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Review Article

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A Literature Review

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THIS REVIEW is a continuation of an annual series originated by McKeehan (1). It represents a comprehensive cross-section of the research and development efforts in various disciplines of the pharmaceutical sciences. Numerous periodicals and *Chemical Abstracts*' Pharmaceuticals and Pharmacodynamics sections published during 1965 were searched and selectively abstracted.

Some of the literature related to the pharmaceutical sciences has been reviewed on an annual basis in other publications and is omitted here. For such associated papers in analytical chemistry, antibiotics, bacteriology, biochemistry, biology, cancer, medicine, medicinal chemistry, microbiology, organic chemistry, pharmacology, physical chemistry, physiology, and plant physiology, the reader is referred to reviews in these areas of study. The "Advances in . . . " series,

the "Annual Review of . . . ." series, and the "Progress in . . . " series are particularly pertinent. In order to maintain continuity with previous pharmaceutical science reviews of *J. Pharm. Sci.*, their general format was retained.

GENERAL PHARMACY

The literature continues to abound with articles of interest to investigators involved in all areas of the pharmaceutical sciences. One paper by O'Reilly listed and discussed many of the pharmaceutical reviews published from June 1963 to June 1964 (2). Vice President Hubert Humphrey described the problems in keeping up with drug literature in a survey performed by the National Library of Medicine (3). Two other surveys attempted to outline the problems associated with the collection, distribution, and effective utilization of the vast amount of drug literature (4, 5). The proper procedure for the approval of a new drug or drug cosmetic has been discussed in an outline of current regulation procedures (6). Kass reviewed the type and scope of information an inspector is entitled to receive upon FDA inspection (7). An article written by a group of four physicians explained the practical aspects of drug therapy from the standpoint of the pharmacist, clinician, researcher, and teacher (8).

One review was concerned with how and why generic and trade names are assigned to new drugs (9); Ansel commented on the qualities of a desirable trade name and the intricacies of determining its legal availability, subsequent registration, and protection (10). The utilization of drugs in aerospace medicine was summarized (11). The chemistry and uses of antifungal (12), anthelmintic (13), and antimalarial (14) drugs were presented in three different articles which contained many useful references. The outlook for dimethylsulfoxide, a new drug from lignin, as a therapeutic agent has been described (15). A paper on historical studies of camphor was also published (16). Kuttel recommended a simple and practical design for aseptic compounding in dispensaries (17). Additional surveys considered the preparation and properties of ophthalmic solutions (18, 19) and some aspects of toiletry technology (20).

Preservatives.—The preservation of ophthalmic products was reviewed in a paper with 68 references (21). In another study, many types of preservatives were evaluated for their antibacterial and antifungal properties (22). Evans applied the Ferguson principle to systems of mixed preservatives to ascertain that biological activity is proportional to the degree of saturation of the aqueous phase (23); the same principle was used to determine and correlate the activity of three quaternary ammonium salts against *M. aureus*, *E. coli*, and *C. albicans* with the surface properties of these compounds (24). Propylene glycol exhibited antimicrobial activity when used topically (25). Thoma carried out galenic and analytical studies on the effect of several cellulose derivatives and alginates on the activity of several antiseptics (26). Alkaline glutaraldehyde has been suggested as a general disinfectant for instruments and apparatus that cannot be sterilized by autoclaving (27). Two studies were concerned with the mechanism of action of phenolic disinfectants. One investigated the effects on induction of and accessibility of the substrate to β-galactosidase in *E. coli* (28), and the other explored the effect of 2,4-dichlorophenol on the incorporation of labeled substrates by *E. coli* (29). Another paper assessed the importance of metal ions and the toxic properties of the formyl group in determining the bactericidal activity of various phenols and salicylaldehydes (30). One other report presented data on the hemolysis of erythrocytes by a series of quaternary ammonium salts (31).

Foster published two different articles on the preservation of ophthalmic solutions (32, 33). Test procedures and test organisms suitable for shortening the time required for the selection of an adequate preservative have been disclosed (34). The use of antimicrobial agents in parenteral products was reviewed in a paper containing 22 references (35). Another summary with 38 references on the activity of antibacterials in a two-phase system was presented (36). Krowczynski and co-workers suggested a preservative for aqueous heparin solutions (37). Also, 8-hydroxyquinoline sulfate was satisfactory as a preservative for tuberculin PPD (38). This agent was effective against two yeasts, three molds, *P. aeruginosa*, and *S. aureus*.

Flavor, Aroma, and Color.—A review has been compiled on the use of flavors in the United States, the various methods used for flavor testing, and the difficulties encountered for the taste correlation of drugs (39). Tilgner proposed a flavor dilution profilogram for characterizing the detailed aroma or flavor sensations of a product in dilution steps between the threshold and some standard extract of the undiluted product (40). A combined electrophysiological and sensory test revealed that the gustatory effect of substances which show taste as sour or salty was reinforced by inhibition of cholinesterase on the tongue (41). No changes were observed for bitter or sweet tastes. Taste sensitivities to quinine and 6-*n*-

propylthiouric acid were determined (42). Five new principles for flavoring antitussives have been developed (43). Sorbitol, saccharin, and *N*-cyclohexylsulfamic acid were found to be effective synthetic sweetening agents in pharmaceutical preparations (44). In addition, Edwards commented on the flavor constituents of citrus oils (45).

The philosophy of and methods for the identification of odor and flavor constituents were reviewed by Wick (46). The theory of odor and the relationship between the odor and the chemical properties of flavors have been surveyed in another paper (47). A review of pioneers in aldehydes and ketones was presented (48), and the synthesis, physiochemical properties, and economic factors of lavender were summarized (49). One status report listed all currently approved U. S. certified colors (50); another outlined the current FDA status of all color additives for cosmetic use (51). The effects of grain size and moisture content have been studied with the Pulfrich photometer against 120 color standards (52). A method was described for classifying and describing colors formed when the concentrations of several dyes and carbon black in compressed tablets were evaluated (53). One other paper discussed the physiology and psychology of color sensation (54).

Adjuvants.—The properties and compatibilities of two dextrans with molecular weights of 40,000 and 70,000 were tabulated by Smith (55). Another investigator assessed the effect of heat on aqueous solutions of dextran by measurements of viscosity and reducing power (56). The use of cation exchangers as carriers of drug components for the improvement of their palatability has been described (57). The application of polyethylene glycols in pharmaceuticals was outlined (58). Anomalies in some of the physical properties of spray-dried lactose and granulated magnesium oxide were traced to the presence of fines which could be removed by washing with selected organic solvents (59). A silicone fluid proved useful as a lubricant for artificial eyes (60); it did not adhere to tissue, was insoluble in water, was stable over a wide temperature range, and did not support bacterial growth. The properties of neutrality, inertness, low surface tension, easy viscosity control, miscibility with eye secretions, and a low tendency to support bacterial growth, all contributed to making methylcellulose a valuable agent for preparing an aqueous vehicle for pilocarpine nitrate ophthalmic solutions (61). Polyvinylpyrrolidone has been recommended for use as a binder in tablet making (62). The characteristics of Neen gum, a polyelectrolyte which behaves as a lyophilic colloid, were disclosed (63). Experimental data were also presented on a new gum prepared by fermentation from glucose that could be used for thickening highly concentrated electrolyte solutions (64). Some of the practical aspects of colloids were commented on by Smith (65). The viscosity control of liquids and the forced flow of solids were accomplished by the use of silicas (66). One worker collected data on the common properties of some clays including dispersion, aggregation, and the difference between clays and other mineral colloids with particular reference to exchange capacity (67). Other researchers conducted an infrared study on structuration in bentonite clays (68).

The importance of propylene glycol as a solvent in dermatology was reported by Barr (69). The attributes of hexadecyl alcohol as a new material for cosmetic and topical formulations have been discussed in detail (70, 71). Another paper described the suitability of higher-boiling fractions of ethoxypolysiloxane oil in ointments and suppositories (72). The formulation of creams, lotions, and ointments with silicones was studied in two different publications (73, 74), and the utility of isopropyl myristate (75) and coconut oil derivatives (76) in cosmetics was also demonstrated. Both cholestanol (77) and germ lecithin (78) were effective emulsifiers in making water-in-oil emulsions. King and Sheffield used the triethanolammonium salts of several alkylsulfuric acids in the formulation of dermatologic vehicles (79). The seed husk of *Plantago ovata* has been evaluated for its emulsifying properties (80); the powder produced poor emulsions, whereas the mucilage gave emulsions that compared favorably with those made with acacia. One investigator proposed microcrystalline cellulose as a new ingredient for the formulation of creams, lotions, and ointments (81). Another researcher outlined the pharmaceutical and cosmetic usage of a new colloidal alumina as a topical formulating agent (82). The synthesis, analysis, and physical properties of several allantoin complexes were determined, and their potential dermatological uses were suggested (83). Other investigators evaluated current problems associated with the effects of synthetic detergents on the skin (84).

Stability.—Current formulation stability problems were discussed in two different review articles (85, 86). Papers by Sawatari (87) and Sabalitschka (88) advocated the use of antioxidants as stabilizers. Another report examined the measurement and prevention of oxidative deterioration in cosmetics and pharmaceuticals (89). The thiobarbituric acid–malonaldehyde

reaction was used to measure antioxidant effectiveness in pharmaceutical oils (90). The oxidation of benzaldehyde and methylbenzaldehyde in hydrous solutions of polyoxethylene glycol ethers was measured by a manometric technique (91). Phenolic antioxidants were found to be quite satisfactory for improving the stability of creams containing vegetable oils (92). The rates of autoxidation of linoleic acid in micellar solution were also studied (93). The influence of heat sterilization and the stability of pharmaceutical solutions were surveyed by Speiser (94). The effect of ultrasonic energy was explored in two different studies; it was used to study the hydrolysis of acetylsalicylic acid solutions at various temperatures and pH values (95), and to evaluate its influence on physical and chemical transformations of purine derivatives (96). In another investigation, the effect of X-rays on dihydrouracil in aqueous solution, with and without the presence of oxygen, was revealed (97).

Acetylcholine bromide solutions were shown to be stable at room temperature for 2.5 months and at 5° for 5 months (98). Optimum stability conditions for adrenaline were achieved by dissolving its bitartrate salt in water containing sodium thiosulfate and boric acid (99). In another stability study, solutions of chlorpromazine were found to develop a precipitate if combined with sodium phenobarbital, sodium bromide, or neospasmin (100). Denoel discovered that ephedrine decomposed rapidly in peanut oil, but was extremely stable in mineral oil (101). Three other investigators tested the effect of self-radiation, pH, temperature, and sunlight on the stability of sodium iodohippurate-^{131}I (102). Experiments were also conducted on the stability of isoniazid and its related compounds (103). Sealing morphine hydrochloride solutions under carbon dioxide or nitrogen gave more protection against decomposition than equivalent solutions sealed under air (104). The effect of aging of aqueous pralidoxime solutions on the assay, toxicity, and antidotal activity has been investigated by Lehman and Bloch (105). Two studies were performed on tetracaine hydrochloride solutions. One study evaluated the effect of an ultraviolet lamp on pH and potency (106); the other examined the effect of sterilization and hydrolysis in the pH range of 4–7 (107). The mechanism of thermal rearrangement and decarboxylation of procaine was disclosed (108). Various methods were suggested for the stabilization of procaine hydrochloride solution. Two papers proposed the addition of carbon dioxide and *p*-aminobenzoic acid as stabilizers (109, 110). The addition of EDTA was observed to prevent solutions of procaine from turning yellow, but it failed to inhibit decomposition of the drug (111). Another local anesthetic, procaine, was stabilized with a mixture of sodium thiosulfate and sodium sulfite (112). The stability of retinol acetate (113) and sodium sulfacetamide has also been investigated (114). A compatibility study with certain sulfonamides indicated that insoluble precipitates were formed with salts of several alkaloids, boric acid, and zinc sulfate (115). Other workers conducted a study on the stability of a 10% solution of sodium sulfadiazine in the presence of copper, iron, and hydrogen peroxide (116). In addition, the stability of triiodothyronine (117) and triiodothyronine-^{131}I (118) was carefully determined under different conditions of storage.

Koshy *et al.* described some of the factors involved in the browning of spray-dried lactose (119). In a similar study, the lactose–amine reaction was discovered to be predominately a primary amine–carbonyl reaction and was similar in nature but distinct from the dextrose-, galactose-, and HMF–amine reactions (120). γ-Rays from ^{60}Co were claimed to accelerate the oxidative decomposition of methyl linoleate mixed with lactose (121). Two compatibility studies have been conducted on powder mixtures. The incompatibility of carbinoxamine maleate (122) and calcium phosphorylcholine hydrochloride (123) with 20 and 84 different powder preparations, respectively, was carefully evaluated. Experiments on powders of dehydroacetic acid revealed that the α-form, which is stable at room temperature, is rapidly converted to the β-form at 80° (124). Diffuse reflectance studies were used to observe solid–solid interactions of oxytetracycline, phenothiazine, anthracene, and salicylic acid with various adjuvants (125). Some of the factors influencing the stability of calcium acetylsalicylate and acetylsalicylic acid tablets have been investigated by Kiss, Rozsondai, and Scholz (126). In a study where acetylsalicylic acid was combined with ascorbic acid in tablets, the effect of water vapor pressure on the moisture sorption and the stability of both components was reported (127). No breakdown of digitoxin was found in tablets, injections, or solutions stored in the dark for 5 years (128). Similarly, no decrease in the alkaloid content of ipecac concentrate was observed after 18 months of storage (129). The sedimentation of thyme tincture was prevented by clarification with talc and cooling to 0 to −5° (130). The stability of helveticoside, a glycoside from strophanthidin, was also studied in a long-term investigation (131).

Stability Kinetics.—Garrett published a review with 198 references discussing the prediction of drug stability in pharmaceutical preparations (132). Two other reviews appeared in the literature. Both of these surveys evaluated the use of chemical kinetics for the prediction of drug stability (133, 134). A nomograph chart was devised in one study to facilitate the analysis of stability data obtained in accelerated testing at elevated temperatures (135). A reciprocal heating machine has been found very useful for investigating single-step stability studies under nonisothermal conditions (136). Other workers used model calculations, based on the statistical-mechanical formulation of isotope effects, to predict how analysis of experimentally measured isotope effects may be used to gain information concerning the differences between the reactants and the transition state in a rate process or between the reactants and the product in an equilibrium process (137).

One paper examined the kinetics of solvolysis of various *N*-alkyl-*N*-nitrosoureas in neutral and alkaline solutions (138). The decomposition of *p*-aminosalicylate was found to be first order while sodium *p*-aminosalicylate was zero order in aqueous solution (139). Pseudo first-order rates of spontaneous degradation were ascribed to apomorphine under varying conditions of temperature and pH (140). The hydrolysis of methyl and ethyl esters of benzoic acid, some sterically hindered acids, and benzonitrile by suspensions of sodium hydroxide in DMSO was 10^4 to 10^5 greater than in hydroxylic solvents (141). Activation energies, frequency factors of the Arrhenius equation, and equilibrium constants between chlorothiazide and its intermediate were calculated from the rate constants on the hydrolysis reaction (142). The rate of autolysis of α-chymotrypsin in the pH region of 7 to 11, in the absence of added salt, has been studied through the rate of acid formation in a pH-stat and through the rate of decrease in enzyme activity (143). Garrett and Notari quantified the kinetics of dehydration of cycloheximide to anhydrocycloheximide in the pharmaceutically useful acetate buffer region (144). Another article compared the rate of hydrolysis of thalidomide, *N*-butylphthalidomide, and phthalimide in sodium hydroxide (145). The degradation of hexamine in aqueous solution was considered to be pseudo first order (146). The solvolysis of 5-iodo-2′-deoxyuridine was revealed as first order over the pH range of 3.9 to 12.0 (147). First-order rate constants were disclosed for the decomposition of molten malonic acid from the volume of carbon dioxide evolved (148). In a stability study on mydeton injection solutions, the rate of decomposition was influenced by pH and temperature (149). Two different papers discussed the rate of hydrolysis of procaine under various conditions of temperature and pH (150, 151). The effects of substitution have been correlated with the acid-catalyzed hydrolysis rates of some oxazolidines (152). Other kinetic studies were carried out on tetracaine, parethoxycaine, leucinocaine, procaine, farmocaine, and larocaine (153). Methyl substitution was demonstrated as providing increased ring stability in a study on the hydrolysis of succinamic acid and succinimides (154). Pseudo first-order rate constants were recorded for the base-catalyzed hydrolysis of urea (155).

Antibiotic Stability.—A buffer solution containing boric acid, sodium borate, and polyethylene glycol did not prevent hydrolysis of chloramphenicol (156). The stability of two antibiotics, cranomycin (157) and erythromycin lactobionate (158), has been studied. Tukamoto, Miyake, and Sato reported on the decomposition of dihydrostreptomycin, chloramphenicol, and tetracycline by drug-fast *E. coli* (159). Other investigators have compared the effect of glycerin, paraffin, propylene glycol, white petroleum jelly, polyethylene glycol, lactose, alcohol, sunlight, and darkness on the stability of hamycin preparations (160). Acid degradation studies were performed on kasugamycin (161). A decrease in the optical rotation of lincomycin showed a direct correlation with microbiological assays (162). One study followed the rates of decomposition of methicillin in aqueous solution (163); another determined the effect of sugars on the browning of neomycin (164).

Several papers were presented on the stability of various penicillins. Losses in potency of 2,6-dimethoxyphenyl penicillin were evaluated iodimetrically, by U.V. absorption, and by microbiological assays on *B. subtilis* (165). The stability of aqueous solutions of certain novel penicillins was observed to be reduced by surfactants, preservatives, and thickening agents (166). The decomposition rates of α-phenoxypropylpenicillin, 2,6-dimethoxyphenylpenicillin, and α-aminobenzylpenicillin have been demonstrated to be first order and obeyed Arrhenius' equations (167). In another study, it was concluded that acacia accelerated the inactivation of penicillin, whereas methylcellulose had no effect (168). Other workers, Olszewski and Grabowska, tested the influence of sodium benzoate on the stability of aqueous penicillin solutions (169). In a physical-chemical study on the relationship between potency and hygroscopicity, the effect of humid-

ity on the potency of four semisynthetic penicillins was investigated (170). Schwartz described the effect of ionic interaction on the catalysis of penicillin hydrolysis by certain catecholamines (171). This investigator also concluded that the degradation of penicillin G involved both the catalyzed hydrolysis of the undissociated molecule and a rearrangement of the penicillin ion following proton attack (172). A different study on some penicillin salts correlated the initial product characteristics and the properties after 3 years by statistical means to predict their shelf-life (173). The catalytic effect of buffers on the degradation of penicillin G in aqueous solution has also been examined (174). Other workers considered the cause of the reddening coloration and pigments in colored solutions of streptomycin (175).

Vitamin Stability.—Elevated temperature storage tests and a graphic method of calculation were used by Tardif to determine thermal degradation rates in three polyvitamin tablet formulations (176). In another vitamin stability study, the same worker found no differences in a polyvitamin suspension that had been stored either in the plant or in the pharmacy (177). In other multiple vitamin stability studies, vitamins A, B_{12}, and ascorbic acid were classified as being the least stable (178). The stability of vitamin A, tocopherol, and unsaturated fatty acids in vitaminized vegetable oil exposed to sunlight was also investigated (179). The stability of vitamin A in concentrates and foodstuffs was determined under various conditions of temperature, atmosphere, and time (180). The effect of material quality and the method of preparation upon the stability of aqueous thiamine injections was the subject of one paper (181); another study examined the effect of salts, vehicles, pH, temperature, and vitamins B_2, B_6, and niacinamide upon the stability of thiamine (182). The effect of cocarboxylase on the hydrolysis of thiamine pyrophosphate was reported (183). Kato claimed that powdered mixtures of thiamine tetrahydrofurfuryl disulfide with sodium bicarbonate and acetylsalicylic acid were completely stable (184). Two separate papers were also presented on the stability of isomers of dihydrothiamine (185, 186). In addition, γ-rays from ^{60}Co were found to accelerate the decomposition of thiamine hydrochloride when mixed with calcium carbonate and dibasic calcium phosphate (187). The stability of riboflavin and its phosphate salt in syrup, propylene glycol, glycerol, 70% sorbitol solution, and water has been assessed (188). Macromolecules, *e.g.*, polyvinylpyrrolidone, polysorbate 80, and sodium decyl sulfate, enhanced the rate of aerobic photobleaching of riboflavin by visible light (189).

