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CONCERNING SCIENTIFIC RESEARCH WORK IN THE INSTITUTES OF THE CZECHOSLOVAK REPUBLIC[1]

[This is a translation of an article written by L. N. Yakhontov, V. V. Kolpakova, Yu. N. Sheynker, and T. D. Pervacheva of the All-Union Scientific Research Chemico Pharmaceutical Institute imeni S. Ordzhonikidze, in Meditsinskaya Promyshlennost' (Medical Industry), No 12, 1959, pages 52-55.]

Physico-Chemical Analytic Methods

In czechoslovakia the most widely used methods of physico-chemical analysis are paper chromatography, polarography, electrometric titration and colorimetry. These methods are used not only in scientific research and control institutes but also in plant laboratories. Spectrophotometric methods are used somewhat less. Conductometric methods and ion exchange chromatography are hardly used at all. Column chromatography is used mainly for preparation purposes.

Chromatography: one of the most interesting chromatographic methods is chromatography in a gas-liquid system. The method consists of dispersion chromatography (of gaseous substances or substances with a boiling temperature up to 250° in vacuum) between a gas (nitrogen, CO_2 and others) and a stationary liquid phase (silicone oil, esters of higher acids and others) on a carrier (kieselguhr, etc.) Attention is being drawn to many different types of detection methods to use after chromatography, from simple gasometric analysis with absorption of carbon dioxide gas to spectrophotometric determination of each component in the yield from chromatographic column. One of the most widely used analyzers is a head-conductivity measuring instrument that automatically records the results of the analysis. The method is used both for analysis of multicomponent mixtures (qualitative and quantative) as well as separation of these mixtures to obtain spectrally pure substances. The method is characterized by high sensitivity (allowing the investigation of 5-10 mg of a multi-component mixture and detection of 0.5 mg of substance in 3 mg of mixture), rapid determination (10-15 minutes) and objectively recorded results.

[1] For the beginning of this article see "Meditsinskaya Promyshlennost' SSSR" 1959, No 11.

Paper chromatography, another very widely applied method, is used for analytical purposes and for solving problems in synthesis. In Czechoslovakia different types of paper chromatography are widely used: ascending, descending, ring chromatography, chromatography over a time period, with chromatography circulating phases, rapid chromatography, paper chromatography for preliminary separation of substances, etc.

The following methods are used for carrying out rapid chromatography: paper with high porosity is selected, the chamber dimensions are reduced (test tube chromatogram), chormatography is carried out at a higher temperature (50°), and systems are used which have a greater speed of solvent front movement. All this makes it possible to reduce the time of the chromatography to 30 minutes.

In the Institute of Pharmacy and Biochemistry, work with paper chromatography is carried out in a special laboratory directed by Dr. K. Macek.

Paper chromatography is used for the following:

a) To determine the purity of substances; chromatography is carried out in certain systems and verifies the absence of side strains.

b) To determine the quantity of the substances obtained in a reaction and the quantitative content of each component (visually or by using planimetry to measure the size of the stain, and also by elution with subsequent chemical or physico-chemical determination).

c) For establishing the identity of substances; it is necessary to use chromatography if there are more than three systems.

d) For studying reaction kinetics and determining the optimal conditions for carrying out reactions; here samples of the reaction mixture after definite intervals of time are placed on paper and undergo chromatography.

e) For solving problems in the structure of organic compounds; the basis of this method is the RF principle of additivity. Having an ingredient Rf for determination of a system and Rf of a new substance in the same system, it is possible to find the structure of the substances; the method was successfully applied by K. Macek for establishing the structure of such complex compounds as the veratrine alkaloids.

In the State Control Institute of Pharmaceuticals paper chromatography methods are used widely for the following purposes:

a) Determining the purity of pharmaceuticals (for example, determination of gitoxin in preparation of digitoxin.)

b) Detecting decomposition products in pharmaceuticals during storage (for example, n-aminobenzoic acid in novocaine and dicaine; Dr Macek).

c) Separating pharmaceutical mixtures into specific ingredients with further quantitative determination (Dr. Jung).

d) Analysis of pharmaceuticals from plants (for example, preparations containing extracts of aloe; Dr. Draus).

