Indeed, service is professional pharmacy's principal commodity.

PHARMACISTS serve the lay public through careful preparation of medicaments and through judicious and intelligent interpretation, in language the layman will understand, of information concerning drugs, insecticides, herbicides, and other scientific or quasi-scientific developments that fall within the domain of pharmaceutical knowledge.

PHARMACISTS serve the physician by disseminating to him reliable and unbiased technical information and advice on the action and properties and available forms of drugs.

Finally, PHARMACISTS serve the community through participation, in their professional capacity, in civil defense and other programs concerned with protecting, maintaining, or improving public health not only at that level but at city, state, national, and international levels as well.

Robertson Pratt, Ph. D.
Professor of Pharmacognosy, College
of Pharmacy, University of California
(Am. J. Pharm. Educ., **17**, 410, 1953)

CHEMOTHERAPY OF CANCER

by **Prof. Amin F. Haddad**

Cancer is a malignant growth of cells which sooner or later, if not eradicated, intrudes upon the structure and impairs the functions of the body, often spreading to form secondary growths (1). Its development is predisposed by a variety of factors, varying with the location of the tumor (1). «The cancer cell was simply a modification of the normal cell. Conversion to malignancy of the normal cell might possibly be brought about by a subtle and elusive change of enzyme constitution quite unaccompanied by any grosser alterations affecting protein structure. On this account there was little or no protective reaction on the part of the body or host, such as occurred in parasitic infections. The malignant cell also appeared to be highly stable in its properties, as was shown by the manner in which its newly acquired characters were transmitted and maintained quite indefinitely. In many ways the processes of cell division were reminiscent of a self-propagating mechanism varying in the degree of control to which it was subject»(3). In brief, the identity of cancer rests on three solid observations - that cancer is a disease of cells; that these diseased cells carry their own stimulus to divide; and that when they divide they reproduce their own kind.

The control of this dreadful disease is being investigated in the light of three main lines of research namely : investigation of the environmental factors which may produce malignant tumors and, then, preventing the disease by appropriate control measures; finding diagnostic tests for incipient neoplastic growth ; and the production of systemic chemotherapeutic agents for the selective destruction of malignant growth (2). At the present time, the volume of research which directly or indirectly is carried along these lines is immense. It is, however, very early to conclude that control of the malignant disease is imminent. Important advances have been made in the understanding of the biology of this malignant disease and fundamental chemical differences between cancer and normal cells have been shown to exist. Increasing knowledge of these differences is making possible the development of chemicals which specifically injure or destroy cancer cells but do not harm normal cells. Recently it has been shown that the desoxyribonucleic acid of the genes of cancer cells is unlike that of normal cells. This is a most important discovery for it offers at least a chance of finding an antimetabolite to block the nucleic acid synthesis of cancer cells without seriously damaging normal cells. (53).

The great majority of cases of cancer at present are treated either by surgery in an attempt to extirpate and remove the tumor cells, or by radiotherapy (1895) to destroy the cells in situ (3). Each of these methods has its limitation particularly in disseminated tumors and tumors located in certain parts of the body where the surgeon's knife can not be safely used and radiotherapy is ineffective. Thus a need was felt for an agent which has a less local and a more general control of malignancy such as could presumbly be brought about by chemical means. Ventures in chemotherapy started a long time ago and at different times in the past there had been applied such agents as belladonna, aconite, mercury, antimony and arsenic. Many of these chemical applications had a merely caustic action, as, for instance, in the local use of concentrated acids and alkalies. The modern era of clinical chemotherapy of cancer, however, started with the introduction of androgen control therapy 12 years ago. Since then, more than 10,000 (4) compounds have been tested of which some were found to be useful in the management of a variety of human malignant diseases. The first series of

compounds found useful were the nitrogen mustards introduced in 1944.

In 1948 Karnofsky (5) suggested possible approaches to tumor chemotherapy. These suggestions are related by Gellhorn (2) as follows: (a) destruction of the «neoplastic component» of the malignant cells; (b) damage to functional and chemical characteristics common to normal and neoplastic cells; (c) stimulation of tissue defenses which limit the growth and spread of malignant cells; (d) alteration of the environment of the cancer cell; (e) interference with the tumor blood supply; and (f) modification of systemic toxicity produced by cancer.

The chemotherapeutic agents used at present are of four types. The first type includes substances like the sex hormones which tend to depress the function of certain specific tissues which in turn accomplish a restraining effect on the tumor growth. The second type includes substances which modify the systemic intoxication produced by cancer such as sex hormones, ACTH and cortisone. Compounds such as urethane, folic acid antagonists, nitrogen mustards, TEM, Myleran, etc. belong to the third type of drugs which cause damage to cellular functions common to normal and malignant cells. More recently 6 - mercapto-purine (Purinethol), closely related to guanine and hypoxanthine, has been introduced and is probably an antagonist of desoxyribonucleic acid of the genes of cancer cells which is unlike that of normal cells. This new product forms the basis of a fourth type of cancer chemotherapeutic agents. Podophyllin will be considered under separate group by itself. The antibiotics have been investigated also and they will be briefly considered.

I. **Drugs which Depress the Function of Certain Specific Tissues.** The clinical application of this therapeutic principle is exemplified by androgen control therapy of disseminated prostatic carcinoma. This method of treatment is based on the findings of Gomori in 1941 and Gutman in 1938 who respectively stated that normal adult prostatic epithelium is rich in an acid phosphatase (7) and that malignant prostatic epithelial cells are also rich in acid phosphatase, and when the tumor has extended beyond the confines of the prostate gland the serum phosphatase is elevated in about 65% of cases (8). On the basis of these facts together with the already known functional dependence of the prostate upon the androgenic hormone Huggins and Hodges (6) demonstrated that the acid phosphatase of serum is reduced in metastatic carcinoma of the prostate by decreasing the activity of androgens through castration or estrogenic injection and that the enzyme is increased by injecting androgens. They concluded that prostatic cancer is influenced by androgenic activity in the body and disseminated carcinoma of the prostate is inhibited by eliminating androgens, through castration, or neutralization of their activity by estrone injection. At the present time, castration, together with the administration of estrogens, is the accepted and generally employed method for the therapeutic management of the disease. If the tumor responds (1), a general feeling of wellbeing and relief of pain occurs within a few days to several weeks which may last anywhere from several months to several years. When found effective, hormonal treatment should be continued for at least three months. A second course may be given if symptoms reappear. Diethylstilbestrol in 10 to 15 mg. daily doses given orally is the estrogen usually used. Castration (orchiectomy) together with the administration of estrogen, is also used in the treatment of the carcinoma of the male breast.

II. **Drugs which Modify the Systemic Intoxication Produced by Cancer.** Gellhorn (2) states that « the systemic toxic manifestations may determine the clinical picture of malignancy. Death in patients with malignant disease is not only caused by mechanical interference with the function of vital structure but also by stable mechanisms which result in fever, anorexia, hypoproteinemia, intravascular hemolysis, depression hematopoiesis, disturbances of carbohydrate metabolism, and probably many other metabolic abnormalities. These

alterations lead to the clinical picture of toxemia and cachexia of malignancy. Although no specific correction of the disturbances just mentioned is recognized, nevertheless chemotherapeutic agents are available which pragmatically support the host against the ravages of his disease». Examples of these chemotherapeutic agents are presented below.

A. **Hormones used in the treatment of carcinoma of the female breast:**

Androgens. In 1919 Loeb (9) demonstrated the relation between the female sex hormone and the incidence of mammary cancer in female mice. The results of his experiments showed that castration of female mice with a high incidence of spontaneous, mammary carcinoma significantly reduced the frequency of occurrence of the tumor. Loeb's observations were confirmed by Lacassagne (10) who showed that the female sex hormone provoked the formation of spontaneous tumors in certain strains of mice. He was not able to explain experimentally the mechanism of production of adenocarcinoma by estrone, but he postulated that the strains slightly susceptible to cancer comprise those mice whose excretory functions rapidly promote an elimination of estrone, while in those mice susceptible to cancer, estrone may be retained, accumulating in certain points in the organism particularly the mammary ducts. He further suggested that estrone by stagnation is transformed into one of the carcinogenic compounds (10). Lacassagne was the first to suggest the use of androgens for the treatment of breast cancer. When first tried, testosterone was given in small doses to women with advanced breast cancer and results were not favourable. Farrow and Woodard (55), in 1942 observed subjective but no objective improvement in about half of 33 patients receiving androgens. Later, in 1946, Adair and Hermann (11) using large doses of testosterone (300 mg./week) reported favourable results with this hormone in the treatment of a proportion of eleven cases of advanced breast cancer.

In 1951 a subcommittee of the Council on Pharmacy and Chemistry (12) of the American Medical Association reported its analysis of 450 cases of advanced breast cancer treated with androgens. Subjective improvement was shown in 80 % of the cases, who had relief of bone pain, increased sense of well-being with improved appetite, and weight gain. Only 20%, however, showed objective improvement.

The mean survival time (12) of those patients improved by androgens, when correlated with the type of metastases, are: soft tissue, 11 months; bone lesions, 13.6 months; lung, 8.7 months. When these data were compared with unimproved patients of the same categories, it was seen that androgen therapy prolonged life only a few months (12), but these brief remissions with some months of enjoyable life are worth while.

Side effects from administration of testosterone to women are very common. The most serious is edema from retention of salt and water. Minor complications include hirsutism, a bass voice, acne, loss of hair, and hot flushes. Care should be exercised in the use of testosterone in elderly hypertensive patients.

Androlone*, Neodrol** (41, 52) is a hormone-like chemical, androstane-17-(beta)-ol-3-one, introduced recently for the control of inoperable carcinoma of the female breast. Its anti-tumor and anabolic effects are very similar to those of testosterone, but with markedly less androgenic effects than the testosterones. The drug is available in the form of a suspension in 10 cc. vials. It is injected intramuscularly in 100 mg. doses daily or three times a week as indicated.

Estrogen. Although estrogen is a carcinogen with respect to the mammary gland in certain species and strains, estrogens have an ameliorative effect on certain patients with advanc-

* **National Drug Co., U.S.A.**

** **Pfizer-Syntex, U.S.A.; Foundation Lab. U.S.A.**

ed mammary cancer. The mechanism of action is unknown, the observation being completely empirical in origin (56).

«The most important basis for the use of estrogens, after it has been determined that conventional surgical or radiotherapeutic measures are inappropriate, is the age of the patient and her temporal relationships to the menopause. Estrogens should be limited to patients at least 5 years post-menopausal. Disregard of this condition may be followed by fulminating progression of the malignant disease (2)».

In brief it can be said that castration is the generally accepted routine for the treatment of female metastatic breast cancer in women who are still menstruating. Castration by radiation is usually done because it is less discomforting than surgery although the latter procedure is quicker and more complete. If symptoms are not controlled, androgen therapy is given. In women past the menopause, estrogens are given for soft tissue and lymph node metastases, and androgen for bone metastases (1).

Other steroids tried are, methylandrostenediol (12, 57, 58, 59), androstenediol (60), progesterone (61) and anhydrohydroxyprogesterone (62).

B. ACTH, Cortisone: Gellhorn (2) summarizes the present knowledge about ACTH and Cortisone in the treatment of leukemia and lymphomas as follows: «... Cortisone and ACTH can modify the manifestations of malignant lymphomas (lymphosarcoma and Hodgkin's disease) but do not affect the neoplastic cells significantly. Their action is apparent only while they are being administered and within days after discontinuation the clinical evidence of the disease returns. The chief value of ACTH and Cortisone in the treatment of the lymphomas is sharply limited to a particular phase of the disease. It is common in the final stages of patients with Hodgkin's disease or lymphosarcoma for a pancytopenia to develop, in part due to the effect of the disease on hematopoiesis and in part due to the treatment with X-ray and/or drugs which depress bone marrow function. At this time the patient usually has severe constitutional symptoms such as fever, malaise, and anorexia. In the past . . . this was recognized as the preterminal phase of the patient's illness. To a certain extent ACTH and Cortisone have altered the prognosis. Following the induction of hypercorticism the temperature may return to normal, a sense of well-being may be restored with improved appetite and strength.

There is no effective therapy for acute leukemia of adults and the chief therapeutic weapon has been blood transfusion. Thrombo-cytopenia with purpura is an almost unvarying characteristic of the natural history of this dyscrasia and death is not infrequently due to bleeding. It has been found that in a significant proportion of patients the purpuric manifestations can be controlled temporarily with ACTH or Cortisone, . . . only symptoms are modified rather than the fundamental disorder. ... Thus, it can be seen that ACTH and Cortisone are temporizing drugs which improve signs and symptoms of constitutional toxicity but do not modify the tumor. The precise mechanism of action of the hromones is unknown.»

III. **Drugs which Cause Damage to Cellular Functions Common to Normal and Malignant Cells.**

Urethane. The idea of using urethane by Haddow and Sexton (13) in the treatment of leukemias and myeloma originated from the studies made by Dustin et al. (14) on various compounds affecting the mitotic cycle either in animals or plants and from an investigation performed by Templeman and Sexton (15) on the effect of arylcarbamic esters and related compounds upon cereals and other plant species. Haddow and Sexton chose for their investigation on Walker rat carcinoma 256, ethyl phenylcarbamate, isopropyl phenylcarbamate and ethylcarbamate (urethane). From the results of their investigations they

concluded that the three compounds had inhibitory effect on the growth of Walker carcinoma 256 and that the activity of urethane was actually greater than that of either of the phenylcarbamates. Later urethane was tried as a therapeutic agent for a variety of human tumors; its chief value is in the treatment of myeloid or lymphoid growths, especially chronic myelogenous leukemia (1). Occasionally remission may be obtained in lymphosarcoma and multiple myeloma (1). The dosage of urethane is usually 0.5 to 1.0 gm. by mouth, three times a day. If there is no response to this dosage an increased amount is rarely helpful (1). The mechanism of action of urethane is not precisely known. There is cytological evidence of interference with cell division, and therefore circumstantially, the site of action is probably on nucleoprotein or nucleic acids (1).

Folic Acid Antagonists. The use of folic acid antagonists in the treatment of acute leukemia in children was begun by Farber et al. (16) in 1948, using 4-aminopteroyl-glutamic acid (Aminopterin). In 1950 Stock et al. (17) experimented with 4-aminopteroyl-glutamic acid (Aminopterin), 4-amino-N-10 methyl pteroyl glutamic acid (Amethopterin), 4-amino-pteroyl aspartic acid (Adenopterin), and 2, 6-diaminopurine. From this study it was concluded «that under (animal) experimental conditions several analogs of folic acid exert an adverse effect upon tumor tissue. Some tumors are not affected by materials markedly inhibitory to other tumors. These effects are not achieved without some toxic manifestations in the host. In addition, none of the compounds at safe levels has damaged the tumor tissue sufficiently to prevent resumption of growth after administration of the drug is stopped.» Other analogs, Aninopterin and Amino-An-Fol, were studied by Sawitsky et al. (18).

Since toxicity of Aminopterin to the host has constituted a limiting factor in the treatment of neoplasia, studies were undertaken by Goldin et al. (20), determine in what manner the quantitative host-toxicity relationships demonstrated with folic acid, citrovorum factor and Aminopterin may relate to their effects on the growth of tumor. Earlier, Nichols and Welsh (19) reported that the lethal action in rats of Aminopterin, 25 micrograms daily, is not prevented by pteroyl-glutamic acid, but the daily administration of 250,000 Units of citrovorum factor (CF) completely counteracts the toxic effects of the antagonist. They also reported that CF is a biologically active derivative of pteroyl-glutamic acid as is shown by the fact that rats, in which growth is arrested by pteroyl-glutamic acid deficiency, and which due to aminopterin are refractory to pteroyl-glumatic acid, grow markedly when given concentrates of CF.

Shoenbach, Colsky and Greenspan (21) reported their results about the efficacy of Aminopterin and Amethopterin in the treatment of patients with disseminated neoplasms and children with acute leukemia. They reported also the signs and symptoms of toxicity produced by these folic acid antagonists. They observed that folic acid in large doses could inhibit minimally toxic doses of the folic acid antagonists. Citrovorum factor, however, was found to be a more potent agent for preventing or reversing toxicity. It is further reported that testosterone or renal insufficiency may enhance the toxicity of Aminopterin. The mechanism of action and the dosage regimen of folic acid antagonists is reviewed by Greenspan (22). These chemicals interfere with cellular metabolism by competing with essential metabolites to which they are structurally analogous. When administered they induce a folic acid deficiency and thereby to some extent arrest the growth of neoplastic cells. The most commonly used folic acid antagonist are Amethopterin and Aminopterin. «The usual dose of Amethopterin, depending upon the age, weight, size and physical condition of the patient, is 2.5 to 5.0 mg. daily given by mouth until a stomatitis, nausea or diarrhea occurs. The drugs are also discontinued if the white cell count falls too rapidly or if the bleeding tendency is increased. Following any of these reactions, treatment is stopped

for about a week, then a maintenance dose, usually half the daily dose that caused the toxic reaction, is given by mouth every other day (1)». «Aminopterin can be given intramuscularly or by mouth in doses of 0.5 — 2 mg. per day. It is advisable to begin dosage at the lower level and to increase it to the higher one if the bone marrow function is sufficiently well preserved. Once there is remission of the process treated (usually acute leukemia), it is well to institute maintenance therapy at from 0.5 — 1 mg. per day, or twice that amount every other day (63)».

Cortisone and ACTH. In acute leukemia of children these hormones produce subjective and objective improvement. «At the present time Cortisone is usually employed initially in the treatment of childhood acute leukemia. This appears to be the agent of choice, because the toxic manifestations of hypercorticism are less dangerous than the toxicity of the antifolic acid drugs. Theoretically, combination therapy of acute leukemia by the simultaneous administration of Cortisone and Amethopterin seems sound, since presumably the drugs are acting through different mechanisms. In practice, however, the efficacy of this regimen is no greater than either drug alone (1)».

Nitrogen Mustards. The nitrogen mustards, introduced in 1944, have been intensively and extensively investigated for their clinical value in the therapy of neoplastic diseases. Mustin or Methyl bis-(2-chloroethyl)-amine Hydrochloride (HN2), which is sold now under the trade name of Mustargen is the form of nitrogen mustard usually administered. «Nitrogen mustards are cytotoxic compounds which concentrate in tumor cells — lymphoid and myeloid — and cause their destruction. These compounds are chiefly used for palliation in the lymphoblastomas, especially Hodgkin's disease, and in leukemia, when symptoms can not be controlled by irradiation or by less generalized toxic forms of chemotherapy (1)». They are not effective in acute leukemias (63). «Cancer of the lung, particularly bronchogenic carcinoma, sometimes responds temporarily to nitrogen mustards. The remissions last only a few weeks but are often worthwhile for the relief afforded from the severe distress that occurs with this type of tumor. The combination of nitrogen mustards and x-ray therapy is sometimes more palliative than either of these agents alone (63)».