The mechanism of color formation, the role of furfural, and the decomposition products of ascorbic acid were delineated (190). In a similar study, the rate of formation of furfural by the hydrogen ion-catalyzed anaerobic degradation of undissociated ascorbic acid was depicted as being equal to the rate of disappearance of the ascorbic acid (191). Another anaerobic study considered the formation of carbon dioxide and furfural by decomposition of ascorbic acid at various pH and temperature conditions (192). Finholt *et al.* also studied the anaerobic degradation of ascorbic acid by following the rate of formation of carbon dioxide (193). Otani detected a linear relationship between the color change and the degradation of ascorbic acid in the pH range 1–7 (194). He presented another paper on the relationship between the color change and the oxidation of ascorbic acid in aqueous solution (195). Additional experimental data compared the stability of ascorbic acid and 2-keto-l-gulonic acid in an aqueous medium (196). Two different manuscripts were concerned with the effect of stabilizers on ascorbic acid. Amino acids improved the stability in liquid formulations (197); rutin retarded the oxidation of ascorbic acid in apple juice (198). Another study analyzed the shelf-life of several liquid formulations with ascorbic acid in different vehicles with and without other vitamins (199). The most stable injectible solutions of ascorbic acid were prepared by using a 5% excess of ascorbic acid, purging with carbon dioxide, and sealing under carbon dioxide (200). In tablets, ascorbic acid remained stable longer if made by dry compression or by using a nonaqueous binder and storing in amber containers without moisture (201). Studies in model systems have indicated that ascorbic acid is more stable in aqueous systems and is a more efficient antioxidant than erythorbic acid (202).

The thiazole moiety of thiamine hydrochloride and selected model compounds had no adverse effect on the cyanocobalamin stability (203). A dose of 9.1×10^4 rads of γ radiation from ^{60}Co destroyed 45% of the vitamin B_{12} under test (204). Steric factors were found to have an important influence on hydrolysis of vitamin B_{12} in aqueous hydrochloric acid–dioxane solution at 50° (205). Hydroxocobalamin in liver extract has been stabilized by the addition of ferric and ferrous sulfate ions (206). Janicki and coworkers conducted a study on the stability of vitamin D_2 in irradiated feed yeasts during storage (207). Thiamine, riboflavin, chlorine, ascorbic acid, manganese sulfate, and calcium hypo-

phosphite were all shown to cause decomposition of folic acid in pharmaceutical preparations (208). The discoloration of isonicotinic hydrazide tablets in tropical climates was attributed to the lactose contained therein (209). Other studies compiled data on the incompatibility of some commercial vitamin K_1 injections (210).

PHARMACEUTICAL TECHNOLOGY

Past, present, and future trends in pharmaceutical product development were summarized by Cooper (211). Two progress reports on solid and solid-fluid systems in pharmaceutical engineering have also been published (212, 213). Some experimental work was conducted on the chemical engineering of foam separation (214). Smith advocated that vibration grinding was a faster process than ball milling (215); he also presented several comments on wet *versus* dry grinding (216). A report was made on some powder properties, their mixing performance, and the development of some new theories of mixing (217). The drying characteristics of three commonly employed tablet excipients have been investigated under vacuum in an instrumented rotary double-cone dryer (218). One review discussed the theory of drying (219); another summary compared the methods used for both batchwise and continuous drying (220). Additional comments on some of the principles and applications of spray drying were also published (221).

Two different papers suggested methods and apparatus for the preparation of gold colloids for medicinal use (222, 223). Another investigator summarized nine different methods for measuring particle size (224). A novel method for evaluating dissolution characteristics of capsules was developed by Paikoff and Drumm (225). The simultaneous mixing and segregation occurring in randomly mixed particulate solid systems subjected to agitation have been investigated (226). Similarly, idealized systems of solid particles as represented by steel and glass spheres were studied with reference to their rates of segregation (227). Four separate papers appeared on the lyophilization of pharmaceuticals. These articles included a study on the effect of certain physical-chemical properties on lyophilization (228), a description of a high-sensitivity resistance bridge for low-conductivity measurements at eutectic temperatures (229), a method for programing a mathematical expression for estimating eutectic temperatures from melting point and solubility parameters (230), and determination of the eutectic temperatures of some inorganic salts (231).

Parenterals.—A review on the formulation of parenterals was published by Parrott (232), while Bedaux outlined various aspects for the preparation of infusion solutions (233). Other researchers recommended the use of demineralized water for the preparation of parenteral solutions (234). A thermoelectric vapor phase osmometer was described for measuring osmotic coefficients, isotonicity values, and sodium chloride equivalents of some univalent electrolytes of pharmaceutical interest (235). Isotonic solution values were tabulated for numerous medicinal agents and adjuvants in three separate publications (236–238). The use of polymers in injectables was surveyed in a discussion with 56 references (239). Also, new formulas were suggested for infusion solutions based on acetates and sorbitol (240). The preparation and development of a chloramphenicol intramuscular injection have been described (241). Pinter reported on a method for the preparation and storage of a citric acid solution for the dissolution of lyophilized plasma (242). Nine commercial parenteral preparations containing calcium salts were mixed with 70 commercial preparations containing salts of organic acids and observed for pH changes and precipitates (243). The same investigators compared the compatibility of thiamine tetrahydrofurfuryl disulfide injection with 136 other commercial parenteral preparations (244). In another compatibility study, 270 unique pairs of medication were tested in 5% dextrose solutions. This test resulted in 23 pairs that were physically incompatible (245). An additional 34 drugs intended for intravenous use were cross-matched to test for physical signs of incompatibility (246). A strain of *Pseudomonas* has been isolated from an injection solution containing 10% bivalent mercury diuretic that was resistant to phenyl mercuric borate and sodium ethyl mercuric thiosalicylate (247). A new disposable hypodermic device, called a hypule, has been evaluated by a biological procedure and tested for compatibility with 117 different parenterals (248).

Sterility.—Advances in sterilization techniques were outlined by Ehrlen (249). Four additional reviews discussed the utilization of gaseous ethylene oxide in sterilization (250–253). A method has been developed for the determination of residual ethylene oxide and ethylene glycol in ethylene oxide sterilized pharmaceuticals (254). The utility of cold sterilization in pharmaceutical products was also disclosed (255). Also, emphasis was placed on the cleaning operation and choice of chemicals and detergents used on metal and rubber parts (256). Sterilization

by radiation was also considered (257); while irradiation of tetracyclines and other antibiotics with ^{60}Co did not diminish their antibiotic power (258). An ultraviolet mercury vapor lamp in a quartz tube was employed for sterilizing water received from an ion-exchange method (259). The addition of small amounts of polymyxin B, benzalkonium chloride, chlorobutanol, or various mercury-containing antiseptics to collyriums prevented bacterial contamination (260). The incorporation of 0.3% phenol and autoclaving for 30 min. at 120° provided a new method for the sterilization of oil solutions (261).

Tablets and Capsules.—Some geometrical considerations concerning tablet design to provide a uniform release rate from solution tablets have been investigated (262). It has been ascertained that half-tablets are poor dosage forms, especially when the dosage must be carefully controlled (263). The influence of many different excipients and lubricants on the chemical and physical stability of several medicinals in tablets was demonstrated by Lachman (264). Other researchers described instrumentation for measuring the sign and magnitude of static charges generated by particles flowing through a tablet hopper (265). They also found that tablet lubricants, such as magnesium stearate, polyethylene glycol 4000, sodium lauryl sulfate, and talc, have the ability to lower the accumulation of static charges resulting from the flow of material through a tablet hopper (266). Tableting difficulties due to the nonwetting of lipophilic and aerophilic substances have been overcome by the addition of detergents to tablets (267). A comparative study was made of the absolute water content with relative dampness and dielectric constants on various granules (268). The equilibrium moisture content of several starches, gums, sugars, and hexamine was determined at different relative humidities and temperatures (269).

Two reports were published on the evaluation of several tablet disintegrating agents (270, 271). The latter article indicated that Moriyo starch was as good as or better than cornstarch and Veegum HV as a tablet disintegrant. An *in vitro* disintegration study was performed on 85 different commercial and 14 different hospital preparations according to the "Danish Pharmacopeia" 48 (272). A comparative evaluation was made on the effect of aging for 24 weeks on seven tablet disintegrants (273). Cornstarch was best. The effect of the viscosity of sodium carboxymethylcelluloses used as binding and disintegrating agents on the rate of disintegration of clay tablets was studied (274). In addition, a study was reported on the properties of experimental granulations produced by using aqueous and alcoholic solutions of celluloses, vinyls, acrylamides, pyrrolidones, oxazolidinones, and ethylene oxide condensation products (275). A technique for determining *in vivo* tablet disintegration has also been proposed (276). Some physicochemical properties, including swelling volume, moisture absorption, particle size distribution, surface area, and ion-exchange properties, of the montmorillonites were examined in relation to their application in tablet making (277).

Kirsop reviewed the fundamentals of tablet compression (278). A comprehensive study on compressed tablets evaluated the effect of the method of granulating, excipient, lubricant, disintegrant, particle size, and pressure on the density, disintegration time, and cohesive force (279). It was discovered that the density of compressible systems may be determined without disturbing the system under study by using a densitometer consisting of a sealed source containing ^{170}Tm and a scintillation detector connected to a preamplifier and pulse-height analyzer (280). A "moving-die" apparatus was described for the investigation of die wall friction during compaction (281). This apparatus was used to determine the die reaction during compression of crystalline acetylsalicylic acid, hexamine, sucrose, sodium chloride, and simple granulations of hexamine and sucrose (282). It was also employed to determine the die reaction following compaction of 100 mesh powders of 11 different lubricants (283). Three different papers reported on the physics of tablet compression. One of these articles, by Seitz and Flessland, was concerned with changes in tablet hardness and friability when the operation of a rotary tableting machine was varied (284). Data collected during the measurement of pressure exerted by various substances on the die wall during and after compression of tablets can be related directly to the ease of formation and ejection of these tablets (285). Another comparative study explored the performance of a food grade dextrose and a spray-dried lactose as excipients in the direct compression of tablets (286).

The form or shape of tablets to be coated was studied and an empirical formula was derived from status analysis for tablet form that would express the ease or difficulty of the coating procedure (287). Coatings prepared from 30% gelatin and 2% methylcellulose mixed in a 1:1 ratio with 1:1 potato starch–talc prevented volatilization of peppermint oil from tablets (288). Some spray-dried formulations of sulfaethylthiadiazole were tested for their prolonged-release action (289). Richman, Fox, and Shangraw prepared nonfriable tablets of glyceryl trinitrate by direct compression

employing microcrystalline cellulose as a tablet matrix (290). Gelatinized starch has been used in the preparation of acetylsalicylic acid tablets (291). In an extemporaneous method of preparing enteric-coated capsules, 29 combinations of polyvinyl acetate resins with plasticizers in various solvents were evaluated along with cellulose acetate phthalate (292). The advantages of direct weighing of filled capsules were compared with the indirect weighing of the capsule content to determine weight variations (293).

Suspensions.—Nash discussed the preparation and properties of suspensions intended for oral, parenteral, or topical use (294). Mean diameters and size distribution curves of aqueous barium sulfate suspensions measured by the sedimentation method were nearly identical to results obtained with the Coulter counter (295). A new method of determining the settling rates of suspensions was studied using a specially constructed absorptiometer and a sealed source of β-excited characteristic X-radiation (296). Guar and colloidal substances from linseeds, in low concentrations, induced flocculation of barium sulfate suspensions but in higher concentration hindered interparticle separation (297). The addition of protalbinic acid, lysalbinic acid, or infusion provided various degrees of dispersion for several bismuth compounds (298). The effect of sodium salts of fatty acids on the thermal stability of aqueous dispersions of kaolinite has been investigated (299). Other studies were conducted on the formulation and stabilization of suspensions containing tetracycline base (300), and suspensions containing alkaloids such as noscapine, papaverine, and methyl ephedrine (301). Particles of clay less than 0.5 mm. in size were found to disperse in water more slowly than particles of a larger diameter, 2–10 mm. (302). The influence of the hydrophile–lipophile balance on oily suspensions was also considered (303).

Emulsions.—A review on the stability of oil-in-water emulsions has been published by Garrett (304). In a unique study, the change in the stability of emulsions according to the number of double bonds in the oil molecule was followed by means of the Lederer equation (305). The kinetic theory of droplet coalescence and its applications to emulsion stability has been discussed by Hill and Knight (306). A γ-globulin fraction was discovered to be responsible for the creaming or complete breakage of intravenous fat emulsions *in vitro* (307). Two studies were carried out on deaggregation in oil-in-water emulsions. In one, the rate of deaggregation of an emulsion system containing 2% hexadecane-in-water stabilized with 0.09% dioctyl sodium sulfosuccinate was studied (308). In the other, the influence of *n*-butanol, *n*-hexanol, *n*-octanol, and dioctyl sodium sulfosuccinate on the deaggregation of 2% hexadecane-in-water emulsions was evaluated (309). Two series of mineral oil-in-water emulsions with varying amounts of sodium dodecyl sulfate or polysorbate 80 were also observed for changes in particle size distribution over a 2-year period (310). Another investigator followed the effect of ethoxylated fatty alcohol combinations on the stability of 4% mineral oil emulsions (311).

The preparation, application, and examination of lotions in dermopharmacy was the subject of a review (312). Lin presented an outline for planning laboratory experiments and interpreting results during the process engineering of cosmetic emulsions (313). He also commented on the advantages of cold emulsification over conventional elevated temperature emulsification procedures (314). Several suggestions were made for determining the role of solubility in the formation of emulsions by using the best solvent for the oil to be emulsified (315). Two methods were described outlining the best technique for using the HLB of emulsifiers (316). The interfacial properties of a glycerin and olive oil emulsion were studied (317). The interfacial tension of various natural and synthetic glycerides did not differ greatly, and none of the glycerides had an interfacial tension sufficiently low to emulsify spontaneously but required additional emulsifiers (318). Paraffin oil-in-water emulsions made with a soap and fatty alcohol complex as an emulsifier were examined microscopically for their physical characteristics (319). A fat emulsion concentrate, transparent and stable to autoclaving and containing very low concentrations of nonphosphatide emulsifiers, has been developed (320). Another publication discussed the emulsification and evaluation of a parenteral contrast medium for lymphography (321). In addition, a report was written on the effect of the dispersed phase (water) content on the structural and thixotropic properties of complex emulsions (322). Muys compiled data on the microbiological quality of edible emulsions during manufacture and storage (323).

Ointments and Creams.—A Hoeppler consistometer was used to measure the effect of temperature variations on the heat stability of ointments and creams (324). Another device was developed for determining the oxidation resistance of both oil-in-water and water-in-oil emulsion vehicles (325). The influence of antioxidant mixtures and physiochemical conditions on the stability of 12 different anhydrous and emulsion-type bases has been investigated (326).

Gretskii examined the stability of water–petrolatum emulsions at −10° and −20° by using 5% pentol, sorbitan oleate, or lanolin and 1–24 hr. freezing time (327). This latter investigator and his co-worker also found that emulsion bases composed of mixtures of petrolatum and pentol or sorbitan oleate gave heat stable emulsions (328). Several formulations for barrier creams (329) and clear gels (330) were suggested. In addition, film-forming bases containing aqueous topical adhesives were discussed (331). One author published two different papers on the use of polyorganosiloxane liquids for ointments and liniments (332, 333). Comparative studies were conducted on the solubility and compatibility of polyethylene glycol, polypropylene glycol, and glycerol–polypropylene glycol ether in various topical preparations (334). Dicarboxylic acid esters were claimed to be suitable additives for increasing water-vapor permeability of ointment bases (335). The hardness of topical creams has been increased by increasing the number of hydroxyl groups of partially acetylated mono- and di-glycerides (336). The addition of quaternary compounds increased the water-holding capacity of petrolatum (337). The ointment pendulum of Fueller and Muenzel was employed to evaluate the smearing properties of water-in-oil and oil-in-water emulsion bases (338).

Suppositories.—Anschel and Lieberman published a two part review on suppository bases (339, 340). An easy method has been proposed for the small-scale production of suppositories by pouring the suppository mass into plastic bottles which terminated in points (341). Experiments on changes in the complete deformation time of suppositories during storage showed that with certain fat vehicles the changes were over 100%; there were no changes with polyethylene glycol suppositories (342). Mixtures of polyethylene oxides were characterized for use in suppositories by their melting point, turbidity point, hardness, viscosity, thermal expansion, and rate of dissolution (343). In another study on suppositories the displacement value was found to decrease by reducing the particle size of the insoluble ingredients (344).

Aerosols.—Five different reviews surveyed the pharmaceutical aspects of aerosols (345–349). Another review summarized the function and application of aerosol packaging in pharmacy and medicine (350). Scriba and Hearn presented an outline on current government requirements for packaging and labeling aerosols (351); the hazards of transporting and storing aerosols and their hazards and toxicity during use have also been discussed (352). Some of the operation and maintenance problems associated with processing aerosols with slow-filling valves with a large propellant charge were disclosed (353). Another paper recommended the application of a statistical quality control procedure to a quality assurance program to improve the efficiency of an aerosol filling operation (354).

A review with 144 references considered the topic of monodispersed aerosols (355). Methods were revealed for selecting the best solvent and propellant for achieving a specific desired effect (356). Johnsen and Haase examined the scope of noncondensable gases as aerosol propellants and the data required for the efficient introduction of such gases by the gasser-shaker method into specific products (357, 358). Another discussion was concerned with the effect of transport and storage on aerosol dispensers, propellants, container construction, dispension methods, and protective covers (359). Additional experimental data have indicated a correlation between aerosol product weight loss from leakage through the valve gasket and the choice of propellant, solvent, valve type, and gasket material (360). At 130° F. the reaction of propellant 11 with water was catalyzed by metal (361). The solubility of some lanolin derivatives decreased but at least one increased with storage in pressurized formulations (362). No direct relation was observed to exist between the dispersion of the aerosol and the surface tension, but the dispersion did depend on the salt concentration and the relative humidity of the compressed air used for atomization (363). Also, it was noted that careful control of the formula, the type of actuator, and valve can be used to adjust the chilling effect of aerosol sprays on the skin (364).

Packaging.—Autian reviewed potential problems of packaging cosmetic products with plastic materials (365). A commentary was also presented on mechanical packaging machines available for use in the hospital pharmacy (366). The merits of polyethylene, the plastic most frequently used in cosmetic and pharmaceutical bottles, were examined in detail (367). Other papers were concerned with the application of aluminum containers for packaging pharmaceuticals (368) and suggested methods for the sampling of acceptable metal containers (369). Various manufacturing, packaging, analysis, and control operations for the continuous production of glass vials by a mechanized process have been delineated (370). Coring, permeability, sorption, and leaching were considered the most pressing problems in present closure applications; comments were offered regarding specific areas of improvement in each of these functions (371). Natural

and synthetic rubber stoppers were tested for turbidity, pyrogens, color, metal content, and reducible materials (372). The sorption and diffusion of formic, acetic, propionic, and butyric acids into nylon 66 has been investigated at a number of temperatures and concentrations (373). A similar binding study of sorbic acid with nylon 66 indicated the interaction is primarily one of hydrogen bonding at the amide linkage (374). Sedova *et al.* compared the effect of some rubber stoppers on the quality of injectable solutions during a 12-month period of storage (375). Two brands of disposable syringes selected at random were examined and found to yield two different types of water-soluble extractives (376). Another study indicated that rubber closures were the source of a precipitate found in physiological saline solutions (377). Other investigators recommended a procedure for screening toxicity of plastic materials based on a tissue culture method using monolayers of strain L 929 mouse cells in modified Eagle's medium (378).