It should also be noted that many types of detection methods have been successfully worked out for use with paper chromatography, from ultraviolet irradiation to actual syntheses in several steps on the paper; for example, to detect aromatic nitroproducts the latter are reduced, diazotized and azo-coupled directly on the paper after chromatography.

Polarography: the leading institute in the area of theoretical and practical questions in polarography is the Institute of Polarography of the Academy of Sciences of the Czechoslovak Republic (Director: Prof. Ya. Geyrovskiy). In this institute work is being done on the application of oscillographic polarography to qualitative and quantitative analysis (Prof. Geyrovskiy, Dr. Karlovoda), building automatic gas analyzers which operate on polarographic measurements, studying molecular structure of organic compounds using polarography (Dr. Zuman), and studying chemical reactions and the mechanism of reduction on a mercury electrode (Dr. Smoler).

In the physical chemistry Laboratory of the Institute of Pharmacy and Biochemistry (Director: Dr. Knobloch) polarographic methods are widely used for the analysis of types of pharmaceuticals and intermediates in the synthesis of pharmaceutical preparations. Polarographic methods have been worked out by the laboratory for the determination of vitamins, hormones, antibiotics and other preparations.

Spectroscope: the most capable and successfully functioning center for molecular spectroscopy in Czechoslovakia is the optical laboratory of the Institute of Organic Chemistry of the Academy of Sciences of the Czechoslavak Republic (Director: Dr. I. Pliva). The laboratory work is closely allied to the work of the whole institute and is primarily concerned with the study of spectra of natural compounds (terpenes and steroids) and silico-organic compounds. Lately work of a theoretical nature is being done in the laboratory. A study is being made of connection between the electronegativity of substituents and the frequency of C-O groups in carbonyl compounds, whereby it may be possible to determine the relationship as a type of empirical Gamet dependence (Dr. Gorak). In addition, in recent years I. Pliva has been carrying out successful work in theoretical calculation of molecular oscillation spectra..

Another laboratory which is functioning successfully in the field of spectroscopy is the laboratory of physical chemistry of the Institute of Pharmacy and Biochemistry (Director: Dr. E. Knobloch). The laboratory work is closely allied to the work of

other laboratories of the institute. Among the analytical methods worked out in the laboratory the following may be mentioned: spectrophotometric determination of apomorphine hydrochloride vitamin B_{12} in injection solutions, vitamin K_1, thiosemicarbazone of n-acetaminobenzaldehyde, pelentan, infra-red spectrum analysis of picolinic fractions for α-, β-, and γ-picolines and 2,6-lutidine, infra-red method for determining o-nitroethylbenzene in n-nitroethylbenzene.

The flame photometer has been used successfully for determination of alkali and alkaline earth metals in preparations or biological liquids. Solutions which are to be analyzed are blown by a stream of gas into the flame of an acetylene burner; adequately grated filters give a spectrum corresponding to the illumination from a given metal; the light falls on a photo-element causing electric currents to flow which are quickly measured with a high degree of accuracy by using the proper circuit.

Some work in the laboratory is of a theoretical nature (for example investigation, using spectra, of the tautomers of 4-oxycoumarin and others).

Among the other laboratories using spectroscopic methods of investigation we should consider the laboratory of physical chemistry in the Institute of Organic Chemistry in Pardubitse-Rybitvi. This laboratory is equipped with the most complete spectral apparatus, among which are a number of valuable instruments that were designed in the laboratory itself: different automatic recording spectral set-ups, and a spectrochromatograph. The latter instrument is of great interest due to the short time it required to carry out a quantitative analysis of complex multicomponent mixtures of aromatic hydrocarbons (or other substances which absorb in the ultraviolet region of the spectrum) in which 1 to 5 mg of mixture are sufficient for a complete analysis. The basic function of the instrument is to separate components of the mixture using gas-liquid chromatography and to register each component spectrophotometrically.

In the State Control Institute of Pharmaceuticals physico-chemical methods, and among them spectral methods, are used for the analysis of vitamins, hormones, anti-biotics and natural substances (Director: Dr. Grda). Spectroscopy is used on a small scale for solving certain analytical problems (determination of vitamins K_1, A, D, terramycin, tetracycline).