The dose is 0.4 mg. per kg. of body weight, divided over a two-or four-day period. The drug must be administered by intravenous saline drip infusion, since direct intravenous injection may cause a thrombosis; extravasation of the fluid causes severe inflammatory changes. The safest method of administration (63) is to start an intravenous infusion of saline solution and inject the required dosage into the rubber tubing after the saline has been running for some time. The saline should be kept running during and following the injection of HN2. Solutions for injections should be prepared immediately before use. Solutions lose their activity very rapidly.

Triethylene Melamine. After the widespread use of nitrogen mustard in clinical cancer therapy, hundreds of chemicals were synthesized and tested in the laboratory, but few were given clinical trial. Research has been directed toward finding a nitrogen mustard with a greater selective effect on tumor as compared with normal tissue and toward obtaining a derivative which can be administered more conveniently, than nitrogen mustard (HN2). The former effort has thus far not been successful and HN2 remains the generally used nitrogen mustard. Progress has been made, however, in the introduction of triethylene melamine (TEM) a substance originally developed for the crease-proofing of cloth, which qualitatively resembles HN2 in its therapeutic and toxic activity. There are two advantages of this drug. It is active when administered orally and causes inconstant and less severe nausea and vomiting than after nitrogen mustard (2). The most widely accepted (63) dosage is a total of 5 mg. per week given on two successive days. This is often administered with 2 gm. of sodium bicarbonate. If hemopoiesis is not depressed during the inter-

vening week, this dosage then may be repeated or increased as the case may indicate. Enteric coated tablets were recently tried (30). Reports on the clinical value of TEM have been made by Karnofsky (23), Wright et al. (24, 25) and others, (26, 27, 28, 29).

Myleran* or (1, 4-dimethanesulfonyloxybutane, GT 41). This compound was synthesized by Haddow and Timmis (32, 33) in the course of studies on bifunctional esters of bishydroxyethyl arylamines. This compound was found to produce depression of granulopoiesis in rats and in man (33). On the basis of this activity, a clinical trial of Myleran was concentrated on cases of chronic myeloid leukemia (34) and the results reported indicate that the drug is a promising therapeutic agent in the management of chronic granulocytic leukemia. The drug was given orally, in schedules of 4 to 10 mg. daily for four to sixteen weeks for a total dose of 200 to 500 mg. or in courses of 25 mg. daily for four to six days for a total of 100 to 150 mg. Later Galton (35) and Ledlie (36) reported an analysis of results of therapy in 56 patients with chronic myeloid leukemia. More recently Petrakis et al. (31) in a study of the effect of Myleran upon leukemia in twenty one cases confirmed the observations of Haddow, Galton and Timmis.

2, 4-diaminopyrimidines. Certain 2, 4-diaminopyramidines, synthesized for possible use as metabolic antagonists, were found to have antimalarial activity. These pyrimidines, including the newly introduced antimalarial Daraprim*, pyrimethamine or 5-(p-chlorophenyl)-2;4-diamino-6-ethylpyrimidine, were also able to inhibit the growth of L. casei and L. citrovorum, and this effect could be reversed by folic acid or folinic acid. For this reason it has been proposed that these pyrimidines probably inhibited the folic acid-folinic acid conversion (45, 46, 47, 48). Recently Nadel and Greenberg (49) reported the synergistic inhibitory action of Amethopterin and an antimalarial 2, 4-diamino-5-(3', 4'-dichlorophenyl)-6-methylpyrimidine (W-50-197) upon leukemia L 1210 in mice.

IV. **Drugs which Interfere with the Nucleic Acid Synthesis of Cancer Cells.** In an editorial, Tice (53) mentioned that, «recently it has been shown that the desoxyribonucleic acid of the genes of cancer cells is unlike that of normal cells. This is a most important discovery for it offers at least a chance of finding an antimetabolite to block the nucleic acid synthesis of cancer cells without seriously damaging normal cells. If this can be done a malignancy can be arrested including all metastases which of course are directly related genetically to primary lesion. Certain of the purine compounds which are nucleic acid precursors provide one avenue of approach in this study».

Already 6-mercaptopurine (Purinethol*) (37, 41) has given some success in treating acute leukemia and chronic myelogenous leukemia. It has not been found to be of value in chronic lymphatic leukemia, Hodgkin's disease, or solid tumors. The drug is available in 50 mg. compressed tablets. The usual initial dose is approximately 2.5 mg. per kg. of body weight per day orally. As a warning, physicians are asked to give the drug personally to patients and not to prescribe more than 3 or 4 days' supply at one time. Blood counts should be taken weekly and the drug should be discontinued or reduced in dosage at the first sign of depression of bone marrow function.

V. **Podophyllin.** For more than 200 years, references to podophyllum, podophyllin, and related substances have appeared in the scientific literature. These materials were popular chiefly as cathartics. About 10 years ago several reports have appeared describing the effectiveness of a 25% suspension of the resin in liquid petrolatum in rapidly curing the lesions of condyloma acuminatum, commonly known as «Venereal Wart» (39, 40). These reports aroused the interest of clinicians and since then a considerable number of

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* **Burroughs Wellcome and Co.**

papers have been published in many parts of the world on the cytological, biochemical, and pharmacological action of podophyllin.

Podophyllin and certain of its components have been shown to have a mitotic colchicine-like action following topical application to the skin (42, 43). These components have also been reported to damage transplanted tumors in mice following subcutaneous injections (44), but no explanation as to its ode of action was given. More recently Algire et al (54) presented experimental evidence showing that the in-vivo action of podophyllotxin and of podophyllin in causing necrosis in transplanted sarcomas results indirectly from its hypotensive effects on the peripheral circulation of the host. An extensive and excellent review on the biological effects and the chemical composition of podophyllin has been published lately by Kelly and Hartwell (38). The following is quoted from the summary with regard to the biological activity of podophyllin in the treatment of neoplastic diseases: «The extension of topical use of podophyllin to treatment of benign and malignant new growth followed demonstration of its therapeutic effect on condyloma, and recognition of its cytotoxic action on normal and pathological tissue. There have been a number of reports of successful treatment of papilloma of various sites, of senile keratosis, and of intradermal carcinoma. The drug is not recommended for infiltrating squamous — or basal-cell carcinoma because of the high incidence of recurrence after apparent healing. It has produced only mild palliative effects on ulcerative carcinoma of the breast.

A few attempts have been made to treat inoperable systemic cancer by parenteral or oral administration of podophyllin or one of its components. No evaluation can be made until more data have accumulated. To date, however, no unequivocal therapeutic effect has been obtained. Some microscopic evidence (mitotic arrest, necrosis) of damage to tumor tissue has been described in biopsy and autopsy material, but no effect on the hematopoietic system has been observed.

There has been some indication that podophyllin sensitizes tissue to the action of X-rays. The usefulness of such an effect in the management of cancer and many other diseases now treated with X-rays is obvious, and it is hoped that future studies will provide definitive information».

The chemistry of podophyllin shows that resins derived from different species of podophyllum differ in composition... «Podophyllin from any source is a complex mixture chemically which may, on future study, yield other substances of whose existence we are not yet aware. The implications of these facts for biological and clinical research seem to be clear, namely, that in working with this material due account should be taken of its non-homogeneity and non-uniformity of composition. The pure compounds derived from the different podophyllins should be of increasing interest in research of many kinds (38)».

VI. **Antibiotics.** Attempts were made to test many of the isolated antibiotics for their ability to retard the growth of Sarcoma 180 in vivo. In 1950 Stock (50) reported preliminary results on a small group of antibiotics. Recently Reilly et al. (51) reported the effects of 33 different antibiotics upon the growth of Sarcoma 180 in mice. None of these is outstandingly effective. Five namely actidione, actinomycin, illudin M, illudin S, and Terramycin — have slight retarding effects which, with the latter four agents, have been achieved only at doses toxic to the host. In addition to the testing of known antibiotics, some 1256 preparations, which included crude microbial culture filtrates as well as partially purified substances, have been screened by Reilly et al. (51) for tumor-inhibiting properties. Five of these crude antibiotic preparations caused sufficient retardation of tumor development to be considered for further work.

CONCLUSION

The present status of cancer chemotherapy is reviewed. Mention is made of those

drugs which have been found to be of definite usefulnss as well as some of the drugs which are still in the experimental stage.

The use of chemotherapy in cancer is becoming more wide spread. But because it is limited in its usefulness by the nature of its agents, it should never be substituted for surgery or radiation if these conventional methods may reasonably be expected to effect a cure. Indications for it limit its usefulness to cases which are otherwise incurable or as an adjunct to the conservative methods of treatment. The neoplasms that are known to be responsive to certain chemotherapeutic agents, and which should be treated with them, once the disease has progressed beyond curability by surgical or other methods, are lymphomas, lymphosarcoma, certain leukemias, and cancer of sex-dependent organs, such as the mammary and the prostate glands.

In the use of these chemotherapeutic agents the physician must be well aware of their limitations, their side actions, and the toxic manifestations they might produce.

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RUTIN

by **Prof. Edward Vorperian**

The isolation in pure form and in maximum yield of the active constituents of plants offers intricate and interesting problems for research. And thus the problem of studying the factors which influence the quality and yield of rutin from tartary buckwheat was assigned to me. Further on, the reader will find a brief summary of my findings.

Rutin, a glycoside of the flavonol quercetin, is finding an extensive use in the treatment of abnormal capillary fragility and permeability associated with a number of hemorrhagic disorders.

Although rutin was first discovered over a hundred years ago by Weiss (1), no mention was disclosed by him in regard to its chemical nature or its pharmacological action and use. The chemical nature of the compound was thoroughly investigated over a period of 25 years beginning with von Kostanecki (2) who, in 1909, succeeded in proving the quercetin fraction of the molecule. Finally, Zemplen and Gerecs (3), in 1934, synthesized the whole molecule and proved it to be identical in all its chemical and physical properties with the natural product obtained from the various plant sources.

A discovery reported in 1936 was received with scepticism by the scientific world and stirred up active controversy concerning the subject. Szent-Gyorgyi (4), a later Nobel prize winner for his work with vitamin C, had observed that certain hemorrhagic disturbances failed to respond to purified vitamin C, and that improvement had occurred only after the administration of lemon juice or Hungarian red pepper. This led him to suspect that the response was due to the presence of some unknown active constituent of the extract other than ascorbic acid, and that this constituent was lost from the natural vitamin C during the purification process. Fractionation of the extract finally brought about the isolation of an active crystalline substance which consisted of a mixture of flavone glycosides. When administered to human beings with abnormally permeable and fragile capillaries, this fraction regularly restored to normal the carpillary resistance and function within a short period of time. The name **citrin** or **citrin flavone** was coined to indicate its origin, and the name Vitamin P. **permeabilitat vitamin,** by its discoverer, to show its vitamin-like effect on tissue permeability.

Other investigators who failed to reproduce the results obtained by Szent-Gyorgyi and his associates in the treatment of permeability defects in capillaries, seriously questioned the existence of the so called Vitamin P (5). This doubt was dispelled to a great extent by the subsequent work of Elmby and Warburg (6), who reported that certain hemorrhagic cases associated with vitamin C depletion were not benefited even by large amounts of ascorbic acid. However, the bleeding tendencies disappeared and a high blood level of vitamin C was noted following the administration of large quantities of lemon juice. Rusznyak and Benko (7) later claimed that lower carpillary resistance in scorbutic guinea pigs was not related to the vitamin C deficiency and that it was corrected only by

the administration of **citrin** . These findings suggested that vitamin P serves as an auxiliary to ascorbic acid, in some way potentiating its pharmacological action.

As time passed, chemical studies on **citrin,** revealed that it was a crystalline mixture of hesperidin and the related glycoside of eriodictyol. Hesperidin alone appeared to be more or less inactive as compared with eriodictyol, by many investigators in the field, was considered to be responsibl for the vitamin P - like activity of **citrin.**

Scarborough (8) , after a thorough study of the matter , called attention to the probable multiple nature of the capillary fragility factor. He pointed out that the activity of pure eriodictyol was not sufficient to account for the potency of many plant extracts possessing similar curative value. He examined these plant extracts chemically and showed that the activity of each of them was due to compounds of related structure belonging to the flavone, flavonol and flavonone compounds. In recent years research has uncovered several substances in the flavonoid series which have been found to exhibit vitamin P — like activity.

Rutin, being a rhamnoglucoside of the flavonol quercetin, has been found to possess considerable activity in increasing capillary resistance in man and in guinea pigs. At present it offers great promise in the treatment of capillary fragility, retinal hemorrhage, apoplexy, certain drug intoxications, excessive after effects, etc.

The definite establishment of the vitamin P — like properties of rutin is due mainly to Griffith and Lindauer (9) . Couch and his co-workers (10) developed commercial methods of extracting and purifying rutin from various plants, primarily from Fagopyrum esculentum, and Fagopyrum tartaricum, known in commerce as Japanese and tartary buckwheat respectively.

Experimental

To provide an adequate supply of the fresh plant needed for the experimental work (11), one pound of tartary buckwheat seeds were planted in early spring. The sprouting of the seeds began ten days later and thirty-seven days after germination the plants had just reached the early blossoming stage.

To determine the influence of age on the rutin content of the buckwheat plant, crops were harvested at three different stages of maturity, namely thirty-seven, forty-six and fifty-four days after sprouting. The fresh plants were analyzed for their original moisture and rutin content. Six assays, using Naghski's method (12) for determining rutin, were run in duplicate in each of the three harvests. The results thus obtained indicated that the rutin content varied with the age of the plant, gradually decreasing from 6.1% at the early blooming stage to 5 % as the seed began to set, calculated on moisture free basis.

The handling of the fresh crop presented some difficulties because of its tendency to lose rutin due to wilting. Experiments conducted to determine the effect of various drying conditions upon the rutin content have invariably shown that the loss was greater when the drying process was prolonged, especially when carried at ordinary temperatures. Leaf meals obtained separately from each of the three harvests, prepared by the sun-drying method, showed an average loss of 38% in rutin content. Of the four different methods of drying, investigated during the experimental work, lyophilization produced leaf meals with greatest extractable rutin content, the average loss of rutin being only 12.6%. However, from a practical point of view, equally good results were obtained with the Stoke's oven-drying method at 80° C., using dry air for the inlet circulation. The average loss of

rutin by this method of drying was found to be only 13.4%.

The rutin-extracting efficiency of four solvents was tested on the fresh and dried buckwheat leaf . The best solvent for optimum rutin yield from the fresh leaf was reconfirmed to be 85 % v/v of hot isopropyl alcohol, and from the dried leaf to be 75 % v/v of hot isopropyl alcohol.

During the experimental work, the various operations involved in the extraction methods, as described in the literature, were tested. The step developed by Couch et al. (10), concerning the removal of fatty matter and pigments, by straining the hot crude liquid concentrate through glass wool and canvas was found to be inefficient and involved some loss of rutin during the straining. Also, the presence of traces of fat in the strained liquid prevented the complete crystallization of rutin from the solution. This step was modified by cooling the crude liquid concentrate to room temperature and defatting it with six or more successive portions of petroleum ether, b.p. 52° C., until the aqueous layer acquired a pale orange color. Any rutin which may have separated out during the cooling or the extraction of the fatty matter did not inferfere, with the subsequent operations. By this modification, improved yields and a purer grade of rutin were obtained.

Pharmacology

The pharmacology of the flavones, flavonols and flavanones has not been studied extensively enough. Based on a comparatively limited number of experiments and observations, some theories in regard to the pharmacodynamics of rutin have been postulated.

Lavollay (13). Parrot and co-workers (14) concluded that vitamin P-like substances, including rutin, exert their various effects on the capillaries by the inhibition of the autooxidation of the circulating epinephrine. According to their observations, the epinephrine sparing action was more prominent with those compounds which possessed greater vitamin P-like activity. This theory, however, throws light on one phase only of the whole pharmacodynamic picture.

Embrose and DeEds (15) produced capillary injury on the depilated ventral surface of albino rabbits by local irritation with chloroform or intracutaneous injection of histamine. They found that the prior administration of rutin decreased greatly the capillary damage from both causes. The extent of damage was determined by injecting intravenously trypan blue and observing the accumulation of the dye in the irritated area. They finally concluded that the protective action of rutin on the capillaries was due to the prevention of the liberation of endogenous histamine.

Another approach to the problem has lead to the study of the effect of certain flavones in inhibiting the action of the **spreading factor** identified as the mucolytic enzyme **hyaluronidase.** As is well known the viscosity of the ground substance including the precapillary sheath, is maintained by the polysaccharide hyaluronic acid. The gels formed by this acid serve, in part, as the cement which holds the cells of the connective tissue together. The normal state of connective tissue permeability and resistance can therefore be influenced by the spreading factor or **hyaluronidase** which catalyzes the hydrolysis of the hyaluronic acid of the ground substance.

The etiology of this abnormal hemorrhagic state therefore remains rather obscure. Any one of a number of causes may be involved in impairing the barrier function of the endothelial cells, as in many infectious diseases, in certain allergic states, in toxic conditions caused by drugs or other substances, in deficiency states resulting from a suboptimal

intake of nutrients other than ascorbic acid, and under certain conditions of unusual stress as in hypertension.

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The more one studies, the more one realizes his ignorance; the more one teaches the more one is conscious of his shortcomings.

Confucius

Silicones in Pharmacy and Medicine

by **Levon M. Karamanukian B. A., Ph. C.**

Since their introduction into industry about a decade ago by the Dow Corning Corporation, silicones have been used to great advantage. Their uses appear to be as unlimited as the number of the possible polymers. In spite of the variation in composition and form of the different silicone polymers, they have certain properties that are common to all: resistance to oxidation, stability to extremes of heat, water repellency, etc. Silicone paints have exceptionally good weathering properties. The water repellent property is made use of in the textile industry to develop shower proofness; for coating of glass, laboratory ware and vials for injections; for water proofing ceramic materials and tiles in masonary etc. Their low surface tension has been made use of in polishes, as mould releasers in the rubber, plastic and metal casting industries. They are also used as antifoaming agents in industry.