A review, citing 49 references, on investigations and standards pertaining to plastic equipment for the collection, storage, transportation, and administration of blood was published with special reference to toxicity problems (379). Two different investigations designed methods for studying the permeability of films and plastic-coated papers (380), and cellulosic or plastic barrier materials, packages, and closures (381). The permeability to water and the stabilities of ascorbic acid and potassium permanganate in several plastic containers were explored by Kimura and co-workers (382). The stability of an enzyme preparation, amylase, was greatly influenced by its packaging material; the activity at 20° and 90% relative humidity decreased in the order of: glass > glassine paper laminated with polyethylene > paper > waxpaper (383). Fluoride solutions in glass containers of aluminum have been stabilized by the addition of EDTA and aluminum chloride (384). Some unique surface tests were utilized for studying the neutrality of glass ampuls for injectable fluids (385). Aluminum tubes provided better protection for anhydrous and hydrated ointment bases containing vegetable oil than orange glass jars (386). Brown tabulated a list of 17 ultraviolet light absorbers used to stabilize plastic packaging materials (387).

EQUIPMENT

Three separate papers discussed automation in the pharmaceutical industry (388–390). Hill published an article on evolutionary operation (EVOP) as a technique for in-plant optimization (391), while Maatman reviewed some of the factors important in the industrial handling and moving of materials (392). Three other investigators evaluated the Sterilab for dispensing sterile products (393). The operation of a simple liquid flow recorder designed to handle a few drops per minute or 50 ml./min. has been revealed (394). The Littleford-Lodige mixer was studied as a method for achieving high-efficiency solid-solid blending; its application as a wet-formulation device was also briefly investigated (395). One other mixer, a stirred flow reactor type, was also tested for its mixing efficiency (396).

A simple constructed device fabricated from materials common to most laboratories was designed for the control of water baths used for nonisothermal studies (397). Another apparatus was developed which permitted rapid determination of thermal diffusivity in foods. A description of its limitations and sources of error was also included (398). Larkins *et al.* described a new automatic recording multigradient capillary viscometer (399). Other workers invented a simple device for measuring the thickness of agar in a Petri dish (400) and illustrated the construction and use of a versatile hot stage microscope for determining phase diagrams of inorganic mixtures (401). During a study on the surface properties of soybean lecithin, a modification of the Wilhelmy or vertical-type film balance was disclosed which is believed to offer certain advantages over other standard film balances (402). One other apparatus has been described for compressing and expanding insoluble monolayers or films present at an oil-water interface (403). A new design was presented for an improved mass-transport cell for the measurement of electrophoretic mobility of concentrated suspensions of particles (404). In addition, a new counter for emulsion photomicrographs was depicted (405). Two papers discussed automated techniques for determining dissolution and reaction rates of antacids. They provided a rapid and accurate profile of the dissolution and reaction rate in addition to the total acid-consuming capacity of the antacid system (406, 407). A new device, called the Heidelberg capsule, has been proposed to telemeter gastric pH (408). The specifications, operation, and production rate of a new encapsulating machine for soft shell products has also been assessed (409).

PHYSICAL PHARMACY

Many pharmaceutical problems were solved through physicochemical means. The theoretical aspects of solid solutions and eutectic mixtures and their application to pharmaceutical systems were discussed by Goldberg, Gibaldi, and Kanig

(410). Other researchers found that the choice of plastic, weight of drug incorporated in the matrix, solubility of the drug used, matrix additives, and the solvent could markedly affect the release rate of drugs from plastic matrices (411). The diffusion coefficients of several physiologically active compounds have been determined in cross-linked thiolated gelatin films (412). It has been shown that stress relaxation effects of gelatin films cross-linked with oxystarch or difluorodinitrobenzene may be represented by the sum of three exponential rates of stress decay (413). Some viscoelastic properties of keratin and collagen fibers immersed in aqueous media have been measured at frequencies between 1 kc./sec. and 20 kc./sec. and at temperatures between 0 and 100° (414). The penetration of chlorpromazine and chlorpromazine sulfoxide into insoluble monomolecular lipid films depended on the surface characteristics of the lipid, pH, and the ionic strength of the underlying solution (415). Additional studies were concerned with the relation between the diffusion coefficients and the electrolytic properties of membranes (416). Measurements of the tensile strength of dry powders of irregular particle shape have been made using a split tilting-plate apparatus based on that described by Thouzeau and Taylor (417). Johnson and co-workers studied the distribution of phenol between water and carbon tetrachloride and the solubility of water in solutions of phenol in carbon tetrachloride (418). Another paper presented a novel means for achieving a superior degree of carbonation with sodium bicarbonate in various latentiated acidifiers (419). The rate of neutralization of hydrochloric acid by dispersed calcium carbonate powder has been examined as a function of pH, temperature, and particle size (420). A tartaric acid buffer has been shown to form a reactive intermediate in aqueous solution capable of rapidly acylating any nucleophilic compound present (421).

Ionization.—The absence of a primary kinetic isotope effect in DMSO was the subject of a paper on ionization rates of weak acids (422). Another article described the mechanisms for the acid dissociation of vitamin B_{12} (423). The acid-base behavior of ephedrine isomers and their oxazolidine derivatives in aqueous and nonaqueous media has been described in detail (424). Also, a new technique was described for measuring the rates of ionization of carbon acids (425).

Solubility.—Wurster and Taylor reviewed the theory of dissolution and methods of study in a paper with 74 references (426). A novel method was developed for determining dissolution rates of multiparticulate systems (427). One other *in vitro* continuous dissolution rate measuring method has been designed and evaluated for determining the dissolution rates of labeled materials from solid dosage forms (428). Results obtained with this method were compared with dissolution rates of similar dosage forms using the U.S.P. disintegration apparatus and the rotating bottle method. An improved holder for rotational disk dissolution studies has been used to determine the relative intrinsic dissolution rates of caffeine monohydrate, aspirin, salicylamide, and acetaminophen (429). The crystal behavior, solubility, and dissolution rates of two anhydrous and one hydrated form of prednisolone in aqueous solution have been investigated (430). The theory for the dissolution rate of polyphase mixtures was probed and applied to several situations involving simultaneous diffusion and rapid equilibria (431). The rate of dissolution of boric acid in aqueous solutions of polysorbates was examined (432); another study explored the effect of complex formation on the dissolution kinetics of *m*-aminobenzoic acid (433). Danckwerts' penetration model was employed to derive equations to explain the theory for the dissolution of solids in a multiparticulate system (434). The dissolution behavior of a weak acid, 1,1-hexamethylene *p*-tolylsulfonylsemicarbazide, and its sodium salt in phosphate buffers has been evaluated by Higuchi *et al.* (435).

One other new method was described for determining the dissolution rate of fine particles of crystalline hydrocortisone acetate (436). A study relating the *in vitro* dissolution rates and solubilities of 45 different compounds representative of various chemical species supported the theory that the initial rate of dissolution of a compound is directly proportional to its solubility (437). In addition, dissolution studies were conducted on both the one-to-one molecular compound and mechanical mixtures of sulfanilamide and sulfathiazole at 15, 25, and 35° (438). As part of a program on the transport, deposition, and dissolution of cholesterol in aqueous medium, the growth, dissolution rates, and nucleation behavior of this compound in saline have been studied by following changes in particle size with the Coulter counter (439). In a similar study, the Coulter counter was used to test the influence of cholate on the precipitation behavior of cholesterol in aqueous media as a function of pH (440).

A new technique has been proposed for determining the solubility product constant (441). Dielectric constants of water–ethanol–sucrose and water–ethanol–sorbitol systems have been experimentally determined and found to be a complex function of composition expressed as weight per

cent (442). The solubilities of acetanilide, *p*-methylacetanilide, *p*-ethoxyacetanilide, aminopyrine, and antipyrine have been measured in dioxane–water mixtures of known dielectric constants (443, 444). Some solubility anomalies were compiled for actinomycin D (445). The water solubilities of five different barbiturates were ascertained by liquid scintillation counting of ^{14}C-tagged compounds using the technique of phase solubility analysis (446). Four different procedures were employed to determine the solubility of cholesterol in water (447). A critical concentration for the solubility of cholesterol chlorobetainate in aqueous solution was detected by specific conductivity, refractive index, and activity coefficient determinations (448). The solubility of iodine has been studied in a series of solvents (449). Nakatani reported on the solubility of compounds related to orotic acid in amine solutions (450). Tagged ^{14}C-pentaerythritol tetranitrate was utilized in determining the solubility of this compound in water and saline (451). Another presentation compared the solubility of polysorbates in simple syrup, glycerol, and propylene glycol (452). The solubilities of several xanthines, including caffeine, theophylline, and theobromine, were examined in dioxane–water mixtures; the solubility curves that were obtained showed a multiplicity of peak solubility values (453). A different type of study provided data on the solubilities of thin films of polyethylene, polypropylene, and polystyrene in many liquid drugs (454). Other investigators studied the solubility of compressed gases in fluorocarbons (455).

Swarbrick published a review article outlining the physicochemical properties of surface-active agents in solution with particular reference to solubilization of materials of pharmaceutical interest (456). One investigation determined the usefulness of test systems consisting of aqueous solutions of anionic surfactants and an excess of ^{14}C-cyclohexane in studying effects related to solubilization (457). The solubilization of several aliphatic and aromatic acids in aqueous solutions of cyclopentamine hydrochloride, ephedrine sulfate, and propoxyphene hydrochloride has been demonstrated (458). A potentiometric method was applied to a study of the solubilization of benzoic acid in systems containing anionic (459) and nonionic (460) surfactants. Another study was concerned with the interaction of urea in varying concentrations with three isomeric monohydroxybenzoic acids (461). The solubilizing capacities for camphor of one anionic, one cationic, and three nonionic surfactants have been investigated and determined by measuring the areas under ultraviolet absorption peaks (462). The use of Z values was proposed as a method for measuring the polarity of the environment in a study on the solubilization of camphor in polysorbate 20 (463). Sorbitan trioleate increased the solubility of hydrous ephedrine alkaloid in liquid petrolatum (464). The effect of various polysorbates on the solubility of sulfanilamide in several different solvent systems was ascertained by Khawam, Tawashi, and Czetsch-Lindenwald (465, 466). Aqueous solutions of urea, 1-acetyl-3-methyl urea, and 1,3-dimethyl urea were discovered to increase the water solubility of testosterone and some other related steroids if the 17-hydroxyl group of the steroid was free (467). The effect of urea on the aqueous solubility of six different dye compounds in water has also been compared (468). In addition, the solubility of theobromine has been increased and stabilized by the addition of various polysorbates in tragacanth mucilage (469).

Complexation.—The formation of copper complexes of sulfur drugs was discussed by Lee (470). Acid dissociation and copper(II) chelate formation constants were compared for glutamic acid and several of its derivatives (471). Data were presented which suggested that coordination complexes may be of major importance in the biological phenomenon of binding with catecholamines (472). Stability constants for complexes of tetracycline with cupric ion have been published (473). An *in vitro* enzyme kinetic study was used to determine the nature of the inhibition of acetylcholinesterase by cupric chelates of glycine and ethylenediamine (474); also, the inhibition of acetylcholinesterase by 1–1 cupric chelates of ethylenediamine and glycine was analyzed and shown to be essentially a noncompetitive type (475). Complexes formed by adrenaline and related compounds with transition metal ions were studied by Jameson and Neillie (476). The inactivation of tetracycline with a cupric–morpholine complex was investigated in another binding study (477). Gel-filtration, ultra-filtration, and ultra-centrifugation were used to study the nature of an iron–dextran complex (478).

Oxytetracycline was shown to form fluorescent complexes with proteins *in vitro* (479); the binding of sulfonamide to serum albumin was also investigated in a similar study (480). Protein binding of radioactive vitamin D_3 added to serum *in vitro* or present in dog serum after intravenous injection has been studied by a variety of methods (481). The interaction of cortisol with bovine

and human serum albumin was observed by an equilibrium dialysis procedure (482). Protein binding of salicylates by rat liver, kidney homogenates, plasma proteins, globulins, and albumin was tested by Stafford (483). Also, the serum albumin binding of several structurally similar xanthine derivatives was evaluated by a spectrophotometric technique (484).

One investigation was conducted to ascertain the interaction of a group of compounds, used in medical and pharmaceutical practice, with several types of insoluble polyamides used in containers or devices for storing or administering drug products (485). The interaction of parachlorometaxylenol with macromolecules was determined by solubility and dialysis procedures (486). An electrophoretic technique was used to illustrate the interaction occurring between sodium carboxymethylcellulose and both methylcellulose and polyacrylamide (487). The interaction between poly-*N*-vinyl-5-methyl-2-oxazolidinone and certain pharmaceuticals in aqueous solution was reported (488). A complex interaction of potato and arrowroot starches with certain drug pharmaceuticals has been noted by Goudah and Guth (489). The binding of certain benzoic acid derivatives by polysorbate 80 and cetomacrogol 1000 was determined by means of an equilibrium dialysis technique (490). An investigation of the binding of polyethylene glycol to carboxymethylhydroxyethylcellulose was also disclosed (491). The hemolytic activity of phenolic preservatives was prevented by their interaction with polyethylene glycols (492).

The reaction of some salts of rare earth metals with group B vitamins has been revealed (493). Another study assessed the interaction of a series of phenyl-substituted carboxylic acids with Schardinger dextrins (494). The equilibrium reactions of caffeine and nicotinamide with lidocaine and saccharin were studied (495); also, flavins and phenols were found to form 1:1 molecular complexes in neutral solution (496). A spectropolarimetric method of determining stability constants of complexes formed through hydrogen bonding has been developed and applied to a camphor–phenol system (497). Gas chromatography was employed during a complexing study of quinine and quinidine with urea, thiourea, and diethylthiourea (498). The binding of chlorpromazine and thioproperazine to rat liver and human leucocytes was reported by Teller (499). The reaction between pyridoxal phosphate and cycloserine has been evaluated (500). Wadke and Guttman presented evidence to indicate that the complexed form of isoalloxazine was resistent to hydrolytic decomposition (501). Complex formation between chlorpromazine and adenosine triphosphate was believed to occur because the surface tension was lowered in the presence of adenosine triphosphate which is not surface active (502). Complex formation involving *cis* hydroxyls in an axial-equatorial position between carbohydrates and dimethylsulfoxide was revealed by proton magnetic resonance data (503).

A study of adsorption complexes formed by the interaction of sodium dodecyl sulfate with gelatin at pH values below the isoelectric point was described (504). Complexation between 1,3,5-trinitrobenzene and several local anesthetic compounds was demonstrated; it was suggested that the amine group was the primary site of reaction, with the tertiary amine taking precedence when present (505). A dark reaction between citrate and iodine was detected by two investigators (506). In addition, Rodgers followed the interaction of hexylresorcinol and amaranth with quaternary ammonium compounds by a conductimetric titration procedure (507). Other studies were concerned with structural determination of complexes by ultrasonic waves (508).

Surface Phenomena.—A review of the basic concepts involved in wetting and adhesion processes was reported by Gray (509). Another review discussed the theory on coagulation of noninteracting particles in Brownian motion (510). Other surveys covered colloidal dispersions, electrokinetic effects, the concept of ζ potential (511), and the coagulation of colloidal powders (512). Higuchi, Rhee, and Flanagan studied the rates of aggregation of polystyrene and polyvinyltoluene particles in aqueous ionic surfactant solutions (513). Solutions to equations for the kinetics of coagulation were analyzed by other workers (514); a mathematical analysis has also been made of two chemically interacting macromolecules settling in a liquid solvent under one-dimensional electrical and cylindrical centrifugal forces that were sufficiently large to overcome diffuse forces (515). Centrifugation current was used to determine the electrokinetic mobility of several electrolytes in the aqueous phase of water-in-heptane emulsions (516). The streaming potential of sulfisoxazole, sulfadimethoxine, and *N'*-acetylsulfisoxazole was measured with Hazel-type cells in sucrose, sodium chloride solution, and sodium chloride in 10% sucrose solution (517).

Two different reviews on the physical chemistry of nonionic detergents have been published (518, 519). Also, a survey on the evaluation of anionic and nonionic emulsifiers according to HLB values was reported (520). The adsorption of three quaternary ammonium salts, having the same

chain length and counterion but differing in the polar group, was measured at the air–water interface (521). The effect of solvent on micellar properties of nonionic surface-active compounds was investigated (522). A conductimetric method was used for determining the critical micelle concentration of sodium decyl and dodecyl sulfates in the presence of sodium chloride (523). Phares predicted reductions in water–air, oil–air, and water–oil interfacial tension produced by nonionic surfactants by using a form of the Langmuir adsorption equation (524). The influence of the sodium chloride concentration on the adsorption of sodium dodecyl, sodium decyl, and sodium octyl sulfate solutions at an air–water interface has been evaluated (525). The Griffin HLB method was utilized to determine the possibility of emulsifying 10 different emulsifiers having HLB values in the range 8–13 (526). The effect of additives on the foaming properties of very dilute surfactant solutions has been reported (527). Some of the physical properties of a series of nonionic detergents with branched hydrocarbon chains of the general formula, $R_2—CH—CH_2O(CH_2CH_2O)_6H$, were described (528).

The adsorption of water on clays was reviewed in a paper with 151 references (529). The relationship between some electrical and thermodynamic properties of adsorbed water on two montmorillonites, a silica gel, and a window glass powder was studied at room temperature (530). The specific surface area of suspensions of montmorillonite and the average thickness of their diffuse double ionic layer were reported (531). The sorption of methylene blue and methylene violet on Fintia bentonite processed by various methods was investigated (532). Bentonite clays have been activated by treatment with 10% hydrochloric acid while heating to improve their adsorptive and catalytic properties (533). Packham examined the coagulation of dispersed clays with hydrolyzing salts while carefully observing the effect of the nature and concentration of clay, pH, and the presence of various ions (534). The adsorption of water on ion-exchange montmorillonite has been discussed (535). It was noted that the heat of wetting of sodium and potassium bentonite was not greatly affected by the addition of small amounts of polyacrylamides (536). Other results were presented which showed clear evidence of discrete charges on clay surfaces (537). The adsorption properties of bentonite clay with regard to vitamin E were considered (538); the adsorption of phenol, *p*-cresol, *p*-nitrophenol, 2,4-dinitrophenol, and puric acid on Fuller's earth was determined (539). The influence of hydrogen ions on the adsorption potential and surface tension of barbital, aminopyrine, and veramon was disclosed in other studies (540). A summary of the effects of the method of preparation on the surface properties of silicas has been presented (541), and the adsorption properties of silica gel precipitated in the presence of some alkaloids has been investigated (542). The reactivities of the surfaces of muscovite, montmorillonite, and chrysotile-asbestos were also explored (543). In addition, Rohdewald evaluated the effect of glycerol, sorbitol, hydrochloric acid, sodium chloride, anionic, cationic, and nonionic surfactants on the properties of talc suspensions (544).

Blaug and Gross reported on the *in vitro* adsorption of nine different anticholinergic drugs by six antacids (545). Steroid adsorption by polyethylene tubing was noted by other workers (546). The critical micel'e concentrations of oxyethylene-oxypropylene polymers were assessed by surface tension and two different spectral absorption methods (547). Additional studies were conducted on the thermodynamic function of the sorption of vitamin B_{12} by the salt forms of sulfo resins (548). The dispersion of inorganic pigments was improved by surface treatment (549). Polypropylene glycols with molecular weights of about 2000 had the highest surface activity and strongest dye dispersing effect (550). It was concluded that with most hygroscopic materials used in pharmacy, the process of water vapor sorption starts to be active in an atmosphere with 50% relative humidity (551). The measurement of interfacial areas of foams and froths has been carried out by a radiographic technique (552). A technique involving reiterated approximations and a high digital computer was employed to solve the problem of surface tension measurement by the Pendant drop technique (553). The hydrophile–lipophile balance of surface-active substances has been determined by a calorimetric technique (554).