Among other physico-chemical analytical methods, electrometric titrations are used in the State Control Institute for Pharmaceuticals. These methods have been worked out for substances which form insoluble precipitates with silicotungstic acid, picric acid and picrolonic acid. These methods are sufficiently accurate, giving an error of 1-2 percent and are used in analyzing not only the drug form but also high-content preparations. During

analysis of the active principle in tablet form it is not necessary to remove the filler in order to carry out the determination.

Colorimetric methods are used mainly for analysis of drug forms (tablets of reserpine, cortizone, vitamins A and D_2, solutions of adrenalin, etc.) and for quantitative determination of substances after their separation on a paper chromatogram.

Most of the laboratories use a Ful'frikh photometer.

Complexonometric methods of titration are being worked out at the analytical laboratory of the Institute of Pharmacy and Biochemistry (Dr Kerbl). Methods are being planned for complexonometric determination of all inorganic preparations and organic pharmaceutical preparations that contain a metal; in addition new indicators are being synthesized for complexonometric titrations.

Some Problems of the Organization of Scientific Work

It is necessary to mention the excellent organization of Scientific work in Czechoslovakia. Attention is being directed toward an accurately supplied scientific information service and summary of material from the literature. As an example one may cite the work carried out in the Institute of Pharmacy and Biochemistry on a review publication: "Exerpta Pharmaceutica."

The publication is issued regularly, every six weeks, and contains about 160 reviews and about 400 annotations on questions of chemistry, medicine and pharmacy. Each scientific journal that is received by the Institute is given to an editorial committee which consists of five members. The committee notes which papers should be reviewed and those which should be annotated. Then the papers are sent to colleagues in the Institute who review these papers during a two week period. The reviews and annotations are printed in a journal in such a fashion that it is possible to cut the journal and obtain cards, each of which is devoted to one paper. The cards are collected in a card index. The card index is well-arranged allowing one to select literature rapidly on various problems of chemistry, biochemistry, biology, medicine, and technology.

The effort of the scientific workers to have at hand all essential original literature is quite valuable. To do this a lively exchange of reprints is carried on with scientists of other countries and in addition, photocopies of papers are made. In the Institute of Pharmacy and Biochemistry there is a special photo-laboratory which photocopies about 1500 papers every month at the request of individual members of the Institute. All this allows the scientific staff to save time by not having to rewrite or summarize papers in the library and by being able to use original sources without leaving the work area.

Czech chemists are doing a lot of work in disseminating data

from the literature and writing monographs and reviews. Practically every leading scientist is doing a monograph or reviews. An example which may be cited is the monograph containing a wealth of material which was edited by Gays and Macek entitled: "Paper Chromatography." It is now coming out in the second Czech edition and has been translated into German. Jizba and Ferles' monograph "The Chemistry of Pyridine" was writted over a period of two years and is currently the most complete review of the chemistry of pyridine in the world literature. Members of the laboratory staff of the R. Lukes Academy are writing a multi-volume review on the methods of organic chemistry. Three volumes have already been printed: I - Reduction, II - Halogenation and Dehalogenation, III - Nitration, Nitrosation and Diazotization. Volume IV, which is devoted to condensation reactions, is being prepared for printing. Finally, every year in the German journal "Die Pharmacie," reviews by Czech chemists are published on new research since the previous year in the field of pharmaceutical chemistry.

Czech libraries are well provided with monographs and periodicals which come from many different countries.

Laboratory glassware is made of Czech glass using ordinary polishing methods. The glass is of high quality. Storage of reagents is a model of organization; the reagents are assigned locations according to the Beilstein system, which not only facilitate locating individual reagents but also makes it possible to tell at a glance what compounds of a given chemical class are in stock.

Also quite valuable is the fact that the institutes are well provided with workshops (glass-blowing, mechinical, etc.) which considerably facilitates and accelerates research. In addition, Czech chemists can carry out without assistance a number of the simplest glass-blowing tasks; in every laboratory there are burners with compressed air which make it possible to pull capillaries, make test tubes, stirring rods, etc. without leaving the work area.

The authors of this paper received the most cordial and friendly treatment from Czech comrades, for which we wish to express our deep gratitude. Czech friends were interested in the work of Soviet chemists and sincerely strove to acquaint us with all of the best in their work and in their country.

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