Silicon is an electropositive element, resembling chemically boron, germanium, tin as closely as it resembles carbon. It shows great affinity to oxygen. It commonly exhibits a covalency of four but is capable of a maximum covalency of six in combination with atoms of relatively small volume and high nuclear charge, e.g. SiF6=(fluorosilicate ion). Under a variety of conditions, unexpected vigorous reactions occur, unknown in analogous reactions of carbon compounds due to its hexacovalency and electropositive nature(1).

The hydrides of silicon form homologous series called silanes, which bear a structural resemblance to the methane series of saturated hydrocarbons. For example, we have monosilane SiH4, disilane Si2H6, trisilane Si3H8, up to hexasilane, the higher silanes being unstable. The halogen derivatives of the silanes are important as starting materials for the synthesis of other silicon compounds.

The true organic compounds of silicon are those in which alkyl or aryl groups are linked directly through carbon-silicon bonds. These could be:

(1) alkyls of silicon having the general formula of SiR4, where the R may represent an aliphatic or aromatic hydro-carbon radical,
(2) alkylsilanes e.g. trimethylsilane, (CH3)3HSi,
(3) alkylhalosilanes e.g. methylallydichlorosilane CH3. Si (C3H5) Cl2,
(4) alkylalkoxysilanes e.g. phenyltriethoxysilane C6H5. Si. (O.C2H5)3.

The above monomer groups, become polymers through repetition of some unit structure within a larger molecule e.g. 1,2 diethyldisilane C2H5.H2Si-SiH2.C2H5. We may also have silicon-carbon chains where alternating carbon and silicon atoms of the type —C—Si—C—Ci—C—Si— serve as structural framework. Or we may obtain siloxane chains, where polymers make use of silicon-oxygen framework —Si—O—Si—O— either in straight chains or in cyclic form. The compounds of the empirical formula (R2SiO—)n were named silicones by Kipping. The silicones form a large number of materials including oils, resins and elastomers (rubbers). The various physical forms assumed reflect the different molecular complexities of the polymers, for the oils are linear molecules, the resins are cross-linked aggregates of cyclic and linear structure, and elastomers are superpolymers of much higher molecular weight and of unknown structure.

The silicone fluids (oils) used in pharmacy are clear oily liquids which are odorless, tasteless, insoluble in water and resistant to oxidation by air and to many chemicals. Their

viscosity depends on the average polymer chain length. Silicone liquids that remain true liquids at high and low temperatures can be produced in any viscosity. Silicone resins have the consistency of petrolatum but show little variation in consistency over a temperature range of —40°C. to 250°C. The silicone rubber has many properties similar to natural or synthetic rubber, but in addition it is stable to extremes of temperature (—90°C to 250°C) and is resistant to many corrosive chemicals. Commercially available silicones are miscible with amyl acetate, benzene, carbon tetrachloride, chloroform, ethylene dichloride, ethyl ether and others.

All these properties have been made use of in industry, research, pharmacy and medicine. The following are some of their pharmaceutical and medical uses.

Water Repellent Properties

When silicone films are applied to the inner walls of pipettes, burettes, beakers, flasks and other analytical glassware, a great saving in time and an increased accuracy are accomplished. Such treatment eliminates frequent rinsing, washing and drying of the apparatus. Usually no rinsing is necessary between pipetting of different solutions. Volumetric ware becomes more precise because there is no residue left in the container. This is of special value in micronalytical work, where silicone treated microliter pipettes give accurate and convenient measurements (2). Coated rods carry no liquid with them, and there will be no loss of solution or suspension down the outside of containers when the poring lip is coated. Additional uses are found in absorption spectrophotometry, flame photometry, electrochemical pH measurements, etc. (3).

Silicone treated vials are now used for parenteral products. Because the vials drain freely, the dosage is complete and waste is cut down considerably(4). These vials are now commonly treated with a dilute (2%) solution of Dow Corning 200 Fluid, in some suitable solvent as carbon tetrachloride, drained free of excess solution and baked at about 300°C for 30 minutes(5)*.

Silicone treated needles, syringes, glass tubing, bottles, and other vessels delay the clotting of blood, hence blood can be stored for longer periods and injected with less danger of quick clotting.

The water repellent properties of silicones have also been made use of in permanent hair-wave, especially in the curly hairs of colored people. The hairs are first straightened, then an emulsion of silicone is applied, and then the hair is set «permanently». This treatment with silicone, prolongs the life of the set, as it is not affected by rain or wind as formerly.

Substances that are used to produce these water repellent properties are alkylhalosilanes such as methyltrichlorosilane, dimethyldichlorosilane, and lauryltrichlorosilane or alkylalkoxysilanes such as ethyltriethoxysilane. The action of these compounds on the glass is a hydrolytic one in which the adsorbed molecular film of water on the surface of glass reacts with the silane liberating a halogen acid such as HCl from an alkylhalosilane, or an alcohol from an alkylalkoxysilane, and leaving, integrally attached to the surface, a film of substituted siloxane. The polar Si—O bonds apparently exhibit an affinity for the similarly constituted structure of the glass surface and the organic radicals, directed outwards, provide the water repellency. Glass surfaces must be completely clean and dry in order to ensure a uniform coating. Once applied, the film is permanent for at least 3 years. Solvents that attack the film are strong alkalies and HF.

*** The vials are covered by patent No. 2,504,482 held by Dow Corning Co. and Premo Pharm Labs.**

Abhesive Properties

Abhesive properties as contrasted to adhesive properties are shown in products treated by silicones. The abhesive property is made use of in the following.

A new British patent issued to Dow Corning Ltd. covers the use of silicones as polishing agents in dentifrices(6). When incorporated in a dentifrice, the silicones are said to aid in preventing the adhesion of food particles to the teeth and the deposition of tobacco stains. It might be expected that such a dentifrice would have little tendency to foam as the silicones are powerful anti-foaming agents.

Special silicone-treated lens tissue is now available for removing dust, dirt, lint and smears from lenses. This tissue leaves, according to the manufacturers (Silicone Paper Co. of America Inc.) an invisible coating of silicone on the lenses which protects them and gives them longer clarity, making cleaning easier, better, faster and more lasting.

If tablets, pills and capsules are coated, they will become moisture repellent, odor free, and resistant to various deteriorating influences and at the same time they acquire a high gloss, a smooth finish, and a non-dusty surface. These tablets, pills, capsules can be coated by allowing vapors of silicone resins to contact the materials or preferably by submerging them in silicone resins dissolved in suitable solvents.

The removal of pills, capsules, etc., from molds previously treated with silicones, is made easier and losses due to cracking or crumbling are greatly reduced.

In the preparation of dry extracts, if the pans are coated before evaporation is started, the extract comes off from the pans with great ease, without sticking to the walls.

Paper treated with silicones, possesses a surface to which no powder will stick and no tape ill adhere. Hence it can be used as weighing paper.

Anti-foam Properties

Because of its powerful anti-foam properties, silicones are sometimes added to aqueous cosmetic lotions containing a solubilized perfume oil. The solubilizer being a surface active material may cause the lotion to foam excessively during mixing or bottling operations. The addition of a trace of Corning's Antifoam A or a similar product is sufficient to control the foam. In some cases, about 1 part per million is sufficient to eliminate foaming. This property is also made use of in fermentation vats of certain antibiotics, saving time and space. The anti-foam property is also made use of in colloid mills and in high speed mixers.

People suffering from pulmonary edema, are constantly threatened with the possibility of death due to foaming of the fluid accumulated in the lungs. Silicone sprays keep the lungs foamless. When silicones are given orally in concentrations as high as 2 per cent of body weight, by inhalation in concentrations as high as 4,500 parts per million, or applied topically to the skin, no untoward effects are observed(7).

Low and High Temperature Stability

A variety of silicone fluid is used in oil sterilizers for instruments used by dentists(8) and physicians. The oil is stable to 250°C for more than 1000 hours, with minor changes in viscosity. It has the advantage of not smoking, not volatilizing or steam

secretions of the mucous membrane. It is usually employed to provide a continuous medicating or germicidal action. It will absorb or give up moisture to the atmosphere, depending upon the humidity. Therefore, it should be stored in tight containers, prefarably of glass. The third type, represented by soap suppositories or Glycerin Suppositories U.S.P. (should not be confused with Glycerin Suppositories B.P. which contain no sodium stearate.) is not expected to melt or dissolve, but to perform its function largely mechanically, producing some irritation, stimulating peristalsis, and causing evacuation of the bowels. It is largely used for children to avoid the use of laxatives(2).

In listing the desirable characteristics of a suppository base, two different aspects should be considered: formulation of the base, and absorption of the drugs from the base. From the standpoint of formulation the ideal base should be stable, pour easily, set quickly in the mold, not require greasing of the mold, have good appearance, be easy to remove from the mold, not be necessary to refrigerate, and be compatible with all medicines. From the standpoint of drug absorption from the base, it should be neutral in reaction, be non-irritating, present the drug in a readily absorbable form, completely melt or dissolve within 30 minutes, and not leak from the rectum(6).

Cacao Butter or Oil of Theobroma. This has been long ago considered to be the ideal base for suppositories intended to melt when inserted into the rectum or other body cavities. It is a bland non-irritating oil and possesses the remarkable quality of maintaining its firmness to within a few degrees of body temperature, when it readily melts to a liquid, without passing through an appreciable softening stage. The melting point of cacao butter is from 30-35°C. but will be lowered if subjected to a higher temperature. It is rarely necessary to raise the melting point of cacao butter by the addition of wax or spermaceti (10-15%), except in the warmest weather, or when phenol, camphor, chloral hydrate, volatile oils or other substances, which will soften cacao butter, form the medicating ingredients (2).

One of the difficulties with a cacao butter suppository is that, when it is inserted, it promptly melts, and leakage occurs frequently carrying with it the medicament. In addition to this, oil-soluble drugs are not readily released from the base. In contrast, suppositories made with glycerinated gelatin slowly dissolve in the secretions and provide a slow and continuous release of the medication. (7).

Glycerinated Gelatin. Gelatin meeting U.S.P. specifications is available in two types known as Pharmagel A and Pharmagel B. Each one is used under different circumstances. Pharmagel A is prepared from acid-treated precursors and is used at a pH of about 8.0.

In making use of gelatin as a suppository base (7), we have to consider optimum conditions for the medicament to be incorporated with the base. Since Pharmagel A is positively charged (cationic) and is available at an acidic pH, it has the incompatibilities of both a positive colloid and a weak acid. For instance, ichthammol suppositories made with Pharmagel A were found to be granular. This is explained by the known incompatibility of ichthammol with acids. Mild silver protein, which is anionic, was also found to be incompatible with cationic Pharmagel A. In some case, however, either one may be used interchangeably .

New Water-Soluble Supositary Bases. Many attemps have been made to find substitutes for cacao butter and for glycerinated gelatin. No generally satisfactory substitutes have been found yet. Few of these will be briefly mentioned.

Carbowaxes are polyethylene glycol polymers introduced in Germany under the name Postonal and known in France as Scurol. Carbowaxes 400, 1540, 4000 , and 6000 were

found to be suitable when used in the proper proportions. They are non-absorbable and non-irritant. Hassler and Sperandio (6) proposed several formulae for this type of water-soluble suppository base. A related base, polyethylene glycol monostearate or Monolene (1) has also been proposed . Gross and Becker (8) proposed a suppository base consisting of a mixture of polyethylene-30 stearate, water, white wax, and aerosol O.T. This base has a high melting point, allows the handling and storage at elevated temperatures, permits a high percentage release of the medicinal substance, and is non-irritant.

Other substances which were recently suggested as suppository bases are hydrogenated peanut oil, coconut stearin, a mixture of oleic and stearic acids, and a mixture of one part of spermaceti and three parts of olive oil (1,5).

Experiments (7) done on the three types of bases (cacao butter, glycerinated gelatin and water-soluble bases) with oil-soluble and with water-soluble antiseptics showed that the glycerinated gelatin base was best for oil-soluble antiseptics. However, if the oil-soluble antiseptic is incorporated in cacao butter it will not diffuse into the water phase in sufficient quantity to affect the organism against which it is supposed to act. The reason for the negative results with the carbowax base is not yet understood, since, like the glycerinated gelatin, this base is water soluble. Experiments with the water-soluble antiseptics were inconclusive. It seems likely that glycerinated gelatin is the best and most reliable vehicle to use for introducing antiseptics into body cavities in suppository form.

Moreover, absorption tests done with different bases showed that the onset of action was more rapid from cacao butter suppositories than from water-soluble ones, but the duration of action was longer from the water-soluble suppositories than from the cacao butter ones (6). Comparison of rectal absorption of sodium salicylate in cacao butter and in 4 synthetic bases — cetyl phthalate, synthetic paraffin waxes, and two polyethylne oxide , bases — showed that the latter bases permitted greater absoption than cacao butter(9). However, according to Hassler and Sperandio each medicament should be tested for the base that would permit its absoption best.

Concerning the compatibility of drugs with water-soluble bases the following drugs have been tried and found compatible : phenobarbital sodium, seconal sodium, amytal sodium, ethylaminobenzoate, camphor, resorcinol, aminophylline, chloral hydrate, tannic acid, quinine sulfate, sulfathiazole, chlorobutanol, thymol iodide, chlorophyll, mercurochrome, and gentian violet (6).

Concerning the release of medication from the base, experiments showed that the inclusion of distintegrating agents, similar to those used in tablets, can increase the percentage of medicinal release of a high-melting base which is only fairly soluble. Furthermore, the addition of small percentages of aerosol O T aided in the solution or dispersion of the base and resulted in a higher percentage of medicinal release. On the other hand, it was found out that the addition of cholesterol, cetyl alcohol or wax decreased the percentage release of medicament from a cacao butter base(10).

The use of a dusting powder to prevent suppositories from sticking to each other or to the mold should be avoided, since non-healing lesions may develop from repeated use of such products (4).

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It is not what we eat but what we digest that makes us strong

Not what we gain but what we save that makes us rich

Not what we read but what we remember that makes us learned

And not what we profess but what we practice that makes us christians.

Roger Bacon

SEMINARS

ABSTRACTS OF SEMINAR PAPERS PRESENTED BY MEMBERS OF THE SENIOR CLASS * +

ARRANGED ALPHABETICALLY BY SUBJECTS

DRUG ADDICTION

by Jerry Zerounian

The Merck Manual (Merck and Co., Rahway, N.J., 1950) defines drug addiction as «a condition in which an individual has become so accustomed to the repeated, daily use of a drug, that he is dependent upon it for his sense of well-being and, if forced to abandon it, suffers a psychic craving and may, though not necessarily will, develop a characteristic 'abstinence syndrome' due to alteration of certain physiologic processes».

«Among the drugs that may cause addiction are the opiates (morphine, heroin, Dilaudid, metopon, Dicodid, eukodal, and codeine), the synthetic analgesics (Demerol, methadone, phenadoxone, etc.), sedative drugs (bromides, barbiturates, chloral, and paraldehyde), cannabis, alcohol, and cortical stimulants (cocaine, amphetamine, etc.).»

Quoting further from the same reference, «three basic facts should be understood: (1) Drug addicts must be treated in a rigidly controlled environment, as in institutions. (2) Withdrawal of drugs is not synonymous with treatment, but is only the first, simplest, and easiest step. (3) Psychotherapy offers the only hope of relief for drug addiction, and it must be carried out continuously for several months or even years if good results are to be expected».

Tetraethylthiuram Disulfide, known under various proprietary names such as Abstinyl, Antabus, Antabuse, and Cronetal is a creamy-white powder, insoluble in water, used in the treatment of chronic alcoholism. The drug is harmless when taken by itself, but if alcohol is absorbed subsequently, unpleasant and potentially dangerous reactions occur. (Martindale, The Extra Pharmacopoeia, V.I., The Pharmaceutical Press, London, 1952).

*** The original texts of these seminars are available for reference at the Director's office, School of Pharmacy. The abstracts have been prepared by Prof. C. ABOU-CHAAR.**

+ Names of graduating students are spelled here according to the transliteration system employed at A. U. B. The spellings of their names as they are written on their diplomas, appear under their photographs in the first part of the yearbook.

NEWER METHODS OF ALKALOIDAL ASSAYS

by Charles Nassar

The seminar paper is a good review of methods of analysis of individual official alkaloids. Two thirds of the paper is devoted, however, to a review of the new methods which are being investigated for the assay of these alkaloids.

The following are extracts from the «conclusion» given by Charles Nassar in his paper :

The extensive work that has been done and is still being done on alkaloids and their determination, is an apparent indication of the desirability in modern analysis of determining to the utmost accuracy the amounts of these constituents as they occur in crude drugs or pharmaceutical preparations.

Among the newer methods, chromatographic procedures seem to be the leading ones and the most widely used (see **The Apothecary** 1953 p. 75). Chromatographic procedures are mainly concerned with the separation of the individual alkaloids when in a mixture or when contaminated with extraneous matter ....

Photometric procedures are next in importance. Compared to chromatography, they are older methods which are widely used at present (see Photometry and its Applications, **The Apothecary** 1952 p. 49). The assays of many alkaloids are being reinvestigated with the intention of adopting photometric procedures to replace the official gravimetric or volumetric methods so very familiar in the pharmacopoeias.

Other methods, such as the polarographic methods, are not yet adequately developed and at present are of limited application in alkaloidal assays, though in future they may prove to be more useful. In polarography, the sample to be examined is dissolved in a base solution containing an excess of a base or supporting electrolyte, and is placed in a special electrolytic cell, which has a pool of mercury as anode and mercury dropping from a capillary at the rate of one drop every 2 to 4 seconds as cathode. When gradually increasing voltage is applied to the cell and the corresponding current is measured on a galvanometer, it is possible to determine from the resulting current-voltage curve both the nature and the concentration of the reducible substances in the sample. See J. E. Page, in J. Pharm. Pharmacol. **4**, 1, 1952).

THE NEWER ANTIBIOTICS

by Arthur Yuhanna

Antibiotics were last reviewed in **The Apothecary** 1952 where the following antibiotics were discussed: Neomycin Sulfate (marketed by Lilly and Upjohn), Polymyxin B Sulfate (**Aerosporin** B. W. and Co.), Chloramphenicol (**Chloromycetin** P. D. and Co.), Chlortetracycline (**Aureomycin** Lederle) and Oxytetracycline (**Terramycin** Pfizer). Excellent revies on these antibiotics may be found in Martindale's Extra Pharmacopoeia, 23rd ed. (The Pharmaceutical Press, London, 1952) and in the N.N.R. 1953 (Lippincott, Philadelphia).