Crystallization.—A review of ultrapurification methods based on zone melting appeared in the literature (555). Nickolics, Bidlo, and Nikolics explored the influence of solvents on crystal structure of resorcinol, sulfathiazole, acetylsalicylic acid, phenacetin, barbital, and phenobarbitol (556). The precise crystal and molecular structure of α-D-glucose by neutron-diffraction analysis was ascertained (557); and the crystal and molecular structure of 1,3-dihydro-1-hydroxy-3-oxo-1,2-benziodoxole was determined by X-ray crystallographic methods (558). Polymorphism in potassium sulfate and thallium sulfate has been reported (559). The physical

properties of various anhydrous and hydrous forms of ampicillin were noted (560). A number of compounds were tested for their inhibitory effect on the needle axis growth rate of sodium acid urate crystal (561). Other data revealed the effect of temperature on the linear crystallization rate of salol, betol, salipyrine, antipyrine, and codeine (562).

Rheology.—A new flow equation for pseudoplastic systems was described by Cross (563). An electrical method has been suggested for determining the areas of hysteresis loops (564). A new viscometer was designed for measurements on dilute polymer solutions but could be equally well used for other liquids (565); also, another new glass rotatory viscometer was recommended for certain rheology studies (566). Hiller reported on the effects of temperature and pressure on the rheological behavior of montmorillonite sols (567). The rheology of silica suspensions was investigated as a function of concentration, particle size, polarity of organic solvents, and the pH and ionic strength of the aqueous phase (568). The factors affecting the rheological properties of clay suspensions were observed in another study (569). The thixotropic behavior of "alki" bentonite suspensions (570) and the physicochemical and technological properties of two kaolin varieties were presented (571). The rheology and suspension characteristics of carboxymethylhydroxyethylcellulose–polyethylene glycol systems, evaluated by means of the power law equation, were outlined (572). The concentration dependence of the steady flow viscosity was discussed for aqueous solutions of high viscosity hydroxyethylcellulose (573). The elastic properties of the particle network in gelled solutions of carboxymethylcellulose have been recorded (574). A treatise was published discussing critical gum solution properties that may be determined through analysis (575). Sugar, when used at high levels, offered a means of providing a delay in the development of the viscosity of guar gum formulations (576).

Procedures and instrumentation have been devised for measuring the stress-relaxation modulus of melts employed as soft gelatin encapsulating formulations (577). Other workers explored the viscosity and stability characteristics of the system ascorbic acid–water–polysorbate 20 (578). The flow properties at 25° of concentrated (30–42%) dicalcium phosphate dihydrate paste suspensions and model systems were determined using a concentric cylinder, cone plate, and capillary extrusion viscosimeter (579); in other studies, the thixotropy and dilatancy in complex emulsions and suspensions were investigated (580). Higuchi and Stehle tested the rheometric properties of silica suspensions in dibutyl phthalate, hexadecane, mineral oil, ethylene glycol, and mixtures with and without different surfactants (581). An apparatus, consisting of a sedimentation tube and capillary viscometer, was designed for particle size determination of suspensions and emulsions (582). In one study, the basis and conclusions for rheological characterizations of some pharmaceutical adjuvants were reported (583). The swelling, hygroscopicity, and viscosity properties of bentonite suspensions caused by water absorption were also evaluated (584).

PHARMACOCHEMICAL ASPECTS

This section of the review considers many of the papers on polymers, antibiotics, and radioisotopes which might be of interest to the pharmaceutical scientist. It is not intended to encompass the vast area of pharmaceutical chemistry concerned with synthesis, structure-activity studies, reaction mechanisms, analysis, etc. These related disciplines are reviewed annually in other publications and are, therefore, omitted from this report.

Polymers.—Rodrigues and Barrosa reviewed the current status of polymers of pharmaceutical interest (585). Good agreement was found between theory and experimental data for the stress cracking of high-density polyethylene in octylphenoxy polyethoxyethanol examined from the viewpoint of critical strain (586). An attempt was made to develop a means of assessing the order in an amorphous polymer from density measurements (587). A discussion has been reported on some of the factors responsible for high thermal stability in polymers along with some results of thermal degradation studies on an aromatic polyimide (588). In another investigation, the melting points of polyethylene crystals and the relation between molecular length and chain folding were presented (589). Also analyzed was the effect of changes in structure on chemical reactivity, the effect of structure on physical properties, and the basic principles of a chain reaction mechanism in polymerization (590). Cooper discussed the toxic dangers and disadvantages of plastic materials used in pharmaceutical systems (591).

The effect of the structure of sulfonated polystyrene ion-exchange resins on the sorption of oxytetracycline and chlortetracycline ions has been investigated (592). Measurements of the swelling ratio and exchange capacity of individual ion-exchange resin beads were used to compare resin samples, to study interparticle differences,

and to help characterize resin degradation (593). Lappas and McKeehan employed several esters of poly(ethylene–maleic anhydride) and poly(vinyl methyl ether–maleic anhydride) as coatings to control the release of drugs upon reaching a specific intestinal pH (594). The use of polyvinyl alcohol as a solvent for pilocarpine ophthalmic solutions was reported in publications by different authors (595, 596). A method for preparing an aqueous colloidal dispersion of organic materials such as β-carotene by using water-soluble polymers like polyvinylpyrrolidone has been revealed (597).

Antibiotics.—Reviews on the chemistry and pharmacology of penimepicilina, a new broad-spectrum antibiotic (598), and on the problems and investigative methods of antibiotic binding by blood serum proteins appeared in the literature (599). The properties of some new antibiotics, cephaloridine (600), kasugamycin (601), and copiamycin (602), were disclosed. Also, the preparation and isolation of anhydroerythromycin (603), antibiotic R-12 (604), neohumidin (605), and lemonomycin (606) have been reported. In addition, a new antifungal antibiotic, trichodermin from *Trichoderma viride* was described (607).

The activity in experimental infections, absorption, and elimination of rifamycin B diethylamide in man have been examined (608); also, the *in vitro* activity, absorption, and excretion of cephalothin in normal subjects have been reported (609). Garrett and Miller showed the generation rate constants for viable counts of *E. coli* were linearly dependent on the concentration of tetracycline and chloramphenicol (610). Definitions, standards of identity, strength, quality, purity, tests, and methods of assay were given for dactinomycin (611). A scheme of classification for the antifungal antibiotics of the pentaene group has been presented (612). Gentamicin was tested *in vitro* against 889 strains of pathogenic bacteria (613).

Radioisotopes.—Radioisotopes in pharmaceutical technology were surveyed (614) along with the production of radioactive isotopes for medical use (615). With the exception of the field of chemical kinetics, a brief survey has been presented of the principles of isotope chemistry and their utility in the ever unfolding panorama of scientific research (616). Another brief review was conducted on the preparation and analytical control of radioactive chemicals of the 16th revision of the U.S.P. and the "British Pharmacopoeia" 1958 (617). The preparation of colloidal solutions of zirconyl phosphate with ^{32}P for radiotherapeutic purposes was described (618). The influence of the sample volume on weak β-counting efficiency at 0° in liquid scintillation counting has been reported (619). The factors influencing the loss of ^{14}C from labeled carbonates were published (620); corrections for grain count in autoradiography were also determined (621).

BIOPHARMACEUTICS

The area of biopharmaceutics considers research efforts directed toward studying the influence of pharmaceutical formulations on the biological activity of drugs. Numerous review articles appeared in the literature. Mann cited 144 references while discussing biological aging and its effect on modification of drug activity (622). The evolution of new concepts on the mechanism of drug action was presented (623). Other topics of review included the absorption of pharmaceuticals by diffusion (624) and transport phenomena in artificial membranes (625). A two-part review covering factors influencing drug distribution in the body and pharmacokinetics also appeared in the literature (626, 627). The mechanism of enzyme and hormone actions was the subject of another review (628). In addition, the theoretical aspects of diuresis and the various therapeutic classes of diuretics were surveyed (629).

The kinetics of drug transfer from a buffered aqueous phase through a lipid phase to another aqueous buffered phase were studied (630). The development of a unified statistical mechanical theory of transport across a membrane model in liquid mixtures and electrolytes was discussed (631). A molecular basis for drug activity was considered (632), while the use of quantum chemistry in drug design was explored by Schnaare and Martin (633). On the assumption that the potassium content of the body cell mass remains constant, it has been possible to estimate body cell mass by measuring ^{40}P activity with a whole-body scintillation counter (634).

Milne discussed the potentiation of excretion of drugs (635). Analog computer studies resulted in an equation that can be used to predict the average asymptotic blood levels during a multiple-dose regimen from basic parameters estimated from single-dose studies (636). A theoretical relationship between dose, elimination rate, and duration of pharmacologic effect of drugs has been suggested (637). The importance of the route of administration was demonstrated in the pharmacodynamics of the antitussive action of codeine and ethylcodeine (638). Three unique, new, highly reactive polymeric compounds of magnesium aluminum oxy hydroxide showed 50–60% more antacid activity than presently known aluminum-magnesium antacids (639).

Effects of Physicochemical Properties.—A review, with 21 references, on physicochemical studies of membrane permeation concerned with absorption and excretion of drugs appeared in the literature (640). It was shown that calcium and pH influence the absorption rate of tetracycline and three of its derivatives (641). The water-insoluble salt, lincomycin hexadecylsulfamate, provided greater absorption and activity than the water-soluble salt, lincomycin hydrochloride (642). Poole, Zeigler, and Dugan demonstrated no significant increase in aluminum blood levels after oral ingestion of a water-soluble aluminum complex, potassium glucaldrate, in normal subjects or in those requiring antacid therapy (643). Certain members of some metal-acid complexes of tetracycline and demethylchlortetracycline resulted in higher blood levels (644). Particle size effects were discussed in relation to formula modifications (645); and the effect of griseofulvin particle size reduction was also determined in relation to drug excretion and absorption (646, 647). The *in vivo* distribution of colloidal chromic radiophosphate having different particle sizes has been studied following intravenous, intramuscular, and intracavitary injection into mice (648). The proportion of a sulfisoxazole dose absorbed did not vary with particle size, but the rate at which this proportion was absorbed did change (649). A correlation between the relative percutaneous absorption of topical corticosteroids and the physical properties of solubility and partition coefficient has been revealed (650). The release of steroids from a topical vehicle was stated to be independent of, and uninfluenced by, the presence of a second noninteracting component (651). Wide individual fluctuations were observed in studies on the influence of the rectal route for the administration of sulfonamides for therapeutic purposes (652). A unique relationship has been discovered between the molecular weight and biological effect of dextran (653). When administered to cats, in quantities representing Hatcher doses, there was a proportionality between the absorption rate and the lipid solubility of various lanata glycosides (654).

Effects of Formulation.—Wurster reviewed some of the factors related to the formulation of medicinals for percutaneous absorption (655). Tablet disintegration and physiological availability of drugs were also surveyed in an article containing 58 references (656). The oral absorption of salicylates was found to be a function of the intrinsic rate of dissolution which was affected by formulation parameters such as particle size, disintegrants, and lubricants (657). Incomplete absorption of aspirin was attributed to an excessively low dissolution rate of the dosage form (658). The importance of dissolution rates in producing effective diazoxide blood levels in man was outlined following administration of solutions, capsules, and tablets (659). A method for the evaluation of antimicrobial activity of a bacteriostatic agent in the presence of a surfactant was described (660). Another study disclosed the relationship between the concentration of a surfactant, polysorbate 80, and the rate of absorption of a drug, salicylamide, from the small intestine (661). Modification of *in vivo* promazine absorption by activated attapulgite and activated charcoal in humans using urinary excretion measurements has been demonstrated (662). Three different dosage forms, namely a liquid concentrate, regular sugar-coated tablets, and substained-release preparations, did not influence thioridazine blood levels (663). Only one-fourth to one-third of orally administered tetracycline was absorbed compared to the amount absorbed after intravenous administration (664). A complex model was presented to illustrate the pharmacokinetic parameters related to the absorption, metabolism, and elimination of nalidixic acid in man (665). The absorption and elimination of salicylic acid was investigated after i.m. injection of aluminum aspirin in a neutral oil (666). Serum salicylate levels were also used to evaluate the relative release rate of aspirin from a commercial aspirin tablet and from a hard gelatin capsule (667). Significant differences in blood levels were found for three different theophylline elixirs (668). Additional studies analyzed the effect of viscosity on the gastric absorption of ethanol and salicylic acid (669).

Indomethacin was absorbed satisfactorily from rectal polyethylene glycol suppositories according to blood level studies (670). A preliminary report on drug absorption from the rectum appeared in the literature (671). Suppository administration of theophylline *p*-aminobenzoate of piperazine provided a rate of absorption equal to, or less than, the rate from an equivalent tablet dosage form (672). The pharmacokinetics of rectal application of 4-sulfanilamido-5,6-dimethoxy-pyrimidine has been published (673). The rectal absorption rates of sulfonamides were reduced by water-soluble bases (674). Nonionic surface-active agents were found to decrease the rectal absorption of sulfonamides; this effect was the result of the micelles being too large to pass through the rectal membrane (675). Comparative studies were carried out on the *in vitro* and *in vivo* release of salicylates from fatty suppository bases (676). Anhydrous lanolin increased drug release when cocoa butter was employed as the

fatty suppository base (677). Cod liver oil and polyethylene glycol bases aided in the penetration of chlortetracycline through intact rabbit skin (678). The percutaneous absorption of an ^{35}S-sulfonated polygalacturonic acid from an oil-in-water emulsion base has been determined *in vivo* by following its disappearance after topical application (679). The cutaneous absorption of *S*-dicarbethoxythiamine was studied from various ointment bases (680). A diffusion study of sulfacetamide and sulfathiazole from three different ointment bases through a membrane into water has been reported (681). Dempski and co-workers discussed an *in vitro* study for testing the relative moisture occlusive properties of several topical vehicles and Saran wrap (682). The percutaneous absorption of heparin from commercial ointments was evaluated (683). A new microbiological "agar tube" method has been developed for measuring the release of antibacterial agents from various ointment bases (684). Several unique factors influencing the topical absorption of idoxuridine were demonstrated by Shell (685). One publication presented the pharmacological evaluation of certain ointment bases (686). The diffusion of neomycin from several ointment bases was examined (687); and the absorption of radioactive salicylic acid from 10 ointment bases was also considered (688). The diffusion of iodine and salicylic acid was studied from 29 different ointment bases by impasting the ointment on an agar-gel disk which contained starch solution or ferric chloride (689). In studies concerning the importance of the vehicle for percutaneous absorption, a small uptake of resorcinol and boric acid was noted, but phenol and salicylic acid were readily absorbed, especially from aqueous solutions (690).

Blaug and Canada observed the relationship of viscosity and contact time on the prolongation of action of methylcellulose-containing ophthalmic solutions (691). The intestinal absorption of certain water-soluble acidic dyes and some of their lipoid-soluble complexes has been investigated (692). An investigation of the effect of solubilization of phenobarbital and several other barbituric acid derivatives on *in vitro* and *in vivo* release rates was discussed (693). Succinic acid was found to promote the absorption of iron from the alimentary tract (694); other authors were concerned with the biological availability of riboflavin solubilized with sodium salicylate (695). The onset of action of tubocurarine has been studied in a program evaluating the skin penetrating properties of drugs dissolved in DMSO and other vehicles (696).

Absorption Control.—*In vitro* dissolution tests were developed which correlated quantitatively with dissolution rate-limited drug absorption in man (697). One investigation was noted on the effect of certain tablet formulation factors on *in vitro* drug release and *in vivo* drug absorption (698). Several authors studied the absorption of aspirin from enteric-coated preparations (699–702). Slow-release tablets of ferrous sulphate showed extremely variable absorption when compared to standard ferrous sulphate therapy (703). A radioisotopic technique for determining the efficiency of an enteric-coated tablet *in vitro* was found to be superior to the U.S.P. method (704).

A review of the effectiveness, safety requirements, rational, and clinical pharmacology of prolonged-release drugs was published (705). Frederik and Cass discussed some principles of the clinical evaluation of sustained-release drugs and suggested clinical methods to determine their duration of action (706). Other researchers observed that the action of procaine, isoniazid, sulfamidochrysoidine, and benzocaine was prolonged by combining them with polymers of dextran (707). Sustained-release aspirin formulations have been evaluated by several researchers (708–710). The sustained-release action of polyvinylpyrrolidinone in tablets containing tetracycline hydrochloride or phenoxymethylpenicillin was examined (711). *In vitro* and *in vivo* evaluations were reported for sustained-release amobarbital tablets (712); and controlled-release nitroglycerin tablets used in the treatment of angina pectoris were also tested (713). A novel system was described in which the dissolution rate of theophylline aminoisobutanol in a prolonged-action system was utilized as a parameter of the blood level concentrations (714). The release rates of sustained-release tablets were followed automatically by employing a photometer (715); another simple apparatus was described that was based on continuous elution for the *in vitro* control of sustained-release preparations (716). By using the half-change method of artificial intestinal and stomach juices, the elution ratio of medically active substances from Bellergot tablets with prolonged action has been investigated (717).

Absorption Mechanism.—Reviews appeared covering the mechanism of absorption of weak acids and alkalies through the lipid barrier (718), and the importance of specific binding, nonspecific binding, and the role of chemical configuration of the effective substance and its receptor (719). Five different models for the transport of methionine and sodium butyrate by intracellular plasma have been described and discussed (720). A discussion of the influence of a drug on its own

absorption was outlined (721). Of particular interest was an article which presented a theoretical study of the potential effect of drug binding by plasma proteins on drug distribution (722). The mechanism of absorption of sulfonamides has been studied by measuring the rectal absorption rate in anesthetized rats (723). The absorption of methyl ethyl ketone under normal, dehydrated, and hydrated skin conditions was investigated by Wurster and Munies (724, 725).

The intestinal absorption of vitamin B_{12} was evaluated by several authors (726–729). Deferrioxamine had no significant influence on the intestinal absorption of hemoglobin iron (730); however, in other studies, desferrioxamine B reduced the intestinal absorption of iron (731). The effect of neostigmine on the intestinal absorption of sulfisoxazole (732) and the effect of acetazolamide on the excretion of sulfisomezole into human parotid saliva were explored (733). Beckett and Rowland examined the urinary excretion kinetics of amphetamine in man and showed that the excretion of the unchanged drug was dependent upon urinary pH (734). The effect of cetrimide and phloridzin on the intestinal absorption of glucose in man was disclosed (735). A significant increase in the excretion rate of sodium salicylate has been observed upon the addition of an equal amount of glucosamine hydrochloride to an orally administered dosage form (736). The modification of protein binding and urinary excretion by the simultaneous use of two drugs was reported (737). The effects of acetazolamide, sodium perchlorate, ouabain, and iodide loading on the processes controlling ^{131}I and inulin-^{14}C distribution in the brain and cerebrospinal fluid were compared in nephrectomized rats (738). Silver proteinate was found to inhibit the absorption of iodine in the rat intestine (739). Benzoyl thiamine monophosphate produced thiamine levels in humans 4 times greater than those produced by thiamine hydrochloride (740). Also, it was noted that chymotrypsin did not augment the absorption or increase the activity of an oral dose of tetracycline (741). In addition, intestinal absorption of glycine was inhibited by phlorizin but not by rutin (742), while fat absorption in rats was delayed by Triton (743).

Kinetic Studies.—The kinetic factors of the digestive absorption of drugs were reviewed in a paper citing 181 references (744). Another article commented on the theoretical aspects of the elimination kinetics for a number of model drugs which have a high affinity for plasma protein (745). Radiophosphorus, ^{32}P, was employed to determine the absorption rate of dibasic sodium phosphate from fatty suppository bases in rabbits (746). In studying the percutaneous absorption of dinitroisopropylphenol in rats, absorption increased with time to reach a maximum after 7 hr. (747). An analog computer program suitable for using blood-level *versus* time data as an input and producing *in vivo* dosage for availability *versus* time pattern as its output was developed and tested by Stelmach, Robinson, and Eriksen (748).