The antibiotics here reviewed are Neomycin, Viomycin (**Viomycin** P. D. and Co.,

Viocin Pfizer), Erythromycin (**Erythrocin** Abbott, **Ilotycin** Lilly), Carbomycin (**Magnamycin** Pfizer), Tetracycline (**Achromycin** Lederle., **Tetracyn** Pfizer), Fumagillin (**Fumidil** Abbott), and Actionomycin C (**Sanamycin** Bayer).

With regard to **Neomycin,** it will only be mentioned here that it has been found toxic when injected intramuscularly and its internal administration is limited to oral use. To quote from the seminar paper, « inspite of its potential value, current practice limits its parenteral use to the following conditions: when a severe gram-negative, Neomycin-sensitive infection does not respond to other less potentially toxic chemotherapeutic agents; when renal function tests reveal no insufficiency; and when intramuscular dosage need not exceed 8 — 10 mg. per kg. body weight per day for no longer than 5-8 days. It is interesting to note that available preparations consist only of the following: a sterile powder for topical use only, tablets for oral use and ointments for topical and opthalmic use. It is also available in combination with Bacitracin (**Neobacin** Tablets and **Neobacin** Ointment C.S.C.), with Cortisone Acetate (**Neosone** Opthalmic Ointment Upjohn), etc.

Viomycin Sulfate is the sulfate of a strong organic base containing a guanidine and a peptide linkage. The base as isolated by two groups of researchers working independently of each other. The Parke and Davis group named the organism which produced it **Streptomyces floridae,** with reference to a soil sample from Florida from which it had been isolated; while the Pfizer group named the organism **Streptomyces puniceus** on account of the purplish-red color of the colony. The two organisms have not yet been proven definitely to be identical. Viomycin sulfate is more or less neutral, freely soluble in water, the solution remaining stable for a whole week if kept in a refrigerator. Viomycin may be assayed by the agar diffusion method using either **Mycobacterium butyricum** or **Bacillus subtilis** as the test organisms; or turbidimetrically by using a broth culture of Klebsiella pneumoniae. It has proved equally effective against both streptomycin-sensitive and streptomycin-resistant forms of tubercle bacilli in concentrations ranging between 1 and 12 micrograms per cc., and also appears capable of potentiating the bacteriostatic ability of other drugs, possibly by means of synergism. Although less active than streptomycin, it is more active than para-aminosalicylic acid. It is intended for the treatment of tuberculosis in combination with streptomycin, dihydrostreptomycin, para-aminosalicylic acid or isonicotinic acid hydrazide for use in patients harboring tubercle bacilli **resistant** to these drugs. 500 mg.

Fumagillin is a crystalline weakly acidic substance with the empirical formula C27 H36 O7 isolated by Mc. Cowen, Callender and Lawlis in 1951 from a culture of **Aspergillus fumigatus.** It melts between 189 and 194° C. It has no antibiotic effect on bacteria or fungi but has a potent direct action on **Entamoeba histolytica,** the causative organism of amoebic dysentery. It does not affect the bacterial flora of the intestinal tract. **Fumidil** is available in 10 mg. capsules in bottles of 30 for the oral treatment of intestinal amebiasis.

Actinomycin C is a yellowish red crystalline antibiotic isolated by Brockman and Grubhofer in Germany from **Actinomyces chrysomallus** and assigned the empirical formula C60 H83 N11 O16. According to **Clinical Excerpts, 26,** 63, 1954, «in animal experiments Actinomycin C showed, even in small doses, a definite inhibitory effect upon the lymphatic system and a cytostatic effect on experimentally induced tumours. Following pharmacological trials, this substance was sent for clinical examination as preparation HBF 386». **Sanamycin** is marketed in ampoules each containing 200 gammas (micrograms) of the antibiotic (in dry form) in boxes of 5 and 25 ampoules for use in the treatment of Hodgkin's disease.

Tetracyline was developed by the Lederle and Pfizer laboratories simultaneously, Its generic name indicates its relationship to Chlortetracyline (Aureomycin) and to Oxytetracyline (Terramycin). It may be obtained from a culture of Streptomyces aureofaciens or chemically from its related compounds. It is slightly yellow in color, soluble in water, more stable in neutral or alkaline solutions than its related compounds and like them has a broad antibiotic spectrum. It does not cause some of the side reactions of Chlortetracycline. It is absorbed easily from the intestinal tract and penetrates tissues and body fluids very readily. It has low toxicity.**Achromycin** is available in 50 and 100 mg. capsules and tablets in bottles of 25, in 250 mg. capsules and tablets in bottles of 16 and 100, in dispersible powder containing 50mg. per teaspoonful as Achromycin Spersoides, and in 100, 250, and 500 mg. vials for intravenous use as Achromycin Injection. **Tetracyn** occurs in the form of 250 mg. sugar-coated tablets in bottles of 16 and 100, in 50 and 100 mg. tablets in bottles of 25 and 100, and as Tetracyn Intravenous in vials containing 250 and 500 mg.

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line 3 for Actionomycin read *Actinomycin*

Viocin Pfizer), Erythromycin (**Erythrocin** Abbott, **Ilotycin** Lilly), Carbomycin (**Magnamycin** Pfizer), Tetracycline (**Achromycin** Lederle., **Tetracyn** Pfizer), Fumagillin (**Fumidil** Abbott), and Actionomycin C (**Sanamycin** Bayer).

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THE IDENTIFICATION OF BARBITURATES

by Bashir ar-Rashid

The large number of available barbiturates, their frequent use, and the numerous cases of poisoning intentional or otherwise resulting from their use make the problem of their identification a difficult and a pressing one. Many schemes and methods have been proposed for a larger or a smaller group of barbiturates. Several of these methods have been reviewed in the seminar paper. The following reference sources will be found useful :

(1) Bamford, F., Poisons: Their Isolation and Identification, 3rd ed., Churchill, London, 1951.

(2) Wickstrom, A. and Salvesen, B., The Separation and Identification of Some Barbiturates by Paper Partition Chromatography, J. Pharm. Pharmacol. **4,** 98 (1952).

(3) Umberger, C.J. and Adams, G., Identification of Mallonyl Urea Derivatives, Anal. Chem. **24,** 1309 (1952).

(4) Goldbaum, L.R., Determination of Barbiturates, **ibid. 24.** 1604 (1952).

(5) McCutcheon, R.S. and Plein E.M., The Identification of some Barbiturates by Means of Xanthydrol as a Reagent, J. Amer. Pharm. Assoc., Sci. Ed. **38,** 1 (1949).

(6) Castle, R.N., Optical Crystallographic Properties of Organic Compounds — I. Barbituric Acid Derivatives, **ibid. 38.** 47, (1949).

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BIOLOGICAL ASSAY METHODS

by Vartkes Apelian

The seminar paper is an attempt at the definition, purpose, scope, limitations, historical background and classification of biological assay methods and a review of the methods applied in the biological assay of the various official drugs such as cardioactive drugs, hormones, some vitamins, antibiotics, serological and bacteriological products, and other drugs such as aconite, ergot, curare and curarizing substances, heparin, anthraquinone purgatives, veratrum, dimercaprol, organic arsenicals, etc. The paper also includes a brief note on microbiological assays and the role and importance of statistical methods in the design and interpretation of the results of biological assays.

The B.P. '53 devotes 58 pages to biological assays and tests. It also gives on pp. 792 - 793 tables giving details of the Standard Preparations used in biological assays, their units, the relation between these units and the international units as well as the form in which the Standard is dispensed and issued. It is interesting to refer here to the article of Prof. Gaddum on «Simplified Mathematics for Bioassays (J. Pharm. Pharmacol., **5,** 345, 1953).

From the beginning of international cooperation an important part has been played by two central laboratories: the state Serum Institute at Copenhagen, and the state National Institute for Medical Research at London. Both have acted and are still acting as important centers for coordination They are also responsible for the distribution of the Standards to the various national centers. The Copenhagen Institute deals with all sera and bacterial products, while the London Institute deals with hormones, vitamins, antibiotics and other drugs.

According to Gaddum, «the object of a well designed biological assay is to estimate the potency of an unknown or test preparation by comparing its effect on living matter with that of a Standard Preparation». The Standard, Reference Standard or, according to the B.P., a Standard Preparation, «is a selected representative sample of the substance for which it is to serve as a basis of measurement. It is essential that Standard Preparations shall be of uniform quality, stable and permanent; these conditions are usually insured by providing the preparations in a dry state, dispensing them in sealed containers free from moisture and oxygen, and storing them continuously at a low temperature and in the absence of light». When a standard becomes official in any of the pharmacopoeias for the time being, it is a provisional standard as e.g. a B.P. or a U.S.P. reference standard. Once it is recognized and adopted by the Expert Committee on Biological Standardization of the World Health Organization, it becomes an International Standard. Very often, whenever these coexist, they are identical and the units are equal in magnitude.

The activity or potency of a crude drug which is biologically assayed is always expressed in terms of units. This potency was previously expressed in term of animal units such as a frog or cat unit. With the establishment of Reference Standards, a unit is now defined as the specific biologic activity of a given weight of the respective Standard Preparation, which is indicated arbitrarily by the responsible authorities, and is expressed in terms of milligrams whenever possible.

The main purpose of bioassay is to establish uniformity by measuring the potency of drugs and their preparations in terms of biological activity when no adequate chemical, physical or other method is available to determine their strength.

The practicability and usefulness of biological assays are bound by various limitations, some of which are inherent in the method employed and others in the skill of performing the assay: animal variability under different conditions, expenses involved in using large numbers of animals, difficulty in getting a sharp end point, lack of agreement on the reliability of suggested methods, the instability of certain drugs, differences in the pharmacological effects of drugs upon various laboratory animals and man, and the unmeasurability of the most promising reaction of certain drugs.

Bioassay methods are usually based upon the therapeutic action of the drugs for which they are designed to be used. Bioassay procedures may depend on a **qualitative** measurement as, for example, the effect produced in all or none of the animals (death), **quantitative** measurement as in the measurement of the graded rise in blood pressure, or on a **time response** measurement as in testing the curative response to thiamine administration.

There two main kinds of bioassay : the **direct assay,** where the potency of the drug is measured directly in terms of a biological effect without a reference standard, and is used in cases where it is not possible to get a stable reference standard as in immunological preparations; and the **orthodox bioassay,** where the potency is measured in terms of a reference standard by comparing the standard and the test preparation under identical

conditions, and is applicable to those drugs where we have a stable reference standard. This stable reference standard may be a well defined and chemically pure substance. In interpreting the results of the orthodox bioassay procedure, Gaddum (see also the B.P.) subdivides it into four methods:

1. **Direct comparison on the same tissue.** Here the effects of the preparations are observed repeatedly on the same tissue. The two samples of the drug, standard and test preparation, are given alternately and the doses adjusted until both give equal biological effects. Thus the activity of the test preparation is calculated by simple ratios with that of the standard.

2. **Threshold dose measured on each animal.** Here the drug is administered slowly to an animal until some observable biological effect is produced such as in digitalis assay with cats, frogs or pigeons, measuring the volume of drug that stops the heart of any of these. Usually two series of such experiments, using the standard and unknown preparations respectively, are carried out and the potency of the test preparation is calculated from the average results.

3. **Response of each animal measured** or assays depending upon measured effects. This method involves the measurement of the effects of drugs on individual biological systems such as the increase in the weight of animals or of organs, or in the size of zones of inhibition of bacterial growth. Two similar groups are used for each test, one for the standard and one for the unknown; and the results are calculated statistically from the conditions. Here the tests may be carried in any one of three ways : **a.** the (2 and 1)and (2 and 2) dose assays; **b.** twin cross-over test; or **c.** the method of constant standard , depending on the case.

4. **Percentage of positive effects measured** or assays depending upon quantal or all-or-none effects. In this method, an effect such as death (frog for digitalis) or hypoglycaemic symptoms (mice for insulin) may be observed as either occurring or not occurring in each animal; and the result depends on the number of animals in which it occurs. The percentage of animals giving a positive response to each dose is converted by means of a table (see B.P.) into a probit, which is then taken as a measure of the effect.

BLOOD PRODUCTS

by Naim (Bandali) Farraj

An abstract on this subject was published in **The Apothecary** 1951 p. 49. This subject is also reviewed , in detail, in The British Pharmaceutical Codex 1949, Part III, p. 1009 and in Remington's Practice of Pharmacy, 10th ed., Chapter 110, p. 1418.

A REVIEW OF THE BRITISH PHARMACOPOEIA 1953

by Nizar Daghir

The 8th edition of the B.P. present many features which are more or less radical departures from the previous editions. Quoting from The B.D.H. Guide To The B.P. 1953: «The most striking change is the use of English in the main titles of the mono-

graphs. Latin titles have not been coined for new monographs.... The monographs on substances, as distinct from preparations of them, are arranged in the alphabetical order of their English titles. The monographs on preparations of a substance are placed immediately after the monograph on the substance.»

Fewer monographs have been added (63) than have been deleted (150). Among the additions may be mentioned the analgesics methadone and phenadoxone, the antiepileptics methoin and troxidone, diiodohydroxyquinoline, sodium aminosalicylate, cyanocobalamin or vitamin B12, folic acid, chlorotetracycline (Aureomycin) B.C.G. vaccine and scarlet fever antitoxin and prophylactic, sterilized surgical catgut, etc... Among the pharmaceutical preparations may be mentioned capsules of both hard and soft gelatin, implants, and the sugar coating of some tablets.

Among the deletions may be mentioned the vegetable drugs aconite, calumba, colocynth ,ergot podophyllum, squill, senega, strophanthus and valerian, and their preparations. Pills are no longer official and the only lozenge remaining is the compressed lozenge of penicillin,

Doses are given only in the metric system. The section on biological assays has been enlarged. The B.P. 1953 is now published for the General Medical Council by The Pharmaceutical Press, 17 Bloomsbury Square, London W.C. 1.

Other than the afore-mentioned B.D.H. Guide To The B.P. 1953, detailed reviews concerning the pharmacy, chemistry, pharmacology, and biological assays of the B.P. have been published in the Pharmaceutical Journal (1953), volume 171, pages 399, 453, 473 by Denston, Linnel and Berry, and in volume 172 (1954), pages 7, 129 by Macdonald and Miles, respectively.

ADVANCES IN THE CHEMISTRY AND PHARMACOLOGY OF VEGETABLE CATHARTICS

by Ilyas Sartan

Constipation may be due to a variety of causes which fall into two main groups : functional and organic. Many of the causes of functional constipation are simple to correct if recognized. «Improper diet due to low roughage, emotional instability, habitual neglect of the normal impulses to defecate, insufficient fluid intake, insufficient exercise, and sedentary habits are but a few causative factors, not to mention the indiscriminate use of laxatives. Organic causes are many among which may be mentioned: elevations in body temperature, allergic reactions, headaches, neuralgia, insomnia,

The chemistry of the anthraquinone purgatives has already been reviewed (Apothecary 1952 p. 58). It is interesting, however, to review here the work of Jorgensen on frangula to correct a printing omission which occurred in that section on p. 59 of the Apothecary 1952 Jorgensen isolated from frangula an anthrone-anthranol glucoside complex which on hydrolysis and oxidation yielded two anthraquinone glucoside complexes A and B. Hydrolysis of fraction A yielded chyrsophanic acid anthrone, frangula emodinanthrone and frangula emodinanthrone monomethyl ether. Fraction B gave on hydrolysis difrangulin which on further hydrolysis yielded frangulin. Lee and Berger isnlated from cascara a microcrystalline substance which they called casanthranol and to which

they attributed the whole laxative action of cascara with the advantage that it dose not cause any nausea or griping. It appears to be a glucoside of aloe emodinanthranol combined with a methyltetrahydroxypentoic lactone and a hexitol residue. Bruce and Whittet found that the most efficient means to extract cascara is to use boiling water followed by autoclaving (J. Pharm. Pharmacol. **5,** 823, 1953) . According to the Extra Pharmacopoeia, «cascara has a mild purgative action and is chiefly used in the treatment of constipation due to colonic stasis and as an habitual purgative for patients with haemorrhoids and in pregnancy . It is preferably given at night».

The action of the convolvulaceous resins jalap, ipomea, Brazilian jalap and scammony is believed to be akin to that of castor oil. They probably act as purgatives by «dissolving the lecithin from the epithelial cells of the intestines. The activity of the resins may be explained by the fact that the alkaline intestinal juices dissolve convolvulin and the resulting solution irritates the mucosa».

Podophyllum resin is a well known drastic purgative producing irritation, griping and sometimes violent peristalsis and so is often combined with hyoscyamus or belladonna. Fairbairn recently reviewed the literature on podophyllum (J. Pharm. Pharmacol, **5,** 281, 1953). He points out the successful use of the resin in the treatment of soft warts commonly known as venereal warts by the topical application of a 25% suspension of the resin in mineral oil. Podophyllotoxin, alpha and beta, peltatin, seem to be the constituents responsible for the colchicine-like mitotic effects. The degenerative effects seem to be more marked in the wart tissue than in normal cells. The resin has been observed to destroy cancer cells both in tissue cultures and in experimental tumors in mice.

It is a common observation that eating plums produces in children and in adults a diarrhea the extent of which depends on the amount ingested. Baum, Sanders and Straub (J. Am. Pharm. Assoc., Sci. Ed., **40,** 348, 1951) recently isolated a diphenyl isatin from California prunes, a substance which has a marked laxative effect.

Of the bulk laxatives, Berberian, Pauly and Tainter (Gastroenterology, **20,** 143, 1952) found that a mixture of both psyllium and carboxymethylcellulose will make an excellent laxative. This mixture had the ability to produce its laxative action after the first day of therapy. It does not irritate the intestinal mucosa and does not interfere with the absorption of the water-soluble vitamins.

NEW CELLULOSE DERIVATIVES AND THEIR APPLICATIONS

by Faris Kuzma Musallam

Cellulose products are legion, among which may be mentioned paper, artificial silk, nitrated cellulose products such as guncotton, pyroxylin, collodion and celluloid. Cellulose nitrate is used in some quick-drying varnishes; cellulose acetate, in addition to its use in preparing acetate rayon, is employed in the film industry, in automobile windows, as a varnish for airplane wings, etc.; viscose rayon is used in making cellophane. Hydrolysis of cellulose yields wood sugar which is then fermented to alcohol. However, the cellulose products with which the seminar paper is concerned, are the new products: the cellulose ethers — methyl cellulose, ethyl cellulose and carboxymethyl cellulose; and oxidized cellulose.

As is well known, cellulose consists of unbranched chains of 1-4-linked beta-d-glucose

molecules in the pyranose form. Each single chain may consist of 2000 to 3000 glucose units. The further aggregation of these chains will not be discussed here. The cellulose ethers are products obtained by replacing one or more of the hydrogens of the hydroxyl groups of the glucose residues by an alkyl group like methyl or ethyl, or a carboxyalkyl group. Replacing the hydrogen atom of the hydroxyl group at C-2 by a methyl group or an ethyl group one obtains methyl or ethyl cellulose, respectively; while replacement of the hydrogen of the hydroxyl group at C-6 by a carboxymethyl group results in the formation of carboxymethyl cellulose. Oxidized cellulose, on the other hand, consists of a product in which the alchoholic group at C-6 is oxidized to an acid group i.e. a carboxylic group.

Methylcellulose is official in the N.F. where it is defined as a methyl ether of cellulose containing not less than 26 per cent and not more than 33 per cent of methoxyl groups (—OCH3). According to the well written monograph on this substance in Martindale's Extra Pharmacopoeia, methyl cellulose «is usually a mixture of alkyl ethers of cellulose, of which the greater part is methylcellulose, with ethylcellulose and carboxymethyl cellulose». Among the proprietary names may be mentioned Cellofas A, Methocel and Tylose. Methylcellulose occurs in both pharmaceutical and technical grades and in various kinds according to the degree of viscosity of their emulsions. Quoting further from the Extra Pharmacopoeia, «(It is) a white to cream-coloured fibrous substance; slowly soluble in cold water; insoluble in boiling water, alcohol, chloroform, and ether; soluble in equal parts of alcohol and chloroform, and in glacial acetic acid .... Methylcellulose forms colourless, odourless, and tasteless, neutral, inert mucilages which are stable in acid or alkaline solution and in the presence of most electrolytes. They do not readily ferment or support bacterial or fungal growth, and the addition of a preservative, although desirable, is in many cases not essential. Prolonged heating lowers the viscosity .. It is employed in the preparation of oil-in-water emulsions, creams and jellies as a 2.5 to 10% mucilage, according to the viscosity required. It is indigestible and is employed as a bulk laxative. It is also used in cosmetic creams and tooth pastes, and as an adhesive in the preparation of tablets». Methylcellulose has recently been used as a plasma substitute, in hemorrhoids, in burn ointments and in opthalmic and nasal medications. Many formulae are given in the seminar paper. Other uses enumerated for it are: stabilizer for D.D.T. suspensions and insect repellent emulsions, as a component in anerobic growth media, as a lining to a metallic drycell anode, in oil-well cement slurries, in polyamide resin suspensoids, to increase detergency of soaps, in the preparation of vitamin concentrates for enriching farinaceous foods, etc.

Carboxymethylcellulose is known by such proprietary names as Cellofas B, Carbose, etc. According to the N.N.R. sodium carboxymethylcellulose has a molecular weight of about 330,000 and contains not less than 99%, calculated on dry basis, of sodium carboxymethylcellulose. Pure sodium CMC is a white to light buff-colored granular or fibrous compound, odorless and tasteless, hygroscopic, soluble or dispersible in water or alkaline solutions, more quickly soluble in hot water and is not precipitated by it. In the words of the Extra Pharmacopoeia, it «produces mucilages similar to those formed with methylcellulose, but is more sensitive to changes in the pH of the solution and more liable to support mould and bacterial growth ... and is used for the same purposes as methylcellulose». CMC was developed originally in Germany as a detergent. Other than its pharmaceutically important qualities as a suspending, thickening, stabilizing and film-forming properties, it has been found therapeutically useful in the management of ulcers as a protective and as an antacid, and has been of help in absorbing irritating toxins from the intestines in diarrhea. It is also finding an extensive use in the food industry as a thickening agent and a protective colloid; in the arts as in adhesives, paints and laquers,

ceramics, the leather industry, etc.

Ethylcellulose has remarkable thermoplastic properties, is stable to heat and inert to alkali. Its best solvents are the fatty acids and the alcohols. It may be incorporated with waxes, resins, higher alcohols, etc. and raises their melting point. This property, and the fact that it is a film forming material and a plastisizer, makes it an excellent ingredient in lipstick formulations and in collodions.

Oxidized Cellulose known under the proprietary names of Oxycel and Hemopak or its calcium salt e.g. Sorbacel exerts a hemostatic effect and is available in the form of cotton pledgets or gauze strips, pads and discs. It is available in sealed sterile containers and should be protected from light. It is used in the control of hemorrhage in surgery. It forms an artificial clot and is later absorbed when buried in the tissues. It is not advisable to use it as a surface dressing except for the immediate control of hemorrhage as it inhibits epitheliation. It seems to inactive penicillin and to delay bone repair. It is official in the U.S.P. and the B.P.C. An account may be read on it in the N.N.R. or in the Extra Pharmacopoeia.

Preparation, physical and chemical properties, identity tests, assays, etc., of these newer cellulose derivatives, can be found in the seminar paper.

MEASURING AND NAMING OF COLOR

by Agop Marcarian

«Color has many different meanings. The chemist and dyer may refer to a pigment or a dye as a color, the physicist may mean a spectrophotometric curve, the psychologist may mean a sensation, but to the man in the street, color is a property of objects and light».

Principles of Color Organization. Colors fall into two classes: **Achromatic,** including white, grey, black and all the steps between them, and these may be modified only one way by being made lighter by the addition of white or darker by the addition of black; and **Chromatic,** including yellow, red, blue, green and all mixtures between them. Chromatic colors may be modified in three ways:

a. a yellow may be made greener or redder, a red may be made yellower or bluer, a blue redder or greener, a green bluer or yellower. This variation is called **hue.**

b. the hue may be retained and an increasing amount of white may be added. The color then becomes progressively lighter.

c. the hue may be retained and an increasing amount of black may be added. The color then becomes progressively darker.

d. a combination of cases **a** and **b** occurs when the hue is retained and various amounts of black and white together (grey) are added. The color becomes progressively duller.

There are four fundamental spectral hues which may be called psychological primaries. These are red, yellow, green and blue.

Munsell defined the three variables of color as hue, chroma and value, terms

which correspond roughly with the present definition of hue, saturation or strength, and lightness.

Colors may be specified or named accurately in different ways and according to one of several systems which have been suggested for this purpose, and may be recorded in terms of instrument color numbers as in the **Lovibond Tintometer** or in terms of standard color charts. Among the systems of color naming may be mentioned the **Ostwald System,** the **Munsell System,** the **Maxwell System,** the **ICI System** (International Commission on Illumination) and the **ISCC-NBS system.** This last system was devised at the request of the American Pharmaceutical Association and the U.S. Pharmacopoeial Convention in 1939. The plan of the method was worked out by the Inter-Society Color Council, and the details were developed at the National Bureau of Standards, hence the abbreviation **ISCC-NBS.** It is based on the Munsell Book of Color. For details of this method consult the N.F.

CHEMICAL METHODS FOR THE ASSAY OF DIGITALIS AND ITS GLYCOSIDES

by Ibrahim Durr

The U.S.P. Digitoxin and the B.P. Digoxin and their preparations are assayed spectrophotometrically and colorimetrically respectively. Lanatoside—C U.S.P., Digitalis and its galenicals are, however, still assayed biologically.

Chemical assay methods of the glycosides fall in two major groups: those which depend on color reactions produced by the aglycone part of the glycoside; and those which depend on color reactions produced by the sugar part of the molecule. The most important of these methods are the following:

a. **Baljet reaction,** this depends on the fact that the aglycone gives a red orange color when mixed with an alcoholic solution of picric acid and sodium hydroxide solution added. Digitoxin U.S.P. is assayed in this manner.

b. **Kedde's reaction,** in this the aglycone produces a brown color with an alcoholic solution of meta-dinitrobenzoic acid.

c. **Raymond's reaction,** this method depends on the production of a bright blue violet color when an alcoholic solution of metadinitrobenzene reacts with the aglycone in the presence of sodium hydroxide. Digoxin U.S.P. is assayed by this method.

d. **Warren and co-workers** suggested a method based on the purple color produced by the aglycone when mixed with sodium beta-naphthoquinone-4-sulfonate and sodium sulfite. The color becomes yellow on acidification with acetic acid. This yellow color is measured spectrophotometrically.

e. **Keller-Kiliani's reaction,** this method depends on the red color produced by digitoxose of the glycoside when mixed with sulfuric acid, glacial acetic acid and traces of ferric chloride. Digoxin tablets and injection B.P. are assayed by this method.

A great deal of research into the application of these reactions in the assay of digitalis and its galenicals is being pursued diligently by many pharmacist researchers in pharmacy schools and in manufacturing firms. It has not yet been possible to obtain

as yet satisfactory agreement between the proposed methods of chemical assay and the biological assay methods which are official for digitalis and its galenicals. The seminar paper reviews the work and results of many of the workers in this field and gives adequate references.

IMPORTANT COMMERCIAL PLANT FIBERS OTHER THAN COTTON AND FLAX

by George Slim

«The commercial importance of a fiber is due to many different factors which depend on the physical properties, namely structure, length, density, fineness, elasticity, tenacity, ductility, tensile strength, moisture content, pliability, spinnability, luster, elongation, durability, permeability, combustibility, etc.; and on chemical properties such as chemical composition, action of heat, thermal properties, action of acids and alkalies, and action of reducing and oxidizing agents, metalic salts, effects towards dyes, and other similar properties. For example, strength and durability of fibers which are desirable characteristics are associated with a high percentage of cellulose; a low moisture content is also indicative of superiority». Availability of the raw material, its cost and its spinnability are important points which affect the use of the fiber.

«Most of the commercially important plant fibers used nowadays are of great antiquity. Which of these fibers was first used is not exactly known, but various specimens of plant fiber clothes and articles dating thousands of years back have been found. Swiss Lake Dwellers of 8000 B.C. grew and wove flax. Specimens of ropes found in Egyptian tombs dating 4000 years back were used in the building of the pyramids (these were mainly made of Papyrus and Palm fibers). Before 2000 B.C. cultivated hemp and cotton were used in India. Record of jute fibers dates back only to 500 B.C. On the other hand, ramie, which is a tough and coarse fiber, is very old and was much used in India and China. This was also used instead of flax in Egypt to wrap mummies of poor Egyptians. Agave fibers such as sisal and henequen were made into cordage and other forms of useful articles in early America».

The seminar paper is a very careful and thorough discussion of the different fibers from the following points of view: history, importance, sources, description and cultivation of the plant; collection and manufacture of the fiber; microscopy and chemical composition of the fiber, as well as uses and storage.

The following fibers were discussed: jute and two of the fibers which are being cultivated as substitutes for it because of its scarcity and relative cost — roselle and kenaf, hemp, abaca, sisal, henequen and related fibers such as istle and maguey, New Zealand hemp, Mauritius hemp, Indian or Sunn hemp, kapok and substitutes such as Indian kapok, milkweeds, cattail and silk cottons. Color test reactions are finally given at the end in table form.

OBESITY — CAUSES AND MANAGEMENT

by Sulayman Abu-Khadra

«Ordinary obesity is quite common, especially in middle life, and is more frequent

in women than in men. Extreme obesity ... suggests unusual etiologic factors. Although heredity may play a contributory role, there only is one immediate cause of obesity: a caloric intake persistently exceeding the caloric output». — **The Merck Manual,** Rahway N.J., 1950.

A REVIEW OF THE NEWER OINTMENT BASES

by Fadlu Shaban

A very brief abstract on the same subject appeared in **The Apothecary** 1951 p. 46. A review of the polyethylene glycols and carbowax compounds appeared in the same number on p. 43, and an abstract, with formulations, of a seminar entirely devoted to these new and important constituents of ointment bases appeared in **The Apothecary** 1952 p. 70. These, therefore, will not be mentioned in the present abstract.

The composition of an ointment base and therefore its efficacy will depend on the function which is required of it: to carry a drug to the skin and hold it there, to influence the penetration of the drug into and through the skin, to alter evaporation from the cutaneous surface, to alter the texture of the skin, to protect the skin or to aid in removal of cutaneous secretions.

Greasy ointment bases act as protectives and can be made to absorb aqueous liquids and form water-in-oil emulsions by the use of such substances as wool fat, wool alcohols, cholesterol, cetostearyl alcohol, beeswax, etc. Good examples of such mixtures are Simple Ointment B.P., Paraffin Ointment B.P. Ointment of Wool Alcohols B.P., White and Yellow Ointment U.S.P., Hydrophilic Petrolatum U.S.P. and Petrolatum Rose Water Ointment U.S.P. Similar non-official mixtures are Aquabase, Aquaphor, Polysorb, Formula Base 20 of Johnson and Lee, etc.

Washable ointment bases or **emulsion bases** or **oil-in-water emulsion bases** are not only more pleasant to use but, more important, they have been found to assist in the absorption of the medicament into and through the skin and therefore enhance the effectiveness of the medicating agent. Official examples of these are Simple Cream B.P., Emulsifying Wax B.P., Emulsifying Ointment B.P., Hydrophilic Ointment U.S.P., and Polyethylene Glycol Ointment U.S.P. In these the oleagenous phase contains one or more of the following ingredients: petrolatum, wax, organic alcohols, polyglycol esters or other grease-like substances. These substances are emulsified with the aqueous phase through the action of surface active agents to produce oil-in-water emulsions. These surface active agents reduce the particle size and increase the stability of the ointment. The oil-in-water emulsion type bases must be protected from water loss, otherwise they will crumble and dry out. Such bases should not be used for the eye or for mucous surfaces. Many non-official formulae of bases of this type are also given such as: Beeler's Base, Cetyl Alcohol-Carbowax Base with Water, Gibson Base, Glyceryl Monostearate Base, Span and Tween Base with Stearic Acid, Bhatia-Zopf Base, Hoffman's Base, Ward-Sperandio Base, and water-soluble Carbowax Bases including the modified Landon-Zopf Base. The use of other substances in water-soluble bases has also been discussed. Among these may be mentioned methyl cellulose and carboxymethyl cellulose — these combined with sorbitol and glycerin, with the addition of a preservative, are useful even for the preparation of eye ointments. Others are sodium alginate, silica gel, bentonite, gelatin, colloidal magnesium aluminum silicate, a magnesium silicate clay called hectorite, Jelene Base — this is

described as a combination of mineral oils and heavy hydrocarbon waxes, and the silicone oils (see p. 49). Many formulations for the use of silicones in ointment bases are given, and their incompatibilities indicated.

IMPORTANT TROPICAL PLANT PRODUCTS

by Nicolas Athanassiades

To the casual observer, the decline in the number of crude drugs in the official compendia may give the mistaken impression that plant products have lost their importance. Perusal of the literature will prove the fact that this is very far from being true. The consumption by industry of products of such familiar names as carnauba wax, papain, chicle gum, cork and maté attains considerable proportions.

Carnauba wax is the most important vegetable wax forming the cuticle of the leaves of the carnauba palm **Copernicia cerifera.** Millions of trees grow in Brazil and constitute a very important export item controlled by the government. Its high melting point makes it useful in a variety of industries and its property of confering high luster creates a big demand for it. The two main uses of carnauba wax are the production of water emulsion floor polishes and the manufacture of carbon paper. It is also used in shoe, automobile and other polishes, in the manufacture of phonograph records, matches, candles, soaps, salves, chalks, as insulating material e.g. in electric bateries, also in the manufacture of inks, leather-dressings, lipsticks and other cosmetics, antifouling paints and for metal drawing as well as a metal stamping lubricant.

The papaw tree, widely grown in the tropics, produces an edible fruit when ripe. When still unripe, the fruit yields on incision a latex consisting of a mixture of enzymes particularly proteolytic enzymes. When dried and purified the later is known as papain. Ceylon and British East Africa are the main producers. Among the uses of papain may be mentioned: as a remedy in dyspepsia, in the production of culture media digests, as an intraperitonial instillation to prevent post-operative adhesions, topically in the treatment of carbuncles, sloughing wounds, etc., in chill-proofing beer, in the food industry in precooked foods and for tenderizing meat, in improving shrinkage resistance of wool and silk in the textile industry, in the chewing-gum industry and in batting skins and hides in the leather industry. The scientific name of the tree is **Carica papaya.**

Chicle is the latex exudate of a tree **Achras sapota** which grows in Central America. It consists mainly of complex hydrocarbons. It is used in large quantities in the manufacture of chewing-gum only about 15% of which consists of chicle, the rest consisting mostly of sugar, corn syrup and a flavor.

Cork is a product of the cork tree **Quercus suber** commercially obtainable in particular from Algeria, Portugal and Spain. The first produced cork is known as male cork and is full of cracks, is hard and brittle, was previously discarded but is now used in composition cork. The cork produced few years later or female cork is superior. Cork has certain properties which make it a very valuable product. Cork is compressible and resilient, is impermeable to liquids, is oil resistant, has a very low specific gravity and a very low thermal conductivity, has frictional qualities which are superior to rubber, is a good sound insultor, is a bad conductor for electricity, is stable and does not deteriorate with age, is tasteless and odorless and is chemically inert. No natural or synthetic substitute has been found for cork. At the symposium on Closures held during the British

Pharmaceutical Conference in London last summer it was disclosed that cork closures were superior to rubber and to screw caps in preserving the contents of containers.

Maté or Yerba Maté is the principal beverage in some countries of South America such as Argentina, Paraguay and Brazil, and is coming into considerable use in this country and in Europe. In amount consumed it comes next to coffee, tea and cocoa and like coffee and tea is used as a stimulating caffeine containing leaf. Maté is the cured leaf of a south American plant **Ilex paraguariensis.** Besides its use as a beverage, it is processed in Brazil for the production of caffeine and chlorophyll.

CHEMOTHERAPY OF HUMAN VIRUS INFECTIONS

by Samih Darwazah

Chemotherapy of virus infections, being in its infancy still, the major part of the seminar paper concerned itself with the definition of viruses and virus infections. Certain of the larger viruses such as the etiological agents of psittacosis, ornithosis, lymphogranuloma venereum, trachoma and inclusion conjunctivitis are influenced by sulfonamide drugs and by some of the wide spectrum antibiotics such as tetracycline and its derivatives which with chloramphenicol have also been found useful in lowering the temperature in primary atypical pneumonia.

Viruses are ultra-microscopic bodies many of which were recently made visible by the aid of the electron microscope. They are all less than one third micron in size. The influenza virus is about one tenth micron while the polio virus is only about 0.02 of a micron.