The determination and significance of the biological half-life of pharmaceuticals were surveyed in a review with 63 references (749). In addition, the biological half-life of several drugs appeared in the literature, namely, 140 min. for psicofuranine (750), 9 min. for noscapine (751), and 11.3 hr. for meprobamate (752). Several investigators studied the pharmacokinetics of aspirin metabolism and distribution (753–755). The utility of goldfish as test animals for evaluating biological membrane permeation led to a detailed analysis of the drug transfer kinetics for 4-aminoantipyrine (756). Data were compiled on the excretion, distribution, and metabolism of doxapram after intravenous injection into dogs (757). A new method was presented for calculating per cent absorbed *versus* time plots from metabolite blood level data (758). Also, a relation between the rate of elimination of tubocurarine and the rate of decline of its pharmacological activity was demonstrated by Levy (759).

Drug Absorption.—The influence of certain factors on the absorption and excretion of drugs was reviewed by two different authors (760, 761). Schlagel discussed the comparative efficacy of topical anti-inflammatory corticosteroids in a review article containing 219 references (762). In other studies, the excretion of ^{3}H-labeled dihydromorphine was presented (763) and whole-body liquid scintillation counting was found suitable for testing the kaliuretic properties of diuretic agents (764).

Blood levels from chloramphenicol palmitate compared well with those from chloramphenicol *per se* at equivalent dosage levels (765). After a single dose of chloramphenicol, both the biologically active form and inactive metabolites have been found in human milk (766). The absorption and excretion of erythromycin and monomycin were measured by Lagert (767), while Fischer and Riegelman evaluated the absorption and distribution characteristics of griseofulvin from other blood level data (768). The absorption, diffusion, and excretion of lincomycin has been studied following oral, i.m., and i.v. administration (769). Plasma appearance times and values of ^{47}Ca did not cor-

relate with the absorption of radiocalcium from the intestine (770). A double isotope method for the measurement of intestinal absorption of calcium in man was presented in another publication (771). The absorption, distribution, and utilization of iron in a fat-soluble form was evaluated against similar data for ferrous sulfate and ferrocene (772). In addition, the absorption of ^{59}Fe-hemoglobin has been investigated in iron deficient and iron supplemented rats and compared with the absorption of ^{59}Fe as ferrous sulfate (773).

The absorption of steroid hormones was assessed by measuring the disappearance rate from the human small intestine during steady-state perfusion of aqueous solutions through a transintestinal tube (774). It was reported that when aloxiprin and aspirin were administered orally, they had similar mean rates of excretion, but aspirin provided higher blood levels (775). Cotty *et al.* evaluated aspirin blood levels following the ingestion of commercial aspirin-containing tablets by humans (776). The absorption, distribution, and elimination of 6,7-dimethyl-4-hydroxyquinoline hydrochloride, administered orally and intravenously to animals has been studied (777), and the absorption and distribution of oxafuradene in the dog were also determined (778). By means of urinary excretion studies in man, the absorption and excretion of ^{14}C-bethanidine were measured (779). It has been suggested that the acetylated phenolic laxatives, bisacodyl and diphesatin, became absorbable from the intestines and active, pharmacologically, after deacetylation (780). Data were presented on the absorption, distribution, and elimination of *N,N'*-dimethyl-*N,N'*-bis[3-(3,4,5-trimethoxybenzoyloxy) propyl] ethylenediamine dihydrochloride (781). Another publication ascertained the absorption, excretion, and metabolic fate of ethambutol in man after oral and intravenous administration (782); the absorption, distribution, and excretion of morphocycline in rabbits were also discussed (783). Other data were compiled showing that only a limited amount of riboflavin can be absorbed from the intestinal tract (784). Another investigator carried out research on the gastrointestinal absorption and pharmacokinetics of selected compounds in man (785). The absorption of isoniazid and some of its derivatives has been noted (786). The absorption, metabolism, and elimination of thiabendazole in farm animals, along with a method for its estimation in biological materials, were presented by Tocco *et al.* (787). Peak plasma levels for sulfamethoxydiazine were found in 6–8 hr. after oral administration (788); also, a similar study by the same authors comparing the antibacterial activity and chemical levels of the same chemical in human serum and plasma was published (789). Amundson, Johnson, and Manthey determined the urinary excretion of *d*-propoxyphene hydrochloride in man (790). The absorption and elimination profile of isoproterenol in anesthetized and unanesthetized dogs has been announced (791, 792). The rate of excretion of a new antiviral agent, amantadine hydrochloride, was discovered to be first order (793). The absorption of terephthalic acid through the digestive tract and its excretion in urine of rats were examined (794). The urinary excretion of three oral cholecystographic agents, iopanoate, tyropanoate, and bunamiodyl, has been studied (795). Another investigation was concerned with the absorption of *d*,1-1-(3-hydroxyphenyl)-1-hydroxy-2-ethyl aminoeltane in the gastrointestinal tract (796).

PHARMACOGNOSY[1]

One review was published on the investigation of *Lupinus* alkaloids (797); another surveyed the physical and chemical properties of aromatic acids from crude drugs of the *Umbelliferae* family (798). Other reviews were concerned with aurones (799), a tabulation of 43 alkaloids used in modern medicine (800), recent advances in the chemistry of *Rutaceae* alkaloids (801), the present status of *Cannabis* research (802), and the application and relationship of plant tissue culture to medicinal plant study (803).

The morphine content of opium from poppy plants under cultivation has been examined by two investigators (804). In a study on the stability of erichroside from *Erysimum cheiranthoides*, it was shown that lower pH's caused hydrolysis, whereas higher pH's caused isomerization (805). Sciuchetti and Born reported on the effect of dimethylsulfoxide alone and in combination with *N*-dimethylamino succinamic acid or 2-chlorethyl trimethylammonium chloride on the growth and alkaloid biosynthesis of *Datura tatula* (806). In a study on morphine losses in poppy capsules (*Papaver somniferum*), it has been revealed that the maximum loss of morphine in freshly crushed poppy capsules occurred in the first 8 days of storage at 20° (807). A description of various rhubarb roots used in the drug trade was listed (808). An interesting article on Mexican witchcraft drugs, *Ipomoea violocea* and *Salvia divinorum*, outlining their active principles, appeared in the literature (809). The production and consumption of opium and coca derivatives

[1] The writers thank Dr. G. H. Svoboda for his suggestions concerning the preparation of this section.

TABLE I.—PHARMACOGNOSTIC INVESTIGATIONS

Plant	Ref.
A	
Abies amabilis	(817)
Acacia angustissima	(818)
Acacia confusa	(819)
Aconitum japonicum	(820)
Actinidia polygama	(821)
Aesculus hippocastanum	(822)
Afzelia xylocarpa	(823)
Alangium lamarckii	(824, 825)
Amanita muscaria	(826, 827)
Amaranthus caudatus	(828)
Amaryllidaceen species	(829, 830)
Ammi majus	(831)
Anabasis aphylla	(832)
Angelica hirsutiflora	(833)
Angelica japonica	(834, 835)
Angelica pubescens	(836)
Aniscocyclea grandidieri	(837)
Anthocleista procera	(838)
Apocynum cannabinum	(839)
Araucaria imbricata	(840)
Arctium lappa	(841)
Ardisia macrocarpa	(842)
Argyreia nervosa	(843)
Arisaema ringens	(844)
Artemisia absinthium	(845)
Artemisia taurica	(846)
Artocarpus heterophyllus	(847)
Asarum europaeum	(848)
Asclepias tuberosa	(849)
Asimira triloba	(850)
Aspidosperma dasycarpon	(851)
Aspidosperma species	(852)
Atropa belladonna	(853)
B	
Baccharis rosmarinifolia	(854)
Berberis hauniensis	(855)
Bixa orellana	(856, 857)
Boletaceae species	(858)
Bryophyllum daigremontianum	(859)
Buxus microphylla	(860)
Buxus sempervirens	(861, 862)
C	
Cassia occidentalis	(863)
Catharanthus lanceus	(864)
Catharanthus roseus	(865–867)
Ceanothus americanus	(868)
Cedrus deodara	(869)
Centaurea species	(870)
Chelidonium majus	(871)
Chionographis japonica	(872)
Chondria armata	(873, 874)
Cinnamomum species	(875, 876)
Cissampelos pareira	(837, 877)
Clausena anisata	(878)
Clerodendron infortunatum	(879)
Cochlospermum gossypiune	(880)
Convallaria keiskei	(881)
Convallaria majalis	(882)
Coptis chinensis	(883, 884)
Corydalis species	(885)
Crotalaria species	(886)
Croton cumingii	(887)
Cyclea madagascariensi	(837)
Cymbopogon mortini	(888)
Cymbopogon nardus	(889)
Cynara scolymus	(890)
D	
Dalbergia lanceolaria	(891)
Daphne genkwa	(892)
Daphne papyracea	(893)
Datura callus	(894)
Datura innoxia	(895, 896)
Datura meteloides	(897)
Datura sanguinea	(898)
Datura tatula	(899)
Daucus carota	(900)
Delphinium species	(901)
Desmodium caudatum	(902)
Digitalis ciliata	(903)
Digitalis davisiana	(904)
Digitalis lanata	(905, 906)
Digitalis purpurea	(908–913)
Digitalis species	(907)
Digitalis thapsi	(914)
Doryphora sassafras	(915)
E	
Eledone moschata	(916)
Embelia ribes	(917)
Enantia species	(918)
Erysimum canescens	(919)
Erythroxylon monogynum	(920)
Eschscholtzia californica	(921)
Eucalyptus staigeriana	(922)
Eupatorium semiserratum	(923)
F, G	
Fumaria species	(924)
Gaillardia pulchella	(925)
Genista lusitanica	(926)
Gentiana bellidifolia	(927)
Glycosmis arborea	(928)
Glycyrrhiza glabra	(929)
Gualteria psilopus	(930, 931)
Gutierrezia sarothrae	(932)
Gymnema sylvestre	(933)
H	
Heimia salicifolia	(934, 935)
Helenium thurberi	(936)
Heracleum candicans	(937)
Heracleum mantegazzianum	(938)
Hibiscus abelmoschus	(939)
Hippophae rhamnoides	(940)
Hydnellum diabolus	(941, 942)
Hyoscyamus albus	(943)
Hypericum perforatum	(944)
I, J	
Indigofera endecaphylla	(945)
Ipomoea digitata	(946)
Ipomoea operculata	(947)
Ipomoea species	(948)
Juniperus virginiana	(949)
L	
Lecidea tenebrosa	(950)
Lepidium sativum	(951, 952)
Libanotis intermedia	(953)
Limnophila rugosa	(954)
Litsea cubeba	(955)
Lophophora williamsii	(956)
Luffa operculata	(957)
Lycium halimifolium	(958)
Lycopodium species	(959)
M	
Machilus species	(960)
Mammea americana	(961)
Mangifera indica	(962)
Mentha piperita	(963)
Mentha pulegium	(964)
Mentha species	(965)
Metaplexis japonica	(966)

(*Continued on next page.*)

TABLE I.—(*Continued*)

Plant	Ref.
M	
Minthostachys verticillata	(967)
Mitragyna speciosa	(968)
Monodora myristica	(969)
N	
Neolitsea acuminatissima	(970)
Neolitsea pulchella	(971)
Nepeta ciliaris	(972)
Nicotiana glutinosa	(973)
Nuphar japonicum	(974)
Nuphar luteum	(975)
O	
Ochrosia sandwicensis	(976)
Ocimum canum	(977)
Ocimum species	(978)
P	
Papaver caucasicum	(979)
Papaver somniferum	(980–982)
Papaver species	(983, 984)
Parmelia cryptochlorophaea	(985)
Peganum harmala	(986)
Pelea christophersenii	(987)
Petasites japonicus	(988)
Peucedanum ruthenicum	(989)
Peumus boldus	(990)
Physalis alkekengi	(991)
Penellia ternate	(844)
Piper methysticum	(992)
Pirus serotina	(993)
Piscidia erythriva	(994)
Plantago asiatica	(995)
Plantago species	(996)
Podophyllum peltatum	(997)
Prunus mahaleb	(998)
Psoralea species	(999, 1000)
Pycnanthemum albescens	(1001)
R	
Rauwolfia mannii	(1002)
Rauwolfia vomitoria	(1003)
Rhamnus frangula	(1004–1006)
Rhizoma zingiberis	(1007)
Rhododendron dauricum	(1008)
Rubus idaeus	(1009)
Rudbeckia species	(870)
Rumex hymenosepalus	(1010)
Ruta graveolens	(1011, 1012)
S	
Salicornia herbacea	(1013)
Salvia officinalis	(1014)
Samadera indica	(1015)
Sapium sebiferum	(1016)
Saracococa pruniformis	(1017, 1018)
Scopolia parviflora	(853)
Securinega suffruticosa	(1019)
Shorea talura	(1020)
Similax sieboldi	(1021)
Solanum atropurpureum	(1022)
Solanum khasianum	(1023)
Sophora flavescens	(1024)
Sterculia candata	(1025)
Sterculia setigera	(1026)
Sterculia urens	(1027)
Strychnos henningsii	(1028)
Strychnos nux-vomica	(1029)
T	
Tabernaemontana laurifolia	(1030)
Talictrum simplex	(1031)
Tanacetum vulgare	(1032)
Taxus baccata	(1033)
Thalictrum minus	(1034)
Thalictrum species	(1035–1037)
Thymus serpyllum	(1038)
Thymus vulgaris	(1039, 1040)
Tinomiscium philippinense	(1041)
Torulopsis utilis	(1042)
Tribulus terrestris	(1043)
Trifolium arvense	(1044)
V	
Vaccinium bracteatum	(1045)
Valeriana procurrens	(1046)
Valeriana species	(1047)
Veratrum album	(1048)
Viburnam opulus	(1049)
Viburnum prunifolium	(1050)
Vinca major	(1051)
Vinca rosea	(1052)
Voacanga bracteata	(1053)
Voacanga globosa	(1054)
W, Y, Z	
Withania somnifera	(1055, 1056)
Yucca glauca	(1057)
Zanthoxylum hamitonianum	(1058)

in France since 1950 were summarized (810). Another report stated the growth of *Atropa belladonna* was strongly inhibited by a heavy water concentration greater than 50% (811). An alfalfa trypsin inhibitor was demonstrated to be thermally stable and also stable in the pH range 2–12 (812). Other studies have been conducted on two sulfur-containing alkaloids from Congo trees (813). The presence of aloin was discovered in *Aloe* species from the section *Anguialoe* Reynolds (814). The effect of dimethylsulfoxide and tributyl 2,4-dichlorobenzylphosphonium chloride on growth and alkaloid synthesis in *Datura ferox* has been described (815). Alkaloid artifacts were difficult to distinguish from active plant alkaloids formed in plant extracts by ammonium hydroxide and acetone (816).

Pharmacognostic Investigations.—This section of the review is primarily concerned with those references pertaining to isolation and identification of plant constituents. Table I lists alphabetically each plant studied, followed by appropriate references to the bibliography.

Methodology.—The pH of the medium and the nature of the organic solvent were the main factors affecting the extraction of alkaloids by organic solvents (1059). A comparison was carried out on turbo-, vibro-extraction, and maceration methods for the preparation of various tinctures in the "Yugoslav Pharmacopeia" II (1060). The extraction of drugs from plants

has been improved by the use of surface-active agents (1061). Laboratory experiments demonstrated the effectiveness of a domestic vibrator for obtaining extracts from various types of plant materials (1062).

Ovadia and Skauen reported that ultrasonic energy had an accelerating effect on the extraction of alkaloids (1063). The kinetics of extraction of alkaloids and other extractables from the rhizome of *Scopolia carniolica* by pressing was studied (1064). Another procedure was described for preparing rye fluid extracts containing 0.05% alkaloids (1065). The properties of clove oils produced under different conditions of distillation from the buds and stems were investigated (1066). Optimum conditions for glycoalkaloid diffusion in the *Solanum laciniatum*–sulfuric acid system were reported (1067), as well as optimum conditions for the extraction of alginic acid from seaweeds on the Saurashtra coast (1068). Various methods for obtaining deterpenated oils were reviewed in a paper with 22 references (1069). In addition, thin-layer chromatographic patterns were noted for Umbelliferous drugs and their adulterants (1070).

REFERENCES[2]