According to Frobisher, animal viruses in general are killed in a few minutes by temperatures like that of pasteurization or even as low as 56° C. They are highly resistant to freezing and will remain alive at — 76° C. for a year or longer. They are rapidly destroyed by ultra-violet light, and disinfectants like iodine, formaldeyde and phenol inactivate them, but they are not affected by sulfonamides, penicillin or streptomycin. With regard to the question of whether viruses are living bodies, Frobisher in his book on Fundamentals of Bacteriology, says that they may exist as living bodies, like elementary bodies, some as crystals which are not living in the sense which biologists attach to this word while others may be mere aggregations of a few protein molecules. There are three hypotheses as to their origin : one, that they take their origin as pathologically active fragments from the cells of higher forms; two, that they represent surviving descendents of primitive procellular forms of life; and three, that they represent degenerate descendants of larger pathogenic micro-organisms -- this view is the one most widely accepted at present.

An important mechanism by which infection is overcome and resistance maintained is the production of specific antibodies. Frobisher says, « three situations may develop : infection may be followed by elimination of the virus and permanent or at least prolonged immunity; infection persists with repeated opportunities for liberation of the virus despite active antibodies production; or infection of the mucous surface is followed by antibody production and an immunity of varying duration. »

CHEMICAL ANALYSIS AND CHEMICAL TREATMENT OF WATER

by Hamid Jabr

The seminar paper is a review from standard books on the subject.

END OF SEMINAR ABSTRACTS

Neuroplégique

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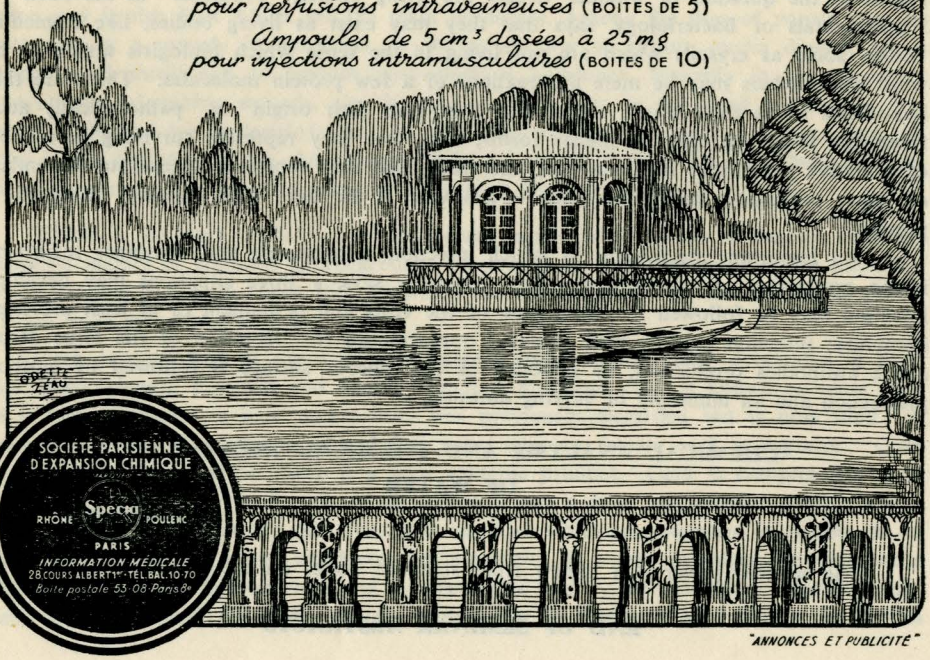
Ampoules de 2 cm³ dosées à 50 mg pour perfusions intraveineuses (BOITES DE 5)

Ampoules de 5 cm³ dosées à 25 mg pour injections intramusculaires (BOITES DE 10)



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THE PHARMACEUTICAL SOCIETY

A Report by the Cabinet

The cabinet elected in May 1953 inaugurated the year's activities by the traditional opening reception in honor of the incoming class of 1957 as well as in honor of Dr. J. McDonald, Dean of the Medical Faculty. Members of the Cabinet consisted of Messrs. Markarian, president; F. Sha'ban, first vice-president; V. Etyemezian, second vice-president; N. Masri, secretary; S. Malak, treasurer. Members of the cabinet, with the exception of the secretary, soon found, for various personal reasons, that they preferred to resign. New elections were held in December, the following constituting the new cabinet: Messrs. F. Sha'ban, president; E. Sartan, first vice-president; N. Masri, secretary; F. Kanj, treasurer; the office of the second vice-president remaining vacant.

From the start, the cabinet had felt the need for the conversion of the Reading Room into a comfortable lounge where students can relax between classes, discuss their problems and read or study in a less formal atmosphere. With the help and enthusiasm of everyone concerned, the old show cases were removed together with one of the two tables, the older benches and most of the oak chairs, thus providing a big floor space to take the two new divans, wicker chairs and stands. All this was accomplished by fund donations from the Ladakis Fund, the School of Pharmacy, the Pharmaceutical Society and the students.

The cabinet tried to do its best to provide the student body of the School of Pharmacy with cultural, professional and social opportunities indicated as objectiyes in the Society's constitution. This was accomplished by means of educational films; the support of the School's yearbook, The Apothecary; the holding of interclass general knowledge contests which were both instructive and recreational; the organization of trips; and the holding of two successful balls income from which will go toward the support of scholarship grants during the next academic year and toward providing further needed fixtures and furniture to the lounge. The activities of the year were finally brought to a close by the farewell party held at the Alumni Club in honor of the graduating class.

The cabinet wishes to thank, in the first place, its adviser, Prof. Edward Vorperian who spared no effort in making its activities and particularly the balls very successful. The cabinet also wishes to thank the Director, Prof. Haddad, and the students who have cooperated to make this school year a successful and a pleasant one.

The following is a list of the activities sponsored by the Society. A pictorial record appears on the next three pages.

Oct. 30, 1953 — Opening Reception (West Hall).
Dec. 10, 1953 — Election of New Cabinet.
Dec. 20, 1953 — Film Show: Plastics, General Anesthesia (MSB).
Jan. 20, 1954 — Film Show: Sulfonamides, Our College (MSB).

Feb. 20, 1954 — Grand Ball (Alumni Club).
April 23, 1954 — General Knowledge Contest: Pharm. II won over Pharm. I (Pharm. Bldg.).
May 6, 1954 — Trip to Naba'-el-Assal wal-Laban.
May 17, 1954 — General Knowledge Contest: Pharm. IV won over Pharm. III (Pharm. Bldg.).
May 21, 1954 — General Knowledge Contest, Championship: Pharm. IV won over Pharm. II (Pharm. Bldg.).
May 31, 1954 — Election of the New Cabinet 1954-55.
June 5, 1954 — Graduation Ball (Alumni Club).
June 9, 1954 — Farewell Reception (Alumni Club).

STRICTLY CONFIDENTIAL

My dear secretary,

Supersaturated as I am with your love, I could not but write to you and state my problem. Your love has caused in me an irreversible chemical reaction that went to completion under the catalytic influence of distilled moonlight. So here I stand, ready for you analysis. Crystallize me , dear, precipitateme, filter me, fractionate me, distill me, and you will find out that my love for you is as valid as the empirical deductions of the second law of thermodynamics.

When I look at you, my heart starts to beat and pang like an internal combustion engine using low octane benzine, and I feel you attracting me with a force similar to the chemical affinity of hydrogen and chlorine. So why are you behaving as if we were two immiscible liquids ? Let my affections for you act as an emulsifier, so that our relations shall become as smooth as fresh cold cream; let my love for you act as a stabilizer, so that we become tied together with bonds as stable as the peptide bonds that tie aminoacids to each other.

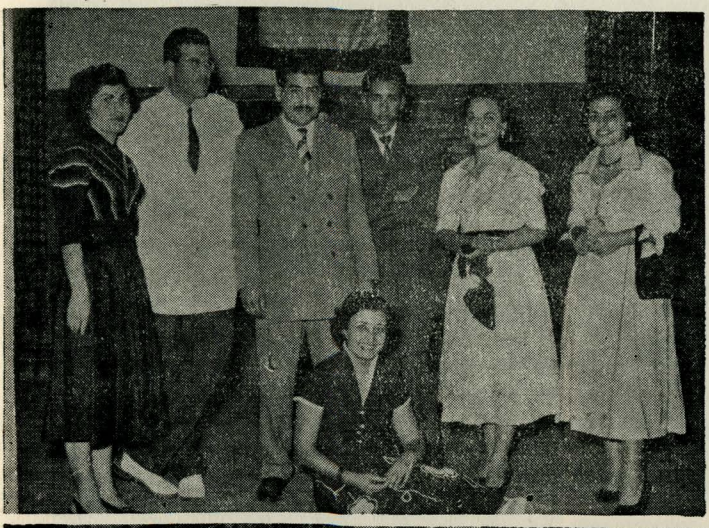
I can never dissolve your image from my memory, for no sooner do you evaporate from my mind than you condense again and return to my imagination. Your eyes, oh dear, are as pure as crystalline carbon, and as green as ferrous sulfate; your skin is as smooth as a water-in-oil emulsion; your hair is as lustrous as nylon, and as fragrant as phenylethyl alcohol; your lips are as red as mercuric oxide, and your teeth as white as freshly precipitated calcium carbonate. You are more precious than gold, more valuable than uranium and more active than radium.

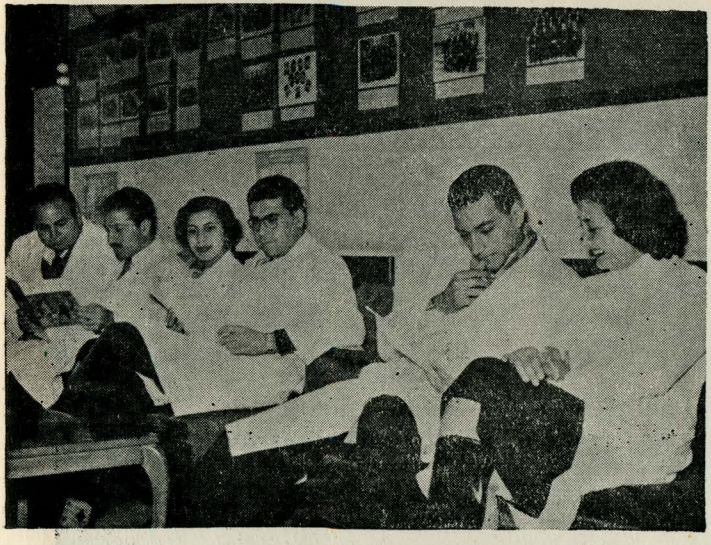
The irresistible electrons of your radio-active charm have chosen my cardiac cavity as their target and have incessantly bombarded it, causing its protoplasm to emit alpha particles that always follow the direction of your motion.

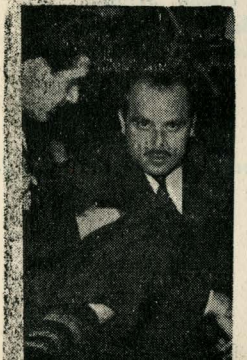
You are better than any compound I know, you are my dearest, most delicate and pretiest molecule. In short, you are the human version of the philosopher's stone, the anatomic edition of the atomic bomb.

Hoping you will not explode soon, I remain, dear molecule,

yours atomically,
H_2O







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PRIZES AWARDED

DURING THE FAREWELL PARTY

JUNE 9, 1954

Prizes offered by the Pharmaceutical Society, A.U.B.

1. **Medals** of the Society were awarded to the following:

   Mr. Levon Karamanukian, previously adviser to the Society, for his interest in the sport activities of the Society,

   Arthur Youhanna, Pharm. IV, for being the most active member of the Society outside the cabinet,

   Rafy Balian, Pharm, II, for coming out second in the interclass ping pong championship of the School of Pharmacy.

   Members of the football team for winning the championship of the Medical Division. The members of the team are: Hamid Jabr (captain), Adib Kuttah, Varoujan Etyemezian, Ziad Habash, Khaled Suleiman, Samir Jurjus, Hussein Tazziz, Nadim Masri, Diran Palanjian. Members of the team also received badges from the Athletic Department.

2. **Books** were awarded to students who have attained the highest average in their classes during the first semester, provided the average attained is 85 or above and provided they had incurred no previous delinquencies. The following received professional book awards:

   Tawfik Karam, Pharm. I ..... B.P. 1953,

   Shibley Bayyuk, Pharm. II ..... B.P. 1953,

   Nicolas Athanassiadis, Pharm. IV....The Extra Pharmacopoeia—Martindale Vol. I.

Prize offered by Mr. Levon Karamanukian

A silver cup to the winner of the School of Pharmacy championship in ping-pong: Khaled Suleiman, Pharm. II.

Prize offered by the Director of the School, Prof. Amin F. Haddad, to the student who has attained the highest grade average during the three past academic years, provided the average is not below 85 and provided no delinquencies were incurred. This prize went to Fadlu Sha'ban, Pharm. IV, who received a copy of the Merck Index.

Prize offered by The Apothecary to Fadlu Sha'ban, its advertizing manager, for his devoted services during the four years he so acted. Fadlu Sha'ban received the Pharmaceutical Formulas Vol. I.

Prize offered by Miss Maria Widacka Ph.C. '50.

A book, Between Life and Death by H. Williams, to the person attaining the highest individual score in the General Knowledge Contest . This prize was awarded to Sami Malak, Pharm. II.

ACHROMYCIN

(CAPSULES) Tetracycline *Lederle*

The antibacterial range of ACHROMYCIN is as great as that of any antibiotic tried to date. It differs, however, from its predecessors in the fact that it is practically free from undesirable side effects.

Dosage — For ordinary infections 1.0 Gm. daily, in divided doses, given with fluids, is the minimal amount required to control infections in the average adult. More severe infections require correspondingly higher dosage.

Dosage may be calculated at the rate of 6–12 mg. of ACHROMYCIN per pound of body weight.

Packages — Bottles of 16 capsules, 250 mg.

ACHROMYCIN is also available in *Intravenous* form, in vials of 100, 250 and 500 mg.; and as SPERSOIDS dispersible powder, in jars containing 26 Gm. and 75 Gm. of ACHROMYCIN.

"MERCURY"

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ATHLETIC TEAMS

Football Team members are mentioned under prizes. The team played against the team of the Medical School and against the Public Health team. Thus the Pharmacy team won the minor league championship for the Medical Division.

Basket Ball Team members are: Diran Palanjian (captain), Artin Malakian, Ghassan al-Mahassini, Haig Gourdikian, Nicola Sassine, Raphy Balian. The team lost to the team of the Medical School.

Volley Ball Team members are Nicolas Athanassiadis (captain), Haig Gourdikian, Nicola Sassine, Diran Palanjian, Raphy Balian, Artin Malakian, Vosgan Anpardjian. The team won against the team of the Medical School but lost twice to the Public Health team.

GENERAL KNOWLEDGE CONTEST

The interclass championship of the School was won by the fourth year team composed of Ibrahim Durr, Faris Mussalam and George Slim. Sami Malak, Pharm. II, scored the highest number of individual points.

Pharmacy Queen

Miss Ibtihaj Kazun, Pharm. I, won the title Pharmacy Queen at the Graduation Ball held by the Pharmaceutical Society on June 5th at the Alumni Club, and was presented with a large silver cup offered by Messrs. A. Neechamal (Grand Magasin Indien - Beirut).

* * *

New Professional Books

THE BRITISH VETERINARY CODEX 1953. The Pharmaceutical Press 17 Bloomsbury Square London W.C. 1, England., Price 45 shillings , plus 1 s. postage).

THE INDIAN PHARMACEUTICAL CODEX. Vol. 1 (Indigenous Drugs). by R. Mukerdji Council of Scientific and Industrial Research, New Delhi, 1953. Price 12 rupees.

FIGURES PHARMACEUTIQUES FRANÇAISES — Notes Historiques et Portraits, 1803 - 1953. Masson et Cie. Paris, 3300 F. francs.

THE PHARMACEUTICAL POCKET BOOK. 16th ed. The Pharmaceutical Press, 17 Bloomsbury Square, London W.C. 1 , England, Price 18 s. 6d.

THE EGYPTIAN PHARMACOPŒIA , 1953. (English Edition). The Cairo University Press, Cairo Egypt. Price 5 Egyptian pounds.

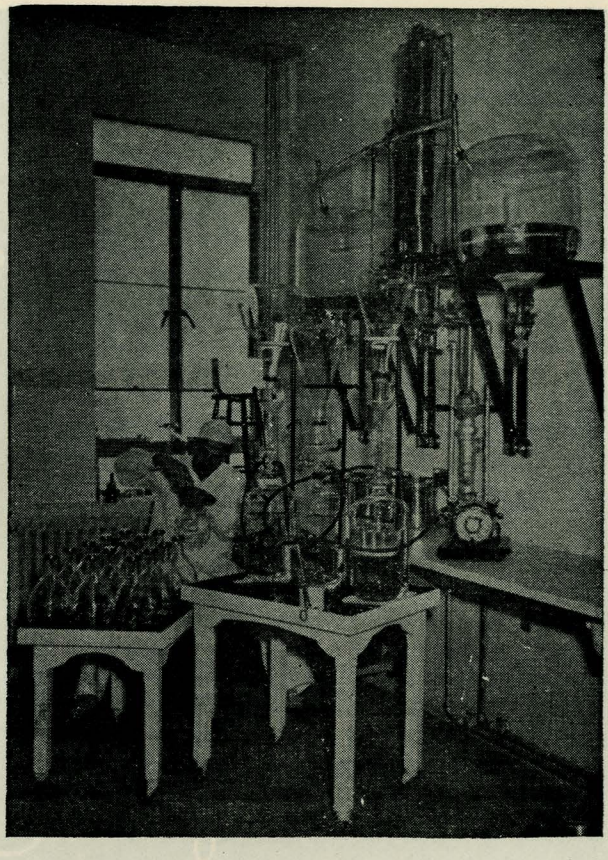
PYROTECHNIQUE

There's poison in the potion
And there's peril in the pill;
And danger's in the distillate
That trickles from the still.
In short, my fellow pharmacists,
In everything we do
There's a modicum of danger—
But we know it, me and you:
We relish no committee-men
To order us about
Lest the pyrogens should get us
if we don't watch out.

Gram-negative bacteria
Of pyrogenic strains
Sail down upon the dust-clouds
Or they threaten from the mains;
But we've got the proper baffles
And the still's not out of date,
Yes, we've surely swilled the bottles
With this morning's distillate.
If we scoff at such precautions
There's a risk, beyond a doubt,
That the pyrogens will get us
if we don't watch out.