(1) McKeehan, W., *J. Pharm. Sci.*, **52**, 613, 717(1963).
(2) O'Reilly, W. J., *Australasian J. Pharm.*, **45**, S114 (1964); through *Chem. Abstr.*, **62**, 8931(1965).
(3) Humphrey, H. H., *Am. J. Hosp. Pharm.*, **22**, 4 (1965).
(4) Anon., *ibid.*, **22**, 7(1965).
(5) Kelsey, F. E., *ibid.*, **22**, 30(1965).
(6) Thiete, F. C., *Am. Perfumer Cosmet.*, **80** (10), 45(1965).
(7) Kass, G. S., *ibid.*, **80** (10), 43(1965).
(8) Sadove, M. S., *et al.*, *Am. Profess. Pharmacist*, **31** (2), 23(1965).
(9) Jerome, J. B., and Alessandri, M. C., *J. Am. Pharm. Assoc.*, **NS5**, 90(1965).
(10) Ansel, H. C., *ibid.*, **NS5**, 160(1965).
(11) Perry, C. J. G., *Clin. Pharmacol. Therap.*, **6**, 771 (1965).
(12) Sciuchetti, L. A., *Pharm. Index*, **7** (8A), 4(1965); through *Chem. Abstr.*, **63**, 9741(1965).
(13) McCutcheon, R. S., *Pharm. Index*, **7** (8A), 14 (1965); through *Chem. Abstr.*, **63**, 9741(1965).
(14) McCutchen, R. S., *Pharm. Index*, **7** (8A), 10 (1965); through *Chem. Abstr.*, **63**, 9741(1965).
(15) Herschler, R. J., and Jacob, S. W., *Tappi*, **48** (6), 43A(1965); through *Chem. Abstr.*, **63**, 6784(1965).
(16) Akamatsu, K., *Showa Yaka Daigaku Kiyo*, **1**, 75 (1963); through *Chem. Abstr.*, **62**, 1509(1965).
(17) Kuttel, D., *Gyogyszereszet*, **8**, 405(1964); through *Chem. Abstr.*, **62**, 3888(1965).
(18) DuBan, G., *Boll. Chim. Farm.*, **103**, 849(1964); through *Chem. Abstr.*, **62**, 8932(1965).
(19) Jecmen, J., *Farm. Glasnik*, **20**, 163, 227(1964); through *Chem. Abstr.*, **63**, 12977(1965).
(20) Kennon, L., *J. Pharm. Sci.*, **54**, 813(1965).
(21) Brown, M. R. W., and Norton, D. A., *J. Soc. Cosmetic Chemists*, **16** (7), 369(1965); through *Chem. Abstr.*, **63**, 8119(1965).
(22) Gaind, K. N., and Bapna, S. C., *Indian J. Pharm.*, **26**, 320(1964); through *Chem. Abstr.*, **62**, 14426(1965).
(23) Evans, W. P., *J. Pharm. Pharmacol.*, **17**, 217(1965).
(24) Weiner, N. D., Hart, F., and Zografi, G., *ibid.*, **17**, 350(1965).
(25) Olitzky, I., *J. Pharm. Sci.*, **54**, 787(1965).
(26) Thoma, K., *Kongr. Pharm. Wiss., Vortr. Originalmitt., 23, Muenster, Ger.*, **1963**, 561; through *Chem. Abstr.*, **62**, 11627(1965).
(27) Snyder, R. W., and Cheatle, E. L., *Am. J. Hosp. Pharm.*, **22**, 321(1965).
(28) Judis, J., *J. Pharm. Sci.*, **54**, 417(1965).
(29) *Ibid.*, **54**, 541(1965).
(30) Burton, D. E., Clarke, K., and Gray, G. W., *J. Chem. Soc.*, **1965**, 438.
(31) Cadwallader, D. E., and Ansel, H. C., *J. Pharm. Sci.*, **54**, 1010(1965).
(32) Foster, J. H. S., *Mfg. Chemist Aerosol News*, **36** (5), 45(1965).
(33) *Ibid.*, **36** (6), 43(1965).
(34) Yambor, T. W., and Boyk, S., *Soap Chem. Specialties*, **41** (3), 91(1965).
(35) Hess, H., *Pharm. Weekblad*, **100** (25), 764(1965); through *Chem. Abstr.*, **63**, 14636(1965).
(36) Bean, H. S., Hemen-Ackah, S. M., and Thomas, J., *J. Soc. Cosmetic Chemists*, **16** (1), 15(1965); through *Chem. Abstr.*, **62**, 8930(1965).
(37) Krowczynski, L., Parafinska, Z., and Zaduminski, M., *Acta Polon. Pharm.*, **20** (3), 265(1963); through *Chem. Abstr.*, **62**, 404(1965).
(38) Pivnick, H., *et al.*, *J. Pharm. Sci.*, **54**, 640(1965).
(39) Pietramaggiori, F., *Farmaco (Pavia) Ed. Prat.*, **20** (5), 266(1965); through *Chem. Abstr.*, **63**, 5445(1965).
(40) Tilgner, D. J., *Food Technol.*, **19**, 25(1965).
(41) Sakai, K., *Chem. Pharm. Bull. (Tokyo)*, **13**, 304 (1965).
(42) Glanville, E. V., and Kaplan, A. R., *Nature*, **205**, 851(1965).
(43) Wesley, F., *J. Am. Pharm. Assoc.*, **NS5**, 162(1965).
(44) Brooks, L. G., *Chemist Druggist*, **183** (4445), 421(1965); through *Chem. Abstr.*, **63**, 2848(1965).
(45) Edwards, J. A., *Food Mfg.*, **39** (11), 59(1964); through *Chem Abstr.*, **62**, 6335(1965).
(46) Wick, E. L., *Food Technol.*, **19** (5), 145(1965).
(47) Majewska, I., *Tluszczei Srodki Piorace*, **9** (1), 47 (1965); through *Chem. Abstr.*, **63**, 12966(1965).
(48) Schofield, M., *Perfumery Essent. Oil Record*, **56**, 451(1965); through *Chem. Abstr.*, **63**, 6781(1965).
(49) Vinot, M., and Bouscary, A., *France Parfums*, **7**, 411(1964); through *Chem Abstr.*, **62**, 8928(1965).
(50) Zuckerman, S., *Am. Perfumer Cosmet.*, **80** (10), 69(1965).
(51) Goulden, H. D., *Drug Cosmetic Ind.*, **96**, 166(1965).
(52) Malysz, D., and Walicka, T., *Acta Polon. Pharm.*, **22** (2), 155(1965); through *Chem. Abstr.*, **63**, 1655(1965).
(53) Goodhart, F. W., Kelly, M. A., and Lieberman, H. A., *J. Pharm. Sci.*, **54**, 1799(1965).
(54) Anon., *Drug. Cosmetic Ind.*, **96**, 464(1965).
(55) Smith, M. C., *Am. J. Hosp. Pharm.*, **22**, 272(1965).
(56) Mondovi, B., *et al.*, *Giorn. Biochim.*, **13**, 415(1964); through *Chem Abstr.*, **62**, 11637(1965).
(57) Spross, B., and Ryde, M., *Acta Pharm. Suecica*, **2** (1), 1(1965); through *Chem. Abstr.*, **62**, 15996(1965).
(58) Kozkik, F., *Farm. Vestnik Ljubljana*, **14** (10–12), 203(1963); through *Chem. Abstr.*, **62**, 2665(1965).
(59) Jones, T. M., and Pilpel, N., *J. Pharm. Pharmacol.*, **17**, 440(1965).
(60) Morgan, J. F., and Hill, J. C., *Am. J. Ophthalmol.*, **58**, 767(1964); through *Chem. Abstr.*, **62**, 4503(1965).
(61) Madden, E. E., Jr., and Piecoro, J. J., Jr., *Am. J. Hosp. Pharm.*, **22**, 195(1965).
(62) Prescott, F., *Drug Cosmetic Ind.*, **97**, 497(1965).
(63) Srivastava, V. K., and Rai, R. S., *Proc. Natl. Acad. Sci. India, Sect. A*, **34**, 338(1965); through *Chem. Abstr.*, **63**, 1241(1965).
(64) Carnie, G. A. R., *Australasian J. Pharm.*, **45**, S80(1964); through *Chem. Abstr.*, **62**, 8933(1965).
(65) Smith, E. A., *Mfg. Chemist Aerosol News*, **36** (5), 54(1965).
(66) Carpenter, F. S., *Soap Chem. Specialties*, **41** (1), 159 (1965).
(67) Mering, J., *Bull. Groupe Franc. Argiles*, **14** (9), 115(1964); through *Chem Abstr.*, **62**, 1113(1965).
(68) Khamraev, S. S., Yagudaev, M. R., and Aripov, E. A., *Kolloidn. Zh.*, **27** (1), 121(1965).
(69) Barr, M., *Am. J. Pharm.*, **137**, 107(1965).
(70) Coopersmith, M., and Rutkowski, A. J., *Drug Cosmetic Ind.*, **96**, 630(1965).
(71) *Ibid.*, **96**, 792(1965).
(72) Endraszka, J., *et al.*, *Dissertationes Pharm.*, **16**, 519(1964); through *Chem. Abstr.*, **62**, 11635(1965).
(73) Mestres, D., and Jose, M., *Quimia (Barcelona)*, **139**, 27(1965); through *Chem. Abstr.*, **63**, 17793(1965).
(74) Jacob, J. T., and Plein, E. M., *J. Am. Pharm. Assoc.*, **NS5**, 431(1965).
(75) Bergwein, K., *Riechstoffe, Aromen, Koerperpflege-Mittel*, **14**, 316(1964); through *Chem. Abstr.*, **62**, 3881 (1965).
(76) Kaufman, T. G., *Drug Cosmetic Ind.*, **97**, 172(1965).
(77) Neuwald, F., and Fetting, K., *Am. Perfumer Cosmet.*, **80** (5), 23(1965).
(78) Neumann, H., *Parfums, Cosmet., Savons*, **7**, 436 (1964); through *Chem. Abstr.*, **62**, 3882(1965).
(79) King, J. C., and Sheffield, W. J., *J. Pharm. Sci.*, **54**, 879(1965).
(80) Mithal, B. M., and Kasid, J. L., *Indian J. Pharm.*, **26**, 316(1964); through *Chem. Abstr.*, **62**, 14427(1965).
(81) Woods, L. C., *Am. Perfumer Cosmet.*, **80** (4), 51 (1965).
(82) Barr, M., *Am. J. Pharm.*, **137**, 127(1965).
(83) Lubowe, I. I., and Mecca, S. B., *Parfums, Cosmet., Savons*, **8** (3), 113(1965); through *Chem. Abstr.*, **63**, 4096 (1965).
(84) Lopukhova, K. A., *Gigiena Truda i Prof. Zabolevaniya*, **8** (12), 38(1964); through *Chem. Abstr.*, **62**, 8930 (1965).

[2] *Index Medicus* abbreviations were used for journals not listed in *Chemical Abstracts*.

(85) Smith, G., *Pharm. J.*, **194,** 219(1965).
(86) Lundgren, P., *Svensk Farm. Tidskr.*, **68** (31), 837 (1964); through *Chem. Abstr.*, **62,** 7592(1965).
(87) Sawatari, K., *Yuki Gosei Kagaku Kyokai Shi*, **23** (8), 734(1965); through *Chem. Abstr.*, **63,** 11247(1965).
(88) Sabalitschka, Th., *Folia Pharm. Istanbul*, **5,** 673 (1965); through *Chem. Abstr.*, **63,** 9741(1965).
(89) Ostendorf, J. P., *J. Soc. Cosmetic Chemists*, **16** (4), 203(1965); through *Chem. Abstr.*, **63,** 428(1965).
(90) Brownley, C. A., and Lachman, L., *J. Pharm. Sci.*, **54,** 1480(1965).
(91) Mitchell, A. G., and Wan, L. S. C., *ibid.*, **54,** 699 (1965).
(92) Pokorny, J., and Fiser, K., *Cesk. Hyg.*, **10** (5), 314(1965); through *Chem. Abstr.*, **63,** 14633(1965).
(93) Swarbrick, J., and Rhodes, C. T., *J. Pharm. Sci.*, **54,** 903(1965).
(94) Speiser, P., *Pharm. Weekblad*, **100** (29), 865(1965); through *Chem. Abstr.*, **63,** 14641(1965).
(95) Mario, E., and Gerraughty, R. J., *J. Pharm. Sci.*, **54,** 321(1965).
(96) Stekol'nikov, L. I., and El'piner, I. E., *Biofizika*, **10** (2), 232(1965); through *Chem. Abstr.*, **63,** 8127(1965).
(97) Vincendon, G., Cier, A., and Nofre, C., *Compt. Rend.*, **260,** 711(1965); through *Chem. Abstr.*, **62,** 11637 (1965).
(98) Vos, T., Kerckhoffs, H. P. M., and Hnizinga, T., *Pharm. Weekblad*, **100** (7), 228(1965); through *Chem. Abstr.*, **63,** 5454(1965).
(99) Moerch, J., and Moerch, K., *Dansk. Tidsskr. Farm.*, **39,** 117(1965); through *Chem. Abstr.*, **63,** 437(1965).
(100) Pawelczyk, E., and Dopierala, T., *Farm. Polska*, **18,** 565(1962); through *Chem. Abstr.*, **63,** 6793(1965).
(101) Denoel, A., *J. Pharm. Belg.*, **19** (11–12), 505(1964); through *Chem. Abstr.*, **62,** 15992(1965).
(102) Kato, S., Kurata, K., and Sugisawa, Y., *Yakugaku Zasshi*, **85,** 935(1965).
(103) Kakemi, K., Sezaki, H., and Inoue, S., *ibid.*, **85,** 674(1965).
(104) Sykulska, Z., and Gorycka, M., *Acta Polon. Pharm.*, **22** (2), 133(1965); through *Chem. Abstr.*, **63,** 9752(1965).
(105) Lehman, R. A., and Bloch, L. P., *J. Pharm. Sci.*, **54,** 1035(1965).
(106) Kuboki, N., Saito, K., and Maki, Y., *Yakuzaigaku*, **24** (3), 255(1964); through *Chem. Abstr.*, **62,** 12985(1965).
(107) Breinlich, J., *Pharm. Ztg.*, **110** (8), 579(1965); through *Chem. Abstr.*, **63,** 5155(1965).
(108) Finnegan, R. A., *J. Pharm. Sci.*, **54,** 928(1965).
(109) Arancibia, A., and Sacre, M., *Farmaco(Pavia)Ed. Prat.*, **19** (11), 567(1964); through *Chem. Abstr.*, **62,** 5146 (1965).
(110) Gonzalez, M. E. S., *Anales Fac. Quim. Farm., Univ. Chile*, **15,** 118(1963); through *Chem. Abstr.*, **62,** 12984(1965).
(111) Parafinska, Z., *Acta Polon. Pharm.*, **20,** 395(1963); through *Chem. Abstr.*, **62,** 1520(1965).
(112) Davydova, V. A., *Sb. Nauchn. Tr. Tsentr. Aptechn. Nauchn.-Issled. Inst.*, **5,** 105(1964); through *Chem. Abstr.*, **63,** 11260(1965).
(113) Milch, G., Toth, T., and Borsai, M., *Gyogyszereszet*, **8** (9), 336(1964); through *Chem. Abstr.*, **62,** 405(1965).
(114) Clarke, P. A., *Pharm. J.*, **194,** 375(1965).
(115) Nerlo, H., *et al.*, *Polski Tygod. Lekar.*, **19,** 1085 (1964); through *Chem. Abstr.*, **62,** 3889(1965).
(116) Gupta, J. L., and Mital, H. C., *Indian J. Pharm.*, **27** (9), 251(1965); through *Chem. Abstr.*, **63,** 16134(1965).
(117) Hernardez, R. I., *Anales Fac. Quim. Farm., Univ. Chile*, **15,** 180(1963); through *Chem. Abstr.*, **62,** 15996(1965).
(118) Anghileri, L. J., *Arg. Rep. Com. Nocl. Energia At. Informe*, **119,** 8(1964); through *Chem. Abstr.*, **62,** 405(1965).
(119) Koshy, K. T., *et al.*, *J. Pharm. Sci.*, **54,** 549(1965).
(120) Duvall, R. N., Koshy, K. T., and Pyles, J. W., *ibid.*, **54,** 607(1965).
(121) Takahashi, T., and Ishihara, S., *Yakugaku Zasshi*, **85,** 808(1965).
(122) Tanako, I., *et al.*, *Yakuzaigaku*, **25** (1), 31(1965); through *Chem. Abstr.*, **63,** 17803(1965).
(123) Ozaki, A., and Inoue, Y., *Yakuzaigaku*, **25** (1), 69(1965); through *Chem. Abstr.*, **63,** 17805(1965).
(124) Kerju, S., and Iguchi, S., *Yakuzaigaku*, **24** (3), 204(1964); through *Chem. Abstr.*, **62,** 12987(1965).
(125) Lach, J. L., and Bornstein, M., *J. Pharm. Sci.*, **54,** 1730(1965).
(126) Kiss, L., Rozsondai, B., and Scholz, T., *Gyogyszereszet*, **8** (9), 341(1964); through *Chem. Abstr.*, **62,** 405 (1965).
(127) Lee, S., DeKay, H. G., and Banker, G. S., *J. Pharm. Sci.*, **54,** 1153(1965).
(128) Samuelsson, G., *Acta Pharm. Suecica*, **1** (6), 227 (1964); through *Chem. Abstr.*, **62,** 12984(1965).
(129) Stawowczyk, A., *Farm. Polska*, **21,** 340(1965); through *Chem. Abstr.*, **63,** 12969(1965).
(130) Ello, I., and Kun, F., *Gyogyszereszet*, **7,** 413(1963); through *Chem. Abstr.*, **62,** 14426(1965).
(131) Lutomski, J., *Biul. Inst. Roslin Leczniczych*, **10,** (2–3), 71(1964); through *Chem. Abstr.*, **63,** 4097(1965).
(132) Garrett, E. R., *Safybi*, **4** (13), 3(1964); through *Chem. Abstr.*, **62,** 8944(1965).
(133) Pinho de Brojo, A., *Bol. Escola Farm., Univ. Coimbra, Ed. Cient.*, **24,** 1(1964); through *Chem. Abstr.*, **62,** 14425(1965).
(134) Kiss, L., and Varsanyi-L., M., *Gyogyszereszet*, **9,** 41(1965); through *Chem. Abstr.*, **62,** 14425(1965).
(135) Lordi, N. G., and Scott, M. W., *J. Pharm. Sci.*, **54,** 531(1965).
(136) Eriksen, S. P., and Stelmach, H., *ibid.*, **54,** 1029 (1965).
(137) Stern, M. J., and Wolfsberg, M., *ibid.*, **54,** 849 (1965).
(138) Garrett, E. R., Goto, S., and Stubbins, J. F., *ibid.*, **54,** 119(1965).
(139) Stefanescu, D., *et al.*, *Farmacia*, **12,** 465(1964); through *Chem. Abstr.*, **62,** 1520(1965).
(140) Burkman, A. M., *J. Pharm. Sci.*, **54,** 325(1965).
(141) Roberts, W., and Whiting, M. C., *J. Chem. Soc.*, **1965,** 1290.
(142) Yamana, T., Mizukami, Y., and Ichimura, F., *Yakugaku Zasshi*, **85,** 654(1965).
(143) Hofstee, B. H. J., *Arch. Biochem. Biophys.*, **112,** 224(1965).
(144) Garrett, E. R., and Notari, R. E., *J. Pharm. Sci.*, **54,** 209(1965).
(145) Champy-Hatem, S., *Compt. Rend.*, **261,** (1) (Groupe 13), 271(1965); through *Chem. Abstr.*, **63,** 9753 (1965).
(146) Woo, C. H., *Vakhak Hoeji*, **7** (2/3), 51(1963); through *Chem. Abstr.*, **62,** 10297(1965).
(147) Garrett, E. R., Chemburkar, P. B., and Suzuki, T., *Chem. Pharm. Bull. (Tokyo)*, **13,** 1113(1965).
(148) Blades, A. T., and Wallbridge, M. G. H., *J. Chem. Soc.*, **1965,** 792.
(149) Takacsi-Nagy, G., and Balkay, A., *Gyogyszereszet*, **9** (5), 190(1965); through *Chem. Abstr.*, **63,** 11260(1965).
(150) Simon, I. S., and Shostenko, Yu. V., *Med. Prom. SSSR*, **19** (3), 33(1965); through *Chem. Abstr.*, **63,** 438(1965).
(151) Tuchel, N., and Antonescu, V., *Farmacia*, **12,** 615 (1964); through *Chem. Abstr.*, **62,** 3889(1965).
(152) Cleary, R. W., *Dissertation Abstr.*, **25,** 4421(1965).
(153) Speiser, P., *Rev. Intern. Serv. Sante Armees Teere Mer Air*, **38** (1), 17(1965); through *Chem. Abstr.*, **63,** 2855 (1965).
(154) Herd, A. K., III, *Dissertation Abstr.*, **25,** 5575 (1965).
(155) Lynn, K. R., *J. Phys. Chem.*, **69,** 687(1965).
(156) Cluzel, R., *Pathol. Biol. Semaine Hop.*, **13,** 392 (1965); through *Chem. Abstr.*, **63,** 6794(1965).
(157) Kondo, S., and Shimura, M., *Meiji Shika Kenkyu Nempo Yakuhiss Bumon*, **6,** 6(1963); through *Chem. Abstr.*, **62,** 5146(1965).
(158) Unterman, H. W., Constantin, E., and Rusan, M., *Farmacia Bucharest*, **12** (10), 625(1964); through *Chem. Abstr.*, **62,** 2673(1965).
(159) Tukamoto, T., Miyake, M., and Sato, H., *Yakugaku Zasshi*, **85,** 41(1965).
(160) Bhate, D. S., Ackarya, S. P., and Parekh, J. H., *Hindustan Antibiot. Bull.*, **5** (4), 99(1963); through *Chem. Abstr.*, **63,** 17803(1965).
(161) Suhara, Y., Maeda, K., and Umczawa, H., *J. Antiobiotics (Tokyo)*, **18,** 182(1965).
(162) Forist, A. A., Brown, L. W., and Royer, M. E., *J. Pharm. Sci.*, **54,** 476(1965).
(163) Schwartz, M. A., *et al.*, *ibid.*, **54,** 149(1965).
(164) Saito, K., *Nippon Nogei Kagaku Kaishi*, **37,** 371 (1963); through *Chem. Abstr.*, **63,** 1664(1965).
(165) Narasimhachari, N., and Rao, G. R., *Hindustan Antibiot. Bull.*, **6** (3), 114(1964); through *Chem. Abstr.*, **63,** 16134(1965).
(166) Thoma, K., Ullmann, E., and Zelfel, G., *Acta Pharm. Hung.*, **35** (1), 1(1965); through *Chem. Abstr.*, **63,** 1664(1965).
(167) Prista, L. N., da Silva, A. R., and Ferreira, S. D., *Rev. Port. Farm.*, **14,** 397(1964); through *Chem. Abstr.*, **62,** 11637(1965).
(168) Modrzejewski, F., and Kaczmarczyk, B., *Farm. Polska*, **20** (23–24), 879(1964); through *Chem. Abstr.*, **63,** 5455(1965).
(169) Olszewski, Z., and Grabowska, J., *Acta Polon. Pharm.*, **21** (2), 175(1964); through *Chem. Abstr.*, **62,** 8945 (1965).
(170) Weiss, P. J., and Palmer, R. V., *Antimicrobial Agents Chemotherapy*, **1964,** 355; through *Chem. Abstr.*, **63,** 6793(1965).
(171) Schwartz, M. A., *J. Pharm. Sci.*, **54,** 1308(1965).
(172) *Ibid.*, **54,** 472(1965).
(173) Narasimhachari, N., Rao, G. R., and Tatke, J. V., *Hindustan Antibiot. Bull.*, **7** (3), 127(1965); through *Chem. Abstr.*, **63,** 16134(1965).
(174) Finholt, P., Jurgensen, G., and Kristiansen, H., *J. Pharm. Sci.*, **54,** 387(1965).
(175) Sugano, Y., and Wadazawa, T., *Nippon Noge, Kagaku Kaishi*, **37** (12), 738(1963); through *Chem. Abstr.*, **63***i* 14640(1965).
(176) Tardif, R., *J. Pharm. Sci.*, **54,** 281(1965).
(177) Tardif, R., *Can. Pharm. J.*, **98** (10), 41(1965).
(178) Weissenberg, E., *Harokeach Haivri*, **10,** 203(1964); through *Chem. Abstr.*, **63,** 2855(1965).
(179) Hillstrom, V., Andersson, R., and Hegedus, L., *Var Foda*, **8,** 57(1964); through *Chem. Abstr.*, **62,** 5146(1965).
(180) Benterud, A., *Acta Polytech. Scand. No. 16. Chem. Met. Ser.*, **1962** (21), 70; through *Chem. Abstr.*, **62,** 6345 (1965).
(181) Zwolinska, Z., *et al.*, *Acta Polon. Pharm.*, **20** (4), 339(1963); through *Chem. Abstr.*, **62,** 405(1965).
(182) Sabri, M. I., and Rao, V. K. M., *Indian J. Technol.*, **3** (1), 28(1965); through *Chem. Abstr.*, **62,** 11638(1965).