But our knowledge is extensive
And our practice up to date;
Our intravenous crystalloids
Are never second-rate:
We busy no cheap and nasty drugs,
And never store them loose;
Our dextrose is the finest
That the country can produce.
The rabbits bear us witness,
The critics we can flout—
For the pyrogens can't get us
while we do watch out !

Peter Cooper
The Chemist and Druggist
December 26, 1953, p. 641



THE SOLUTION ROOM LABORATORY

The Solution Room Laboratory has been moved last April from the Laundry Building into the fourth floor of the new Hospital wing. It now occupies a two-room section for the preparation of sterile solutions, and a store room. The autoclaves are housed in a separate room, while the two stills which supply the water used in the preparation of the solutions are housed in the two-room section. The older still is a Stokes' still. The newer still is a reflux Castle still delivering distilled water directly into inverted carboys which in turn supply the water directly into Fenwal flasks (see photograph). This closed system is thus far superior to the older one. The two-room section is made as dust proof as possible, and positive-pressure ventilation is produced by means of a fan and an air filter.

Due to the increase in the Hospital bed capacity, after the construction of the new wing, the monthly average of flasks dispensed, containing solutions for both parenteral and external use, increased from 1500 prior to January 1954 to 2000 flasks during the first four months of 1954. Mr. Nadim Khallouf, Ph.C. '50, is in charge of the Solution Room Laboratory and is assisted by three aids.

The Order of Pharmacists of Lebanon

The following alumni are serving on the Cabinet of the Order : Messrs. Spiridon Metni, Ph. M. '10, secretary; Adib Kaddurah, Ph. C. '38, Hassan Kaidbey, Ph. C. '38, and Luder Ishkhanian, Ph. C. '38, members.

Prof. Amin F. Haddad, Ph. C. '33, is chairman of the Scientific Committee and editor of **The Lebanese Pharmaceutical Journal.** Prof. Charles Abou-Chaar, Ph. C. '36, is member of the Scientific Committee.

A new scholarly work on an old subject.

PLANTS OF THE BIBLE

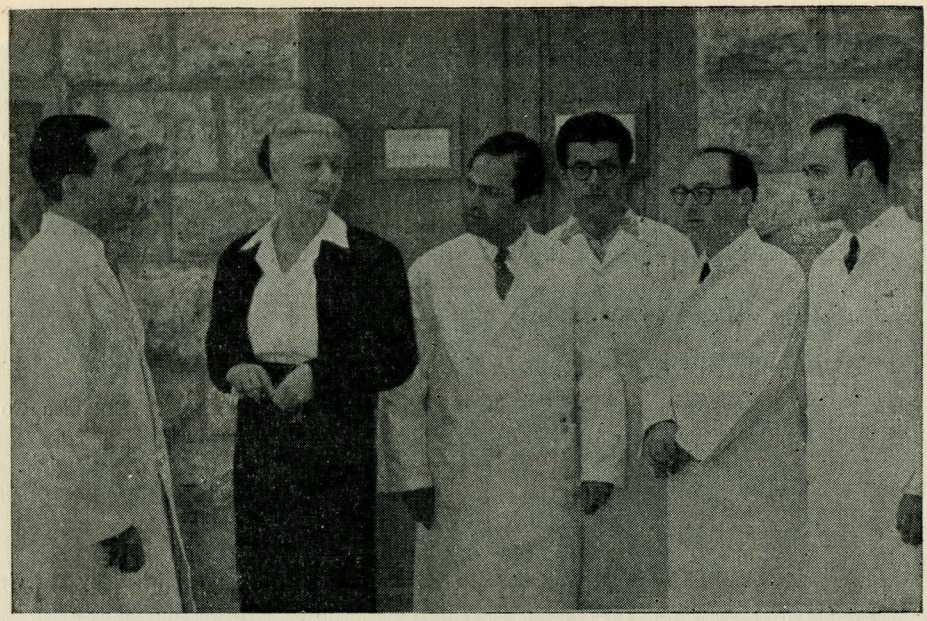
by H.N. Moldenke and A.L. Moldenke, published by the Chronica Botanica Co., Waltham, Mass., U.S.A. , 1952. Price 7.50 dollars.

A good companion

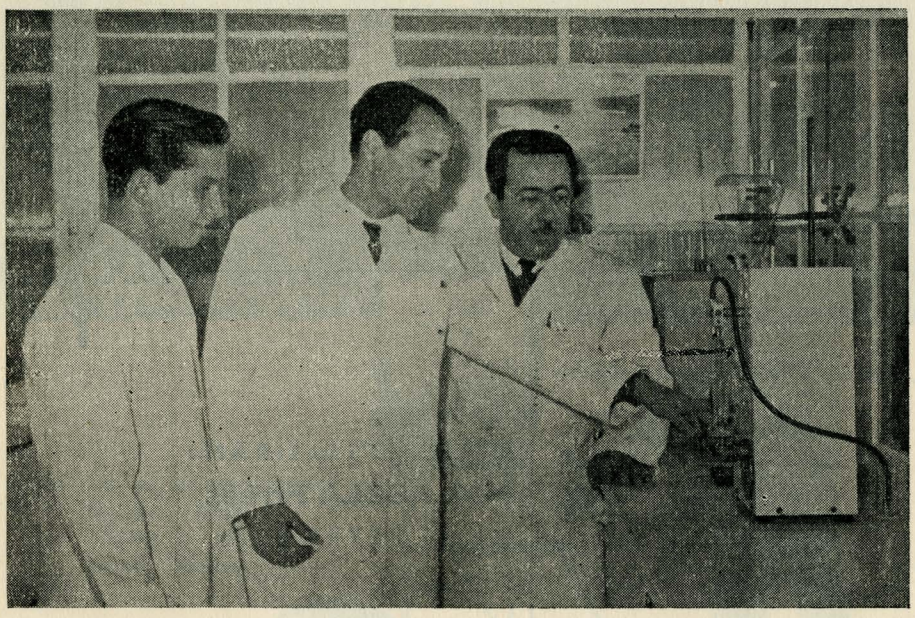
THE BOOK OF HEALTH

by R.L. Clark, Jr. and R.W. Cumley (Editors - in - Chief) published by Elsevier Press Inc., New York, 1953. Price 10 dollars.

One aim of the editors is to present sufficient information to the layman to enable him, when and if necessary, to be an informed patient and to know something about living to avoid being a patient . — J Amer. Pharm. Assoc. Sci. Ed. **43,** 128 (1954)

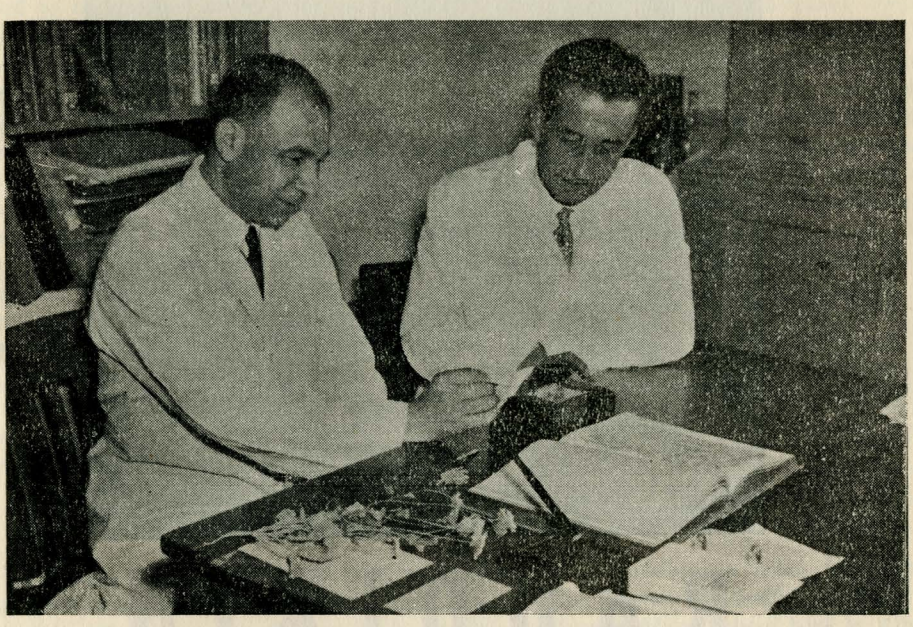


The University Pharmacy staff are able, for a rare moment, to get together for an informal shot. From l. to r., J. Barghash Ph.C. (Pharmacist), Mrs. S. Sivinsky (Secretary), J. Adel (dispenser), M. Costantin (aid), H. Derghazarian Ph.C. (Asst. Pharmacist), A. Zantut (aid).



«Do you see how the syringe is filling up ?» -- Hani Shaar seems to say, while M. Butrus (right) and F. Nahhas look on. Mr. Shaar is in charge of preparing injectables and Mr. Butrus tablets, for the University Pharmacy.

«You see, the Merck's Index has it», Mr. Uthman Kanafani seems to say to Assistant Professor Edward Vorperian. Prof. Vorperian obtained his M.Sc. degree last summer from Ohio State University.



Mr. Levon Karamanukian appears to agree with Associate Professor Charles Abou-Chaar that the plant specimen is very interesting. Prof. Abou-Chaar spent two weeks in London last summer attending the British Pharmaceutical Conference and visiting schools of pharmacy in England. He also attended the meeting of the International Pharmaceutical Federation held in Paris and visited the school of pharmacy there.

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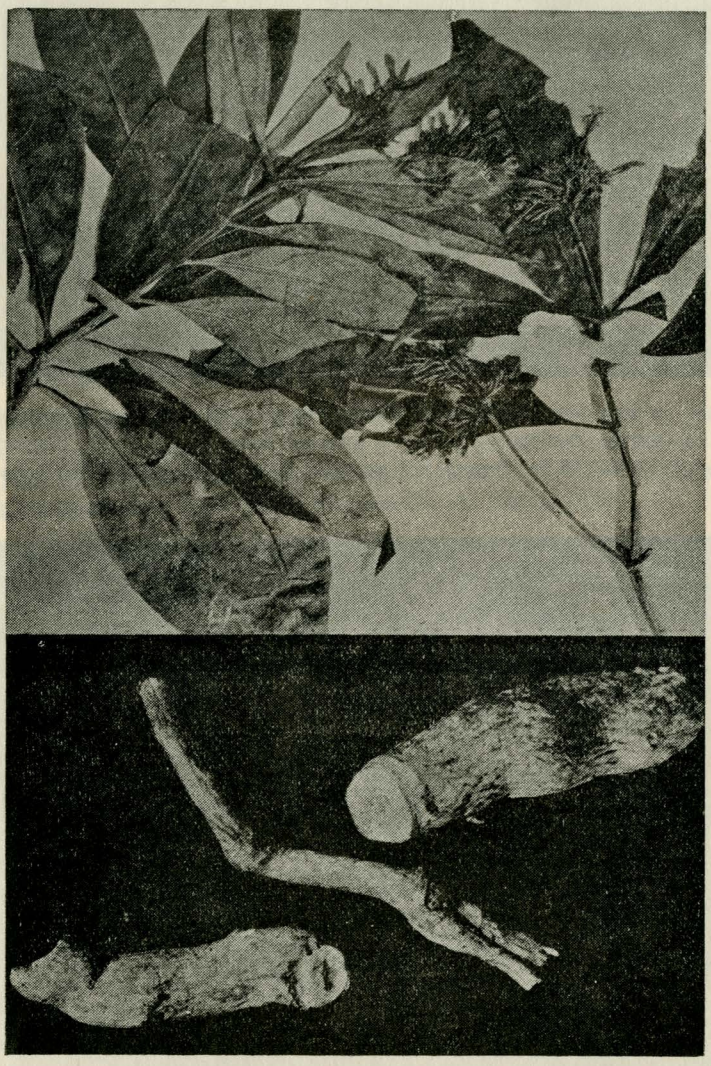
to the ideal drug
for treating hypertension...



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SQUIBB RAUWOLFIA

Available in 50 mg. tablets of the whole root of Rauwolfia serpentina, in bottles of 25 and 100.

SQUIBB

Excerpts

FROM OUR MAIL

Mr. Hamdi Dûrûst Ph. C. '51, Turkey:

Writing as Lt. Pharmacist acting as head of the Stock Control Group of the Master Medical Depot at Ankara while spending his term of Military service, last August, Mr. Dûrûst says: «Work in this Master Medical Depot here at Ankara has been very interesting so far ..... As I have written before, almost all ranks of the pharmacy profession in military service are represented here. In addition, there is a fairly well equipped Armed Forces' Medical Manufacturing Plant within the organization and grounds of the Depot , where the galenicals, tablets, injections and capsules on demand by the Army, Navy and Air Force Medical Corps are manufactured and packed on a large scale. Although I am primarily attached to the more-or-less administrative unit(the stock control group) , I find occasion to walk into their labs and plants to see various pharmaceutical processes and machinery at work , to see standardization techniques, assays of suspected open-container powders and drugs turned in by distant Armed Forces units for analysis..... The library has a very good collection of the recent additions of the U.S.P., B.P., D.A.B., U.S.D., French and Turkish Pharmacopoeias, Merck's Index and Manual, the Therapeutic Index and various other standard and official books on pharmacy and pharmaceutical analysis. I often go there and to the Manufacturing Plant and discuss recent methods with its well-trained director, himself a public analyst and pharmaceutical chemist, with the rank of Lt. Colonel .... Not only the Manufacturing Department, but other departments of the Depot are of great interest to the young pharmacist : there is one department dealing with sanitary and surgical dressings and supplies ; another where all instruments and apparatus needed in the modern practice of surgery, dentistry, roentgoenology, bacteriology, pharmacy and pharmacognosy are available and are supplied .... according to demand and available stock. Still another section deals with field supplies .... to be used in war or in maneuvres by the medical corps, such as portable beds, stretchers, tents, portable cooking units, mess kits, snake- and scorpion-bite kits, first aid kits, water-purifying packages, field medical and surgical chests, tags for the wounded and dead, etc. Another department deals with stationary used by the medical corps including medical books ranging from Cecil's Internal Medicine to Gray's Anatomy , to be supplied to the military hospitals and infirmaries of ships as needed, and all sorts of medical literature in English, French, German and Turkish. That would explain, in short, why this Master Medical Depot is a pharmacist's paradise. My list does not include such purely technical departments where the X-ray and other appartus of the Armed Forces are repaired and fitted....»

Dr. R. J. Pauly writes from Albany, N. Y.

«Ralph, Lore, and Heidel each spent their Spring Vacation at home, but as they all go to a different college none of them were at home together as vacation time did not overlap. After they were all gone again Hansie's vacation at Milne School here in Albany began. Ralph is doing graduate work at the University of New Hampshire, majoring in Marine Biology. This summer he expects to spend some time at Woods Hole, Mass. —

The Wellcome Research Institution, Euston Road, London

IN THE CAUSE OF HEALING

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AGENTS FOR LEBANON: ABELA FRÈRES, B.P. 45, BEYROUTH,

the famous marine biology station. Lore has had occasion to use the languages she acquired in Beirut, by being called upon twice at college to act as student hostess at International College Affairs where many foreign students come for a visit to Keuka College».

Mr. Adel Maksad Ph.C. '51, Sudan :

Readers will remember that Adel Maksad was in Juba in the Southern Sudan. Lately he wrote, «I was transferred to Khartoum in February ... I really enjoyed my stay in Southern Sudan, I was always interested in serving the underprivileged (Adel was a very active member of the CWL during his student days — editor) and I found my chance and opportunity in Southern Sudan where I did what I could to help those who needed my help. I also had the chance of training some young eager men in the art of dispensing. I am now in Khartoum resuming my former work at the Civil Hospital pharmacy.... I expect to arrive in Beirut in June for a short leave. I have met all alumni friends and colleagues in Khartoum. All the pharmacist alumni are doing well..... I am bringing their subscriptions to the 1954 Apothecary with me to Beirut...».

Mr. Nizar Jardanah Ph.C. '48, Amman :

Nizar Jardanah has discovered one of the secrets of success and long life and that is to concentrate fully on one single problem at a time leaving all others for the moment. As a result of this philosophy he finds time to accomplish a great many things. He is always beaming and has put on weight. This is all true for he recently paid the School a visit. Previous to his visit he had written, «together with other colleagues we have succeeded in having the Ministry of Health, the Ministry of Justice and the cabinet of the Prime Minister approve a draft of a law to establish a Jordanian Order of Pharmacy. The bill will come before parliament next November and we hope it will be passed. Credit goes to the Pharmaceutical Society of Amman for their efforts in writing up the draft and pushing it up the ladder of officialdom. If passed, the law will give the cabinet of the would-be Order wide jurisdiction on professional matters such as pricing, organization of the profession, and application of diciplinary measures».

Mr. Anis Muasher B.Sc. '53, writes from Amman:

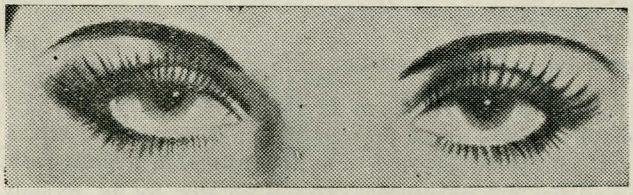
«As to my pharmacy it is running well and I am preparing to establish a drugstore. I have finished the preparation of hexylresorcinol capsules and they proved to be good... Life in Amman is work and only work, no fun what-so-ever, because it is not easy to make a good living in a poor country like Jordan .... The situation at the Israeli border is awful and no body feels that he is safe or that he will reap his toil for himself. But we all wish and look for the better and that is how we live in hope...»

Mr. John Shakarjian Ph.C. '51, writes from Aleppo :

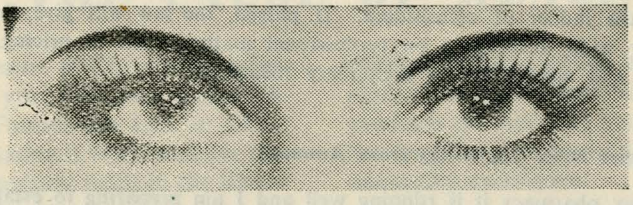
«My ambition now is to form a Pharmaceutical Society in Aleppo. ... May be under such an organization the pharmacists, at least the A.U.B. graduates, could be brought together once in a while to meet their colleagues, discuss their common problems and try to find, together, a solution to these problems. Still more important would be to revive in them an interest in the science and art of Pharmacy by regular talks on the new scientific discoveries ... And once this is achieved, it may be that such a group will be able to spread their constructive virus to other pharmacists».