(183) Zaduminski, M., *et al., Acta Polon. Pharm.*, **20** (5), 399(1963); through *Chem. Abstr.*, **62**, 404(1965).
(184) Kato, Y., *Yakuzaigaku*, **24** (3), 241(1964); through *Chem. Abstr.*, **62**, 12985(1965).
(185) Kawasaki, C., Okada, K., and Ono, Y., *J. Vitaminol.*, **9**, 257(1965); through *Chem. Abstr.*, **62**, 1519(1965).
(186) Kawasaki, C., and Okada, K., *J. Vitaminol.*, **10**, 135(1964); through *Chem. Abstr.*, **62**, 10297(1965).
(187) Takahashi, T., *Yakugaku Zasshi*, **85**, 804(1965).
(188) Gana, R. I. M., *Anales Fac. Quim. Farm., Univ. Chile*, **15**, 112(1963); through *Chem. Abstr.*, **62**, 14426(1965).
(189) Kostenbauder, H. B., DeLuca, P. P., and Kowarski, C. R., *J. Pharm. Sci.*, **54**, 1243(1965).
(190) Otani, S., *Yakugaku Zasshi*, **85**, 521(1965).
(191) Finholt, P., Alsos, I., and Higuchi, T., *J. Pharm. Sci.*, **54**, 181(1965).
(192) Yamamoto, R., and Yamamoto, E., *Yakuzaigaku*, **24**, 309(1964); through *Chem. Abstr.*, **63**, 1663(1965).
(193) Finholt, P., *et al., J. Pharm. Sci.*, **54**, 124(1965).
(194) Otani, S., *Yakuzaigaku*, **25**, 36(1965); through *Chem. Abstr.*, **63**, 17803(1965).
(195) Otani, S., *Yakuzaigaku*, **24**, 293(1964); through *Chem. Abstr.*, **63**, 1663(1965).
(196) Yamamoto, R., and Yamamoto, E., *Yakuzaigaku*, **25**, 42(1965); through *Chem. Abstr.*, **63**, 17803(1965).
(197) Das, S., Dutta, B. K., and Dutta, B. N., *J. Proc. Inst. India*, **36**, 296(1964); through *Chem. Abstr.*, **63**, 1663(1965).
(198) Charlampowicz, Z., and Gajewski, A., *Zeszyty Probl. Postepow Nauk Rolniczych*, **53**, 121(1965); through *Chem. Abstr.*, **63**, 12976(1965).
(199) Das, S., Dutta, B. K., and Dutta, B. N., *J. Proc. Inst. Chemists*, **36**, 245(1964); through *Chem. Abstr.*, **63**, 1662(1965).
(200) Galczynska, M., and Zuk, J., *Acta Polon. Pharm.*, **20**, 441(1963); through *Chem. Abstr.*, **62**, 6346(1965).
(201) Seth, S. K., and Mital, H. C., *Indian J. Pharm.*, **27** (4), 119(1965); through *Chem. Abstr.*, **62**, 15995(1965).
(202) Borenstein, B., *Food Technol.*, **19** (11), 115(1965).
(203) Doerge, R. F., Ravin, L. J., and Caldwell, H. C., *J. Pharm. Sci.*, **54**, 1038(1965).
(204) Audisio, G., and Pucini, L., *Giorn. Med. Mil.*, **115** (1), 81(1965); through *Chem. Abstr.*, **63**, 6794(1965).
(205) Bonnett, R., Raleigh, J. A., and Redman, D. G., *J. Am. Chem. Soc.*, **87**, 1600(1965).
(206) Saccani, F., and Boselli, M., *Boll. Chim. Farm.*, **104**, 362(1965); through *Chem. Abstr.*, **63**, 9752(1965).
(207) Janicki, J., *et al., Przeglad Zbozowo-Miynarski*, **8**, 262(1962); through *Chem. Abstr.*, **62**, 3889(1965).
(208) Madiwole, M. S., Rao, S. S., and Dutta, N. K., *Indian J. Pharm.*, **27** (4), 113(1965); through *Chem. Abstr.*, **62**, 15996(1965).
(209) Ritschel, W. A., and Rahman, M., *Sci. Pharm.*, **33** (2), 105(1965); through *Chem. Abstr.*, **63**, 12977(1965).
(210) Ozaki, A., *et al., Yakuzaigaku*, **25** (1), 75(1965); through *Chem. Abstr.*, **63**, 17805(1965).
(211) Cooper, J., *J. Am. Pharm. Assoc.*, **NS5**, 373(1965).
(212) Fowler, H. W., *Mfg. Chemist Aerosol News*, **36** (1), 75(1965).
(213) *Ibid.*, **36** (5), 57(1965).
(214) Wace, P. E., and Banfield, D. L., *Nature*, **206**, 1131(1965).
(215) Smith, E. A., *Mfg. Chemist Aerosol News*, **36** (2), 47(1965).
(216) *Ibid.*, **36** (8), 28(1965).
(217) Ridgway, K., and Wibberley, K., *Chemist Druggist*, **183** (4443), 366(1965); through *Chem. Abstr.*, **63**, 4098(1965).
(218) Swartz, C. J., and Suydam, W. L., Jr., *J. Pharm. Sci.*, **54**, 1050(1965).
(219) Rankel, A., Lieberman, H. A., and Paruta, A. N., *Drug Cosmetic Ind.*, **97**, 836(1965).
(220) Stratton, R. A., *Chem. Ind. (London)*, **1965**, 67.
(221) Cook, E. M., *Drug Cosmetic Ind.*, **96**, 45(1965).
(222) Knoll, P., and Leuschke, W., *Kernenergie*, **4** (8), 637(1961); through *Chem. Abstr.*, **62**, 4651(1965).
(223) Iya, V. K., *et al., Indian J. Chem.*, **3** (9), 317(1965); through *Chem. Abstr.*, **63**, 16126(1965).
(224) Smith, E. A., *Mfg. Chemist Aerosol News*, **36** (6), 47(1965).
(225) Paikoff, M., and Drumm, G., *J. Pharm. Sci.*, **54**, 1693(1965).
(226) Faiman, M. D., *Dissertation Abstr.*, **26**, 109(1965).
(227) Olsen, J. L., *ibid.*, **26**, 324(1965).
(228) DeLuca, P., and Lachman, L., *J. Pharm. Sci.*, **54**, 617(1965).
(229) Lachman, L., DeLuca, P. P., and Withnell, R., *ibid.*, **54**, 1342(1965).
(230) DeLuca, P., Lachman, L., and Yost, W., *ibid.*, **54**, 1348(1965).
(231) DeLuca, P., and Lachman, L., *ibid.*, **54**, 1411(1965).
(232) Parrott, E. L., *Drug Cosmetic Ind.*, **96**, 320(1965).
(233) Bedaux, F. C., *Pharm. Weekblad*, **100** (21), 653 (1965); through *Chem. Abstr.*, **63**, 5445(1965).
(234) Ebels, J. J., and Moeys, W. A., *Pharm. Weekblad*, **100** (21), 654(1965).
(235) Johnson, R. D., Goyan, F. M., and Tuck, L. D., *J. Pharm. Sci.*, **54**, 1176(1965).
(236) Vaille, C., and Souchard, M., *Ann. Pharm. Franc.*, **23** (5), 323(1965); through *Chem. Abstr.*, **63**, 12201(1965).
(237) Hammarlund, E. R., and Van Pevenage, G. L., *J. Am. Pharm. Assoc.*, **NS5**, 324(1965).
(238) Hammarlund, E. R., Deming, J. G., and Pedersen-Bjergaard, K., *J. Pharm. Sci.*, **54**, 160(1965).
(239) Weil, G. P., *J. Pharm. Belg. (N.S.)*, **18** (45), 445 (1963); through *Chem. Abstr.*, **63**, 5455(1965).
(240) Koerber, G., *Deut. Apotheker-Ztg.*, **103**, 181(1963); through *Chem. Abstr.*, **63**, 2856(1965).
(241) Kosa, L., *Gyogyszereszet*, **8** (10), 389(1964); through *Chem. Abstr.*, **62**, 3259(1965).
(242) Pinter, J., *Gyogyszereszet*, **8** (9), 339(1964); through *Chem. Abstr.*, **62**, 406(1965).
(243) Aoki, M., *et al., Yakuzaigaku*, **24**, 331(1964); through *Chem. Abstr.*, **63**, 1662(1965).
(244) Aoki, M., *et al., Yakuzaigaku*, **25** (1), 59(1965); through *Chem. Abstr.*, **63**, 17805(1965).
(245) Dunworth, R. D., and Kenna, F. R., *Am. J. Hosp. Pharm.*, **22**, 190(1965).
(246) Misgen, R., *ibid.*, **22**, 92(1965).
(247) Lang, B., *Gyogyszereszet*, **8**, 402(1964); through *Chem. Abstr.*, **62**, 3883(1965).
(248) Guess, W. L., Berg, H. F., and Autian, J., *Am. J. Hosp. Pharm.*, **22**, 180(1965).
(249) Ehrlen, I. R., *Svensk Farm. Tidskr.*, **68** (30), 818 (1964); through *Chem. Abstr.*, **62**, 7593(1965).
(250) Yalcindag, O. N., *Kim. Sanayi*, **12** (59), 120(1961); through *Chem. Abstr.*, **62**, 12985(1965).
(251) Marzouk, Y., *Harokeach Haivri*, **10**, 2(1964) through *Chem. Abstr.*, **62**, 7593(1965).
(252) Synek, J., *Boll. Chim. Farm.*, **103** (11), 790(1964); through *Chem. Abstr.*, **62**, 7593(1965).
(253) Howard, P. J., *J. Sci. Technol.*, **10** (4), 172(1964); through *Chem. Abstr.*, **62**, 7593(1965).
(254) Adler, N., *J. Pharm. Sci.*, **54**, 735(1965).
(255) Marzouk, Y., *Harokeach Haivri*, **10**, 187(1964); through *Chem. Abstr.*, **63**, 2856(1965).
(256) McCulloch, W., *J. Soc. Dairy Technol.*, **18** (1), 36 (1965); through *Chem. Abstr.*, **62**, 16519(1965).
(257) Ley, F. J., and Tallentire, A., *Pharm. J.*, **195**, 216 (1965).
(258) Pochapinskii, V. I., Ermol'eva, Z. V., and Breger, A. Kh., *Antibioliki*, **9**, 926(1964); through *Chem. Abstr.*, **62**, 3889(1965).
(259) Saunders, L., *Dechema Monograph*, **55** (955-975), 275(1964); through *Chem. Abstr.*, **63**, 11261(1965).
(260) Guven, K. C., Tali Cetin, E., and Aykan, T. B., *Eczacilik Bulteni*, **6** (5–6), 64(1964); through *Chem. Abstr.*, **63**, 439(1965).
(261) Dahlgren, P., *Farm. Revy*, **64** (8), 180(1965); through *Chem. Abstr.*, **62**, 15996(1965).
(262) Cleave, J. P., *J. Pharm. Pharmacol.*, **17**, 698(1965).
(263) Chafetz, L., and Hodges, J. R., *Am. J. Hosp. Pharm.*, **22**, 382(1965).
(264) Lachman, L., *J. Pharm. Sci.*, **54**, 1519(1965).
(265) Gold, G., and Palermo, B. T., *ibid.*, **54**, 310(1965).
(266) *Ibid.*, **54**, 1517(1965).
(267) Ritschel, W. A., and Rahman, M., *Australasian J. Pharm.*, **45**, S552(1964); through *Chem. Abstr.*, **62**, 8946 (1965).
(268) Langauer, Th., and Steiger-Trippi, K., *Kongr. Pharm. Wiss., Vortr. Originalmitt., 23. Muenster (Westfalen) Ger.*, **1963**, 575; through *Chem. Abstr.*, **62**, 6346(1965).
(269) Shotton, E., and Harb, N., *J. Pharm. Pharmacol.*, **17**, 504(1965).
(270) Modrzejewski, F., and Wochna, L., *Gyogyszereszet*, **9** (9), 335(1965); through *Chem. Abstr.*, **63**, 14633(1965).
(271) Patel, R. P., and Pancholi, J. M., *Indian J. Pharm.*, **26**, 313(1964); through *Chem. Abstr.*, **62**, 14425(1965).
(272) Nuppenau, H., *Arch. Pharm. Chemi*, **72**, 435(1965); through *Chem. Abstr.*, **63**, 6793(1965).
(273) Bergman, L. A., and Bandelin, F. J., *J. Pharm. Sci.*, **54**, 445(1965).
(274) Jaminet, Fr., *J. Pharm. Belg.*, **19** (3–4), 144(1964); through *Chem. Abstr.*, **63**, 6795(1965).
(275) Willis, C. R., Jr., Banker, G. S., and DeKay, H. G., *J. Pharm. Sci.*, **54**, 366(1965).
(276) Steinberg, W. H., *et al., ibid.*, **54**, 747(1965).
(277) Wai, K.-N., *Dissertation Abstr.*, **25**, 6550(1965).
(278) Kirsop, W., *Australasian J. Pharm.*, **45**, S73(1964); through *Chem. Abstr.*, **62**, 8946(1965).
(279) Raff, A. M., *Dissertation Abstr.*, **25**, 4661(1965).
(280) Chase, G. D., and Parsons, W. H., *J. Pharm. Sci.*, **54**, 528(1965).
(281) Lewis, C. J., and Train, D., *J. Pharm. Pharmacol.*, **17**, 33(1965).
(282) *Ibid.*, **17**, 1(1965).
(283) *Ibid.*, **17**, 577(1965).
(284) Seitz, J. A., and Flessland, G. M., *J. Pharm. Sci.*, **54**, 1353(1965).
(285) Higuchi, T., *et al., ibid.*, **54**, 111(1965).
(286) Duvall, R. N., Koshy, K. T., and Dashiell, R. E., *ibid.*, **54**, 1196(1965).
(287) Hasegawa, K., *et al., Yakugaku Zasshi*, **85**, 796 (1965).
(288) Bujar, H., and Olszewski, Z., *Acta Polon. Pharm.*, **20**, 447(1963); through *Chem. Abstr.*, **62**, 6346(1965).
(289) Asker, A. F., *Dissertation Abstr.*, **25**, 7211(1965).
(290) Richman, M. D., Fox, C. D., and Shangraw, R. F., *J. Pharm. Sci.*, **54**, 447(1965).
(291) Saber, A. H., *et al., Bull. Fac. Pharm.*, **2**, 129(1963); through *Chem. Abstr.*, **62**, 6346(1965).
(292) Cook, C. H., Jr., and Webber, M. G., *Am. J. Hosp. Pharm.*, **22**, 95(1965).
(293) Czetsch-Lindenwald, H. v., and Tawashi, R., *Pharm. Ind.*, **27**, 146(1965).
(294) Nash, R. A., *Drug Cosmetic Ind.*, **97**, 843(1965).