You Can Get Quick Relief from Tired Eyes

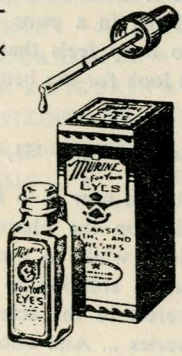
Make this simple test today !



EYES FEEL TIRED ? You can soothe and refresh them in seconds with two drops of gentle, comforting Murine in each eye. You get —



QUICK RELIEF. Instantly your eyes feel refreshed. Murine's scientific blend of seven ingredients cleanses and soothes eyes tired from overwork or exposure to sun, wind and dust.



MURINE
FOR YOUR EYES

ALUMNI NEWS

The Apothecary takes pleasure in extending the greetings and sincere goodwishes of the Director and Faculty of the School to all its graduates wherever they may be. Only news which has become available to us, and not previously published, is included below.

BIRTHS

Sweetest li'l feller, everybody knows ;
Dunno what to call him, but he's mighty lak' a rose ;
Lookin' at his mammy wid eyes so shiny blue
Mek' you think that Heav'n is comin, clost ter you.

Frank L. Stanton

Aftim Acra '46, A.U.B., a son Michel, on December 8, 1953.

Tanas Atallah '37, Droguerie T. Atallah and Co. , Beirut, a daughter Myrna, on March 18, 1954.

Samih Darwazah '54, Amman a daughter May , on July 25, 1953.

Adib Jidawn '49, director of the branch office of Frosst and Co. Damascus, a daughter Mouna, on December 21, 1952.

Morris Karam '52, Pharmacie Orientale, Tripoli, a daughter Nabeelah-Thérèse, on August 24, 1953.

Barkev Mugrditchian '49, Barkev's Pharmacy, Ras Beirut, a daughter Rina, on September 4, 1953.

Subhi Khuri Nasr '51, Kuweit Health Department, a daughter Mouna, end of September 1953.

Nazim Sukhn '44, al-Razi Pharmacy , Nablus, a son Tareef, June 1953.

ENGAGEMENTS

He'd nothing but his violin,
I'd nothing but my song ;
But we were wed when skies were blue,
And summer days were long.

Mary Kyle Dallas

Hanna Doany '44, A.U.B., to Miss Leila Shaer. The wedding will be in August, after which the couple will leave to the Univ. of Minneapolis where

Doany will prepare for his Ph. D. in Bacteriology and his wife for her M.A. in Sociology.

Wajih Mishriki '47, Helwan, Egypt to his cousin Miss Leila Mishriki.

Majid Yarid '50, Inspector of Pharmacy, Amman, engaged.

WEDDINGS

Do you know you have asked for the costliest thing
Ever made by the Hand above —
A woman's heart, and woman's life,
And a woman's wonderful love ?

Mary T. Lathrop

Mamduh Abu-Hijleh '47, Nablus to his cousin, summer of 1953

Ramiz Afifi '47, Beirut , to Miss Faouzié Nsouli, on March 28, 1954

Samih Afifi '52, Beirut , to Miss Samir Hashem Husayni, on August 28, 1953.

Abdel-Al Awad '52, Abdel-Al Pharmacy, Port-Said, in March 1954.

Noubar Babikian '50, Babikian's Pharmacy, Aleppo, to Miss Mary Kantarjian, on February 2, 1954.

Fahd Farraj '50, Amman, to Miss Hind Succar, on September 20, 1953.

Assadour Gulvartian '47, Pharmacie Ideale, Beirut, to Miss Sonia Tchintchinian, on February 21, 1954 .

Amin Kamal Ismail '52, Health Department, Kuweit, to Miss Joumana Sughayyar, in September 1953.

Wasfi Khazin '53, Sukhtyan Pharmacy, Tulkarm, to Miss Aida Lathkani, on December 31 , 1953.

Muhammad A. Kurdi '52, chief biochemist, Government Central Laboratory ,Amman, to Miss Salwa Také, on December 14, 1953.

Samuel Manushakian '51, Midan Pharmacy, Aleppo, to Miss Heripsime Kantarjian, On August 31, 1953.

Maria Michajlow '48, Toronto , Canada , to Mr. Stanley Mocarski. on December 26, 1953.

Mohammad Rifi '48, Rifi Pharmacy , Tripoli (Lebanon).

Karekin Sagherian '51, Pharmacie Sagherian, Beirut, to Miss Knar Merdjanian. on July 9, 1953.

Hagop Shirinian '45, Shirinian's Pharmacy, Dora - Beirut, to Miss Verjine Shirinian M.D., on November 22, 1953.

George Tarazi '49, New Sha'b Pharmacy, Jerusalem, to Miss Nadia Ilias Sliheet, on August 30, 1953.

MISCELLANEOUS NEWS

Eugenie Abouchdid '53, Beirut , is in charge of Pharmacie Abouchdid.

Amal Abu-Ghazalah '53, Nablus, is in charge of Abu-Ghazalah Pharmacy.

George Adrouny '40, Emory University , Atlanta , Ga. expects to complete this summer the requirements for Ph. D. in biochemistry.

Philip Akl '29, Bikfaya, Lebanon, runs his own Pharmacy and manufactures «Hydrobase --- the first water-soluble ointment base to be made in Lebanon on a large scale.

Riad Alami '51, Ohio State University, Ohio, obtained his M. Sc. from Michigan University expects to complete this summer the requirements for Ph. D. Pharmacognosy, He will probably teach at the University of Southern California.

Joseph Andonian '53, Beirut , is scientific representative of Hoechst.

Zuhayr Annab '48, Amman , now captain, Army Central Hospital, is chief chemist and bacteriologist. He will soon be leaving to England for a year of study at the London School of Hygiene and Tropical Medicine to obtain a Diploma in bacteriology.

Nubar H. Arsenian '35, Jerusalem, is senior radiographer at the Augusta Victoria Hospital and directs the Jerusalem Grand Pharmacy.

Goubran Atallah '52, Cairo, runs his own Zamalek Pharmacy at Zamalek, Cairo.

Nabih Atiyyah '49, Tripoli, is in charge of the I.P.C. Hospital Pharmacy.

Musa Awad '52, Jerusalem, operates the Government Hospital Pharmacy.

Nuha Baddurah '53, Beirut, is pharmacist at the Ministry of Agriculture.

Adib Bashshur '49, Tripoli works with the I.P.C.

Badi Batshon '51, East Lansing , Mich., is studying for his M. Sc. in pharmacy at the Michigan State College.

Fawzi Bicharah '33, New Delhi, is adviser to the regional director of WHO. at the South East Asia Regional Office

Edward Bortcosh '53, Kirkuk, Iraq, works at the Training Center of the I.P.C. instructing apprentices in chemistry to fit them in departmental work.

George Dayian, 53, Aleppo , bought the late Bashkounji's Pharmacy and changed its name to Al-Markaz Pharmacy. Tilal St.

Loris Dirlik '32, Cairo, proprietor of Norton Pharmacy, summers regularly in Lebanon and , like all the alumni who come to Beirut, never fails to visit his Alma Mater. He is representative of **al-Kulliyah Magazine.**

Hovig Etyemezian '39, Los Angeles, Calif., is an cultural advisor to the Armenian Community.

Elias Farah '53, Kuweit, is in charge of a government pharmacy, Kuweit City.

Tahir Faydi '51, Amman, obtained the Public Health Certificate from A.U.B. in Sept. 1953 and is now the chief serologist at the Central Government Laboratory .

Farid Goussous '50, Amman, opened a clinical laboratory for bacteriological and biochemical analysis.

William L. Habashi '53, Khartoum is now manager of Morhig's Pharmacy and plans soon to open his own pharmacy in the new quarter of the city.

Fuad Haddad '33, Cairo, is proprietor of Wilson's Pharmacy and directs the Manufacturing Pharmaceutical Laboratory for Protectinge Products.

Anwar Hakim '50, Berkeley, Calif, after obtaining his «Docteur en Pharmacie » from Geneva, did research in Switzerland, Belgium, England and the U.S.A. and published papers in the Biochemical Journal.

Fuad Hakim '50, Tripoli, is in charge of the I.P.C. Medical Stores and Dispensary and was recently promoted to staff grade.

Sami F. Halabi '53, A.U.B. is research assistant to Dr. W. Adolph. Nutrition Department.

Fuad Hamdan '47, Kuweit City , runs his own Hamdan's Pharmacy.

Elias Hawwa '52, Kuweit , is in charge of the village pharmacies of the Health Department.

Anwar Husseini '53, Jerusalem , operates Dawudy's Pharmacy in Jericho.

Edward Ishkhanian '50, Beirut , is scientific representative for Upjohn.

Hagop Ishkhanian '50, Aleppo , is doing his military service in the Syrian Army.

Luder Ishkanian '38, Aley, Lebanon . is in charge of his father's pharmacy.

Ara Israbian '53, Beirut , runs his own pharmacy, Israbian's Pharmacy at Bourj Hammoud.

Nuruddin Issa '43, Aleppo, owns his newly established Droguerie al-Chamal.

Edmond Kayyaleh '38, Jordan, is chief pharmacist of the East Jordan with UNRWA

Sarkis Kevorkian '51, Aleppo, bought the late Kenderji's Pharmacy. and changed its name to al-Aman Pharmacy.

Safwat Kutub '52, Austin, Texas, is studying at Texas University.

Abdul-Fattah Mallah '37, Baghdad, has been appointed director of the Royal College of Pharmacy, Iraq.

Anis Mouasher '53, Amman , opened his own de-luxe Pharmacy Ibn-Sina.

Sami Naman '53, Beirut, directs Richany Pharmacy.

Husam Nimr '53, Jenin, opened a beautiful pharmacy in Janin.

Rauf Salfity '50, Amman, spent two terms (1952-53) at Notingham University taking bacteriology and biochemistry. During vacations he trained in a hospital laboratory for experience in morbid clinical pathology and spent an extra term in the laboratories of Guys and St. Pancras Hospitals. He returned home last summer after successfully completing the requirements, and is still manager of the Jordan Medical Supplies Co. Ltd.

John Shakarjian '51, Aleppo, is technical director of Droguerie Diquaz and acting head of the science department at Aleppo College where he teaches qualitative and quantitative chemistry.

Fuad Stephan '32, Beirut has resigned his position as dean of the Royal College of Pharmacy, Baghdad.

Adli Suleiman '45, Khartoum, is now manager of Watania Pharmacy Khartoum North.

Yahya Safi '38, Khanakine , Iraq, is chemist at Khanakine Petrolium Co. He has been recently to England to study developments in petroleum chemistry.

Jamal Tabari '46, Aleppo, is technical director of Droguerie Sultanem in Tilal St.

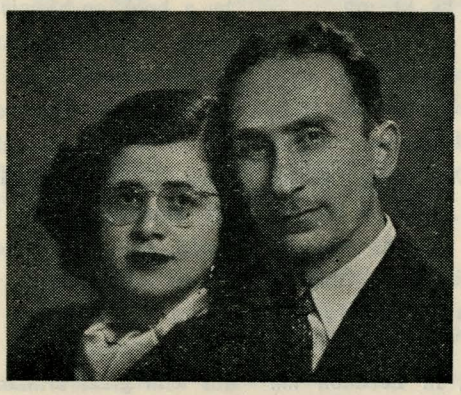
Berin Tutunji '53, A.U.B. , is research assistant to Dr. G. Fawaz, Pharmacology Department.

Nicolas Trochalakis '53, Jerusalem, is at Tutunjian's Pharmacy.

Sami Tukan '40, Temple University, Philadelphia, is studying for the Ph. D. degree. He received his M. Sc. degree at P.C.P. and S.

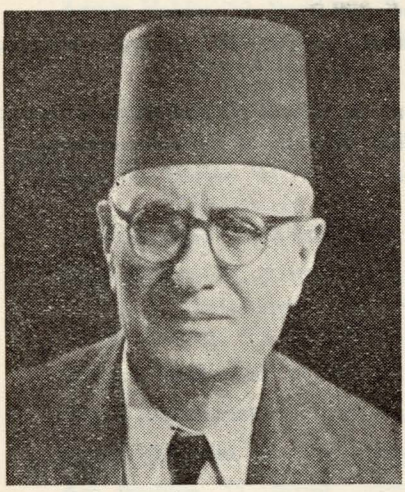
Anis Wahbah '53, A.U.B. , is research assistant to Dr. W. Adolph Nutrition Department.

Fuad Zaru '50, Chapel Hill, N.C., is studying at the School of Pharmacy, University of North Carolina, and doing part-time teaching at the same school.



Mr. and Mrs. N. Babikian

IN MEMORIAM



Nicola Haddad, Ph. M. '02

« One of the Arab world's most unique personalities , and also one of its best known and most loved savants -- Alumnus **Nicolas Haddad** (Ph. M. '02), passed away in Cairo on March 1, 1954, at the age of eighty-four .... In his time he was a successful journalist, novelist, poet, sociologist, scientist, political pamphleteer, and a few other things as well.... Mr. Haddad was born in Joun, near Saida, in Lebanon ..... Upon graduation, he went to the states.... He returned to Egypt .... and established Haddad's Pharmacy in the Shubra district of Cairo .... His intellectual activity was just about all-consuming and together with his wife he started a magazine called «Majallat er-Rijal was-Sayidat» ..... he spent a great deal of time writing books in various fields. One of his most famous was on sociology. He was also author of some thirty novels, dealing mostly with a variety of social, intellectual, and political life in the Arab world. And yet, with the advent of the modern scientific age.... he spent a great deal of time studying these advances in science, and eventually wrote « Architecture of the Universe» published in **al-Muktataf** under the editorship of A.U.B. 's present Vice-President in Charge of Relations — Fuad Sarruf . These were followed in recent years by a book on atomic energy and the atomic bomb. Lately, he participated in a novel contest organized by the Egyptian Ministry of Education. The work was based on the life of Kha'ed ibn el-Walid,..... it won first prize ..... With the rise of political Zionism, Mr. Haddad foresaw the danger to the Arab world, and .... wrote no less than sixty articles on the subject, in the weekly **Al-Rissala.** At 84, he was invited to lecture at the Oriental Club in Cairo late in January, 1954, He did this with great brilliance, but the effort proved to be too much for his advanced years.... He is survived by his widow, one son (Fuad Haddad, Ph. C. '33), and two married daughters.»

— Quoted from the al-Kulliyah Magazine, May 1954, p. 35.

Muhyiddin Raad, Ph. C. '35, passed away suddenly on December 28, 1953, in Tripoli.

FACULTY 1953-1954

Administration

Bayard Dodge, D.D., L.L.D., President Emeritus of the University
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Musa Ghantus M.D., Associate Dean of the Medical Division
Amin F. Haddad, Ph. C., M.S., Director of the School of Pharmacy.
Farid Amin Fuleihan, B.B.A., Registrar of the University

Teaching Personnel

From the School of Pharmacy

	Name	Courses taught	Class	
1.	**Amin Farid Haddad, Ph.C., M.S.**	Jurisprudence and Ethics	Pharm.	IV
		Pharmacy IV	Pharm.	IV
		Seminar	Pharm.	IV
		Pharmacy II	Pharm.	II
		Pharmacy I	Pharm.	I
2.	**Charles Abou-Chaar, Ph.C., M.S. (Abu-Shar)**	Drug Chemistry	Pharm.	IV
		History of Pharmacy	Pharm.	IV
		Pesticides	Pharm.	IV
		Seminar	Pharm.	IV
		Pharmacognosy	Pharm.	III
		Library Practice	Pharm.	III
		Pharmaceutical Botany	Pharm.	II
3.	**Edward Vorperian, B.A. Ph.C., M.S.**	Inorganic Pharm. Chem.	Pharm.	III
		Organic Pharm. Chem.	Pharm.	III
		Theory of Solutions	Pharm.	I
4.	**Levon Karamanukian, B.A., Ph.,C.**	Drug Chemistry Lab.	Pharm.	IV
		Pharmacy III	Pharm.	III
		Qualitative Chemistry	Pharm.	I
		Quantitative Chemistry	Pharm.	I

continued on next page

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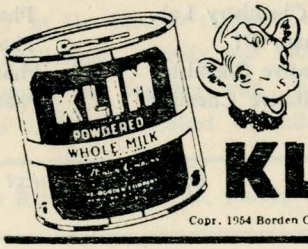

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5.	**Uthman Kanafani, Ph.C.**	Pharmacy IV Lab.	Pharm.	IV
		Drug Chemistry Lab.	Pharm.	IV
		Pharmacy III Lab.	Pharm.	III
		Pharmacy II Lab.	Pharm.	II
		Phamacy I Lab.	Pharm.	I

From the School of Medicine

6.	**Stanley E. Kerr, Ph.D.**	Biological Chemistry	Pharm.	IV
7.	**Munir As'ad Kan'an, M.D.**	Pharmacodynamics	Pharm.	IV
8.	**S. Boulus, M.D.**	Physiology	Pharm.	III
9.	**Hanna B. Doany, Ph.C.**	Microbiology	Pharm.	II
10.	**George Abu-Haydar, B.A., M.A.**	Biological Chemistry Lab.	Pharm.	IV

From the School of Arts and Sciences

11.	**Nicolas D. Constan, Ph.M., D.Sc.**	Organic Chemistry	Pharm.	II
12.	**R. Gulen.**	Organic Chemistry Lab.	Pharm.	II
13.	**John I. Mirhij, Ph.D.**	Biology	Pharm.	I
14.	**J. Keehn, Ph.D.**	Psychology	Pharm.	I
15	**Miss S. Khallouf, B.A.**	Psychology	Pharm.	I
16.	**Levon G. Babikian, B.A., M.A.**	Biology	Pharm.	I
17.	**L. Armstrong, Ph.D.**	Sociology	Pharm.	I
18.	**Mufid Abu Khadra, B.B.A.**	Business Methods	Pharm.	II
19.	**Fuad Badr, B.B.A.**	Business Methods	Pharm.	IV
20	**Miss P. Mavrides, B.A.**	Biology Lab.	Pharm.	I

CONTENTS

Acknowledgement

Mr. Haigaz Artinian, University Photographer, took the photographs on pages 7, 83, 86, 87.

The editor wishes to thank, too, Messrs. Achkar Frères, the printers, for their kind cooperation and for their promptness.

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1. Glass, S. J., The Advantages of Combined Oestrogen-Androgen Therapy of the Menopause, J. Clin. Endocrinol., 10: 1616, 1950.

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