(295) Fujiwara, H., *Takeda Kenkyusho Nempo*, **21 (Oct.)**, 54(1962); through *Chem. Abstr.*, **62**, 15995(1965).
(296) Benedict, L. K., Banker, G. A., and Kessler, W. V., *J. Pharm. Sci.*, **54**, 1659(1965).
(297) Tufegdzic, N., Tufegdzic, E., and Georgijevic, A., *Acta Pharm. Jugoslav.*, **12**, 121(1962); through *Chem. Abstr.*, **62**, 8944(1965).
(298) Makitantova, A. E., *Tr. Vses. Nauchn.-Issled. Inst. Vet. Sanit.*, **18**, 167(1964); through *Chem. Abstr.*, **62**, 2672 (1965).
(299) Bahr, A., *Z. Erzbergbau Metallhuetenw.*, **17**, 467 (1964); through *Chem. Abstr.*, **62**, 4647(1965).
(300) Trandafilov, I., *Farmatsiya (Sofia)*, **14** (3), 56 (1964); through *Chem. Abstr.*, **62**, 10297(1965).
(301) Kigasawa, K., *et al.*, *Yakuzaigaku*, **24** (3), 231 (1964); through *Chem. Abstr.*, **62**, 12987(1965).
(302) Demyanova, E. A., *Razvedka i Okhrana Nedr*, **27** (1), 40(1961); through *Chem. Abstr.*, **63**, 17187(1965).
(303) Motawi, M. M., Czetsch-Lindenwald, H. v., and Nassif, N., *J. Pharm. Sci. U. Arab Rep.*, **4**, 63(1963); through *Chem. Abstr.*, **63**, 11261(1965).
(304) Garrett, E. R., *J. Pharm. Sci.*, **54**, 1557(1965).
(305) Stefanescu, D., and Tuchel, T., *Farmacia (Bucharest)*, **12**, 641(1964); through *Chem. Abstr.*, **62**, 8412(1965).
(306) Hill, R. A. W., and Knight, J. T., *Trans. Faraday Soc.*, **61** (1), 170(1965); through *Chem. Abstr.*, **62**, 4642(1965).
(307) LeVeen, H. H., Giordano, P., and Johnson, H., *Am. J. Clin. Nutr.*, **16**, 129(1965).
(308) Lemberger, A. P., and Mourad, N., *J. Pharm. Sci.*, **54**, 229(1965).
(309) *Ibid.*, **54**, 233(1965).
(310) Rowe, E. L., *J. Pharm. Sci.*, **54**, 260(1965).
(311) Millar, A., *Proc. Sci. Sec. Toilet Goods Assoc.*, **43**, 28(1965); through *Chem. Abstr.*, **63**, 5441(1965).
(312) Hohnjec-Mihaljinac, S., *Farm. Glasnik*, **21**, 283 (1965); through *Chem. Abstr.*, **63**, 11248(1965).
(313) Lin, T. J., *Am. Perfumer Cosmet.*, **80** (1), 39(1965).
(314) *Ibid.*, **80** (3), 35(1965).
(315) Rimlinger, G., *Parfums, Cosmet., Savons*, **7** (9), 396 (1964); through *Chem. Abstr.*, **62**, 735(1965).
(316) Burt, B. W., *J. Soc. Cosmetic Chemists*, **16**, 465 (1965); through *Chem. Abstr.*, **63**, 13581(1965).
(317) Hamill, R. D., Olson, F. A., and Peterson, R. V., *J. Pharm. Sci.*, **54**, 537(1965).
(318) Singleton, W. S., *Am. J. Clin. Nutr.*, **16**, 16(1965).
(319) Hebeisen, F., *Promotionsarb Zurich*, **1963**, 3353; through *Chem. Abstr.*, **63**, 47(1965).
(320) McQuarri, E. B., and Andersen, H. P., *Am. J. Clin. Nutr.*, **16**, 23(1965).
(321) Kann, D. E., and Tester, W. W., *Am. J. Hosp. Pharm.*, **22**, 606(1965).
(322) Vol'fenzon, I. L., *Kolloidn. Zh.*, **27** (1), 8(1965).
(323) Muys, G. T., *Chem. Ind. (London)*, **1965**, 1245.
(324) Motawi, M. M., Czetsch-Lindenwald, H. v., and Nassif, N., *Kongr. Pharm. Wiss., Vortr. Originalmitt., 23. Muensler, (Westfalen) Ger.*, **1963**, 551; through *Chem. Abstr.*, **62**, 6345(1965).
(325) Golucki, Z., and Wisniewski, W., *Dissertationes Pharm.*, **16**, 513(1964); through *Chem. Abstr.*, **62**, 11639 (1965).
(326) Golucki, Z., *Dissertationes Pharm.*, **17** (2), 205 (1965); through *Chem. Abstr.*, **63**, 16135(1965).
(327) Gretskii, V. M., *Aptechn. Delo*, **14** (1), 10(1965); through *Chem. Abstr.*, **62**, 11636(1965).
(328) Gretskii, V. M., and Blagovidova, Yu. A., *Aptechn. Delo*, **13** (6), 12(1964); through *Chem. Abstr.*, **62**, 6347(1965).
(329) Alexander, P., *Mfg. Chemist Aerosol News*, **36** (7), 55(1965).
(330) Kaufman, T., and Blaser, R., *Am. Perfurmer Cosmet.*, **80** (12), 37(1965).
(331) Lange, W. E., and Gonet, F. R., *J. Soc. Cosmetic Chemists*, **16** (10), 563(1965); through *Chem. Abstr.*, **63**, 14640(1965).
(332) Alyushin, M. T., *Aptechn. Delo*, **14** (4), 69(1965); through *Chem. Abstr.*, **63**, 16137(1965).
(333) Alyushin, M. T., *Sb. Nauchn. Tr. Tsentr. Aptechn. Nauchn.-Issled. Inst.*, **5**, 7(1964); through *Chem. Abstr.*, **63**, 11262(1965).
(334) Macda, S., *Bull. Pharm. Res. Inst. (Osaka)*, **53**, 1 (1964); through *Chem. Abstr.*, **63**, 14634(1965).
(335) Weitzel, G., and Fretzdorff, A. M., *Fette, Seifen, Anstrichmittel*, **67** (3), 228(1965); through *Chem. Abstr.*, **63**, 2846(1965).
(336) Pokorny, J., Pokorna, V., and Tomankova, I., *Sb. Vysoke Skoly Chem.-Technol. Praze, Potravinarskee Technol.*, **7** (1), 167(1963); through *Chem. Abstr.*, **63**, 5444 (1965).
(337) Fumaneri, A. E., *Boll. Chim. Farm.*, **103**, 681 (1964); through *Chem. Abstr.*, **62**, 1519(1965).
(338) Makedonska, R., *Acta Polon. Pharm.*, **20**, 185 (1963); through *Chem. Abstr.*, **62**, 1520(1965).
(339) Anschel, J., and Lieberman, H. A., *Drug Cosmetic Ind.*, **97**, 341(1965).
(340) *Ibid.*, **97**, 507(1965).
(341) Marqversen, J., *Arch. Pharm. Chemi.*, **72** (13), 579 (1965); through *Chem. Abstr.*, **63**, 14640(1965).
(342) Krowczynski, L., *Acta Polon. Pharm.*, **22** (2), 149 (1965); through *Chem. Abstr.*, **63**, 9752(1965).
(343) Gluzman, M. Kh., Dashevskaya, B. I., and Tridman, G. M., *Med. Prom. SSSR*, **19** (5), 16(1965); through *Chem. Abstr.*, **63**, 4096(1965).
(344) Adel, M. S., *Acta Pharm. Hung.*, **35** (3), 110(1965); through *Chem. Abstr.*, **63**, 16137(1965).
(345) Harrison, M., *Lebanese Pharm. J.*, **8** (1), 1(1963); through *Chem. Abstr.*, **62**, 12983(1965).
(346) Leberl, O., *Kosmetik-Parfum-Drogen Rundschau*, **11** (11/12), 178(1964); through *Chem. Abstr.*, **62**, 5138(1965).
(347) St. Laurent, G., Mintzer, H., and Weissman, F. T., *Drug Cosmetic Ind.*, **96**, 627(1965).
(348) Guillot, M., *Prod. Probl. Pharm.*, **20**, 5(1965); through *Chem. Abstr.*, **62**, 10298(1965).
(349) Marsden, R., *Soap, Perfumery Cosmetics*, **38**, 129 (1965); through *Chem. Abstr.*, **62**, 14419(1965).
(350) Orban, E., *Gyogyszereszet*, **8**, 369(1964); through *Chem. Abstr.*, **62**, 1511(1965).
(351) Scriba, G. T., and Hearn, N. J., *Drug Cosmetic Ind.*, **97**, 343(1965).
(352) Phillips, G. F., *Soap, Perfumery Cosmetics*, **38**, 35(1965); through *Chem. Abstr.*, **62**, 14420(1965).
(353) Schuler, P., *Soap Chem. Specialties*, **41** (8), 78 (1965).
(354) Parker, D. N., *ibid.*, **41** (9), 164(1965).
(355) Feeks, N. A., and Sutugin, A. G., *Usp. Khim.*, **34** (2), 276(1965); through *Chem. Abstr.*, **62**, 12483(1965).
(356) Bergwein, K., *Riechstoffe, Aromen, Koeperpflegemittel*, **15**, 117(1965); through *Chem. Abstr.*, **63**, 2857(1965).
(357) Johnsen, M. A., and Haase, F. D., *Soap Chem. Specialties*, **41** (7), 73(1965).
(358) *Ibid.*, **41** (8), 92(1965).
(359) Phillips, G. F., *Perfumery Essent. Oil Record*, **55**, 597(1964); through *Chem. Abstr.*, **62**, 8882(1965).
(360) Flanner, L. T., *Soap Chem. Specialties*, **41** (12), 208 (1965).
(361) Sanders, P. A., *ibid.*, **41** (12), 117(1965).
(362) Herzka, A., *J. Soc. Cosmetic Chemists*, **16** (1), 31 (1963); through *Chem. Abstr.*, **62**, 8931(1965).
(363) Walkenhorst, W., and Dautrebande, L., *Staub*, **24**, 505(1964); through *Chem. Abstr.*, **62**, 11184(1965).
(364) Broderick, G. F., and Flanner, L. T., *Soap Chem. Specialties*, **41** (6), 98(1965).
(365) Autian, J., *Proc. Sci. Sec. Toilet Goods Assoc.*, **43**, 14(1965); through *Chem. Abstr.*, **63**, 5145(1965).
(366) Jeffrey, L. P., and Fish, K. H., Jr., *Am. J. Hosp. Pharm.*, **22**, 532(1965).
(367) Gogler, W. C., Jr., *Am. Perfumer Cosmet.*, **80** (5), 37(1965).
(368) Glowacki, E. Z., *Mfg. Chemist Aerosol News*, **36** (1), 37(1965).
(369) McKloskey, R., *Soap Chem. Specialties*, **41** (6), 117(1965).
(370) Gurney, H. W., and Raper, A. H., *Mfg. Chemist Aerosol News*, **36** (6), 48(1965).
(371) Hopkins, G. H., *J. Pharm. Sci.*, **54**, 138(1965).
(372) Voisin, A., Campion, D., and Rebeyrotte, A., *Prod. Probl. Pharm.*, **19**, 468(1964); through *Chem. Abstr.*, **62**, 3890 (1965).
(373) Berg, H. F., Guess, W. L., and Autian, J., *J. Pharm. Sci.*, **54**, 79(1965).
(374) Rodell, M. B., *et al.*, *ibid.*, **54**, 129(1965).
(375) Sedova, K. D., *et al.*, *Sb. Nauchn. Tr. Tsentr. Nauchn.-Issled., Aptechn. Inst.*, **5**, 34(1964); through *Chem. Abstr.*, **63**, 5456(1965).
(376) Inchiosa, M. A., Jr., *J. Pharm. Sci.*, **54**, 1379(1965).
(377) Johannesen, B., *Medd. Norsk Farm. Selskap*, **27** (2), 15(1965); through *Chem. Abstr.*, **63**, 438(1965).
(378) Rosenbluth, S. A., *et al.*, *J. Pharm. Sci.*, **54**, 156 (1965).
(379) Gullbring, B., *Plastvarlden*, **15**, 454(1965); through *Chem. Abstr.*, **63**, 6783(1965).
(380) Hadorn, H., and Zuercher, K., *Mitt. Gebiete Lebensum. Hyg.*, **55** (3), 154(1964); through *Chem. Abstr.*, **62**, 398(1965).
(381) Lockhart, H. E., *Dissertation Abstr.*, **26**, 659(1965).
(382) Kimura, O., Oda, R., and Ueda, Y., *Yakuzaigaku*, **24**, 329(1964); through *Chem. Abstr.*, **63**, 1666(1965).
(383) Ogiso, T., and Sugiura, M., *Yakuzaigaku*, **24** (3), 201(1964); through *Chem. Abstr.*, **62**, 12983(1965).
(384) Mellberg, J. R., *J. Pharm. Sci.*, **54**, 615(1965).
(385) Bourgeois, *Labo-Pharma*, **127**, 39(1964); through *Chem. Abstr.*, **62**, 7594(1965).
(386) Golucki, Z., *Acta Polon. Pharm.*, **22** (3), 259 (1965); through *Chem. Abstr.*, **63**, 17804(1965).
(387) Brown, A. R., *J. Soc. Cosmetic Chemists*, **16**, 221 (1965); through *Chem. Abstr.*, **62**, 14420(1965).
(388) Heyworth, G. M., *Mfg. Chemist Aerosol News*, **36** (7), 49(1965).
(389) Seymour, R. B., *ibid.*, **36** (9), 58(1965).
(390) Greensmith, D. E., *ibid.*, **36** (10), 55(1965).
(391) Hill, R. A., *Am. Perfumer Cosmet.*, **80** (9), 25(1965).
(392) Maatman, K. B., *Drug Cosmetic Ind.*, **96**, 467 (1965).
(393) Gupta, S. K., Mehta, S. C., and Mattocks, A. M., *J. Am. Pharm. Assoc.*, **NS5**, 538(1965).
(394) Ai-Seng, L., and Lin, R. C. Y., *J. Pharm. Pharmacol.*, **17**, 48(1965).
(395) Hutchins, H. H., *et al.*, *J. Pharm. Sci.*, **54**, 776 (1965).
(396) Sullivan, J. M., and Houser, T. J., *Chem. Ind. (London)*, **1965**, 1057.
(397) Eriksen, S. P., and Bird, H. E., *J. Pharm. Sci.*, **54**, 455(1965).
(398) Dickerson, R. W., Jr., *Food Technol.*, **19** (5), 198 (1965).
(399) Larkins, J. H., *et al.*, *J. Chem. Educ.*, **42**, 555(1965).
(400) Anagnostopoulos, G. D., and Woodbine, M., *Chem. Ind. (London)*, **1965**, 948.

(401) Glasser, L., and Miller, R. P., *J. Chem. Educ.*, **42**, 91(1965).
(402) Poulsen, B. J., and Lemberger, A. P., *J. Pharm. Sci.*, **54**, 875(1965).
(403) Blight, L., Cumper, C. W. N., and Kyte, V., *J. Colloid Sci.*, **20**, 393(1965).
(404) Long, R. P., and Ross, S., *ibid.*, **20**, 438(1965).
(405) Narasimham, P., *et al.*, *ibid.*, **20**, 473(1965).
(406) Steinberg, W. H., *et al.*, *J. Pharm. Sci.*, **54**, 625 (1965).
(407) *Ibid.*, **54**, 761(1965).
(408) *Ibid.*, **54**, 772(1965).
(409) Anon., *Mfg. Chemist Aerosol News*, **36** (9), 65(1965).
(410) Goldberg, A. H., Cibaldi, M., and Kanig, J. L., *J. Pharm. Sci.*, **54**, 1145(1965).
(411) Desai, S. J., Simonelli, A. P., and Higuchi, W. I., *ibid.*, **54**, 1459(1965).
(412) Johnson, R. H., *ibid.*, **54**, 327(1965).
(413) Jopling, D. W., *J. Polymer Sci.*, **3A**, 513(1965).
(414) Mason, P., *Kolloid-Z.*, **202**, 139(1965).
(415) Zografi, G., and Auslander, D. E., *J. Pharm. Sci.*, **54**, 1313(1965).
(416) Fridrickhsberg, D. A., and Pavlova, L. V., *Kolloidn. Zh.*, **27** (1), 113(1965).
(417) Morgan, B. B., *Nature*, **205**, 36(1965).
(418) Johnson, J. R., Christian, S. D., and Affsprung, H. E., *J. Chem. Soc.*, **1965**, 1.
(419) Higuchi, T., *et al.*, *J. Pharm. Sci.*, **54**, 1273(1965).
(420) Notari, R. E., and Sokoloski, T. D., *ibid.*, **54**, 1500 (1965).
(421) Higuchi, T., Uno, H., and Shimada, I., *ibid.*, **54**, 302 (1965).
(422) Hofman, J. E., Schriesheim, A., and Nickols, R. E., *Tetrahedron Letters*, **1965**, 1745.
(423) Bellomonte, G., and Cingolani, E., *Farmaco (Pavia), Ed. Sci.*, **19**, 1066(1964); through *Chem. Abstr.*, **62**, 6345(1965).
(424) Soliman, S. A., *Dissertation Abstr.*, **25**, 7213(1965).
(425) Russell, G. A., and Bemis, A. G., *Chem. Ind. (London)*, **1965**, 1262.
(426) Wurster, D. E., and Taylor, P. W., *J. Pharm. Sci.*, **54**, 169(1965).
(427) Goldberg, A. H., *et al.*, *ibid.*, **54**, 1722(1965).
(428) McClintock, W. J., *et al.*, *ibid.*, **54**, 1782(1965).
(429) Wood, J. H., Syarto, J. E., and Letterman, H., *ibid.*, **54**, 1068(1965).
(430) Taylor, P. W., Jr., *Dissertation Abstr.*, **25**, 5875 (1965).
(431) Higuchi, W. I., Mir, N. A., and Desai, S. J., *J. Pharm. Sci.*, **54**, 1405(1965).
(432) Kuroda, K., *Yakuzaigaku*, **24** (3), 227(1964); through *Chem. Abstr.*, **62**, 12985(1965).
(433) Wurster, D. E., and Kildsig, D. A., *J. Pharm. Sci.*, **54**, 1491(1965).
(434) Goyan, J. E., *ibid.*, **54**, 645(1965).
(435) Higuchi, W. I., *et al.*, *ibid.*, **54**, 8(1965).
(436) Edmundson, I. C., and Lees, K. A., *J. Pharm. Pharmacol.*, **17**, 193(1965).
(437) Hamlin, W. E., Northam, J. I., and Wagner, J. G., *J. Pharm. Sci.*, **54**, 1651(1965).
(438) Sekiguchi, K., and Ito, K., *Chem. Pharm. Bull. (Tokyo)*, **13**, 405(1965).
(439) Higuchi, W. I., and Saad, H. Y., *J. Pharm. Sci.*, **64**, 74(1965).
(440) Saad, H. Y., and Higuchi, W. I., *ibid.*, **54**, 1303 (1965).
(441) Goodman, R. C., and Petrucci, R. H., *J. Chem. Educ.*, **42**, 104(1965).
(442) Sorby, D. L., Liu, G., and Horowitz, K. N., *J. Pharm. Sci.*, **54**, 1811(1965).
(443) Paruta, A. N., Sciarrone, B. J., and Lordi, N. G., *ibid.*, **54**, 1325(1965).
(444) Paruta, A. N., and Irani, S. A., *ibid.*, **54**, 1334 (1965).
(445) Petri, I., *Monatsber. Deut. Akad. Wiss. Berlin*, **7** (3), 201(1965); through *Chem. Abstr.*, **63**, 14641(1965).
(446) Sedam, R. L., Gennaro, A. R., and Osol, A., *J. Pharm. Sci.*, **54**, 215(1965).
(447) Saad, H. Y., and Higuchi, W. I., *ibid.*, **54**, 1205 (1965).
(448) Botre, C., Brufani, M., and Riccieri, F. M., *ibid.*, **54**, 919(1965).
(449) Shinoda, K., and Hildebrande, J. H., *J. Phys. Chem.*, **69**, 605(1965).
(450) Nakatani, H., *Yakuzaigaku*, **24** (3), 223(1964); through *Chem. Abstr.*, **62**, 12985(1965).
(451) Merrill, E. J., *J. Pharm. Sci.*, **54**, 1670(1965).
(452) Gan, K. H., *Pharm. Weekblad*, **100** (8), 263(1965); through *Chem. Abstr.*, **63**, 11261(1965).
(453) Paruta, A. N., Sciarrone, B. J., and Lordi, N. G., *J. Pharm. Sci.*, **54**, 838(1965).
(454) Artem'ev, A. I., *Aptechn. Delo*, **14** (4), 13(1965); through *Chem. Abstr.*, **63**, 16137(1965).
(455) Dantzler, E. M., Holler, F. C., and Smith, P. T., *Soap Chem. Specialties*, **41** (1), 125(1965).
(456) Swarbrick, J., *J. Pharm. Sci.*, **54**, 1229(1965).
(457) Arambulo, A. S., *Dissertation Abstr.*, **25**, 5574 (1965).
(458) Conine, J. W., *J. Pharm. Sci.*, **54**, 1580(1965).
(459) Rhodes, C. T., and Donbrow, M., *ibid.*, **54**, 1069 (1965).
(460) *Ibid.*, **54**, 1130(1965).
(461) Altwein, D. M., Delgado, J. N., and Cosgrove, F. P., *ibid.*, **54**, 603(1965).
(462) Bjaastad, S. G., Hall, N. A., and Thakkar, A. L., *ibid.*, **54**, 1529(1965).
(463) Bjaastad, S. G., and Brown, K. F., *Australasian J. Pharm.*, **45**, S116(1964); through *Chem. Abstr.*, **62**, 8945 (1965).
(464) Bellafiore, I. J., *J. Am. Pharm. Assoc.*, **NS5**, 557 (1965).
(465) Khawam, M. N., Tawashi, R., and Czetsch-Lindenwald, H. v., *Sci. Pharm.*, **33** (2), 90(1965); through *Chem. Abstr.*, **63**, 12977(1965).
(466) Khawam, M. N., Tawashi, R., and Czetsch-Lindenwald, H. v., *Sci. Pharm.*, **32**, 271(1964); through *Chem. Abstr.*, **62**, 8945(1965).
(467) Lata, G. F., and Dac, Le K., *Arch. Biochem. Biophys.*, **109**, 434(1965).
(468) Katayama, A., *et al.*, *Kolloid-Z.*, **202**, 157(1965).
(469) Trandafilov, T., Mihailova, D., and Mincov, E., *Farmacia*, **12**, 257(1964); through *Chem. Abstr.*, **62**, 1520 (1965).
(470) Lee, W. K., *Yakhak Hoeji*, **7** (1), 13(1963); through *Chem. Abstr.*, **62**, 10297(1965).
(471) Nyberg, M. H. T., and Cefola M., *Arch. Biochem. Biophys.*, **111**, 321(1965).
(472) Colburn, R. W., and Maas, J. W., *Nature*, **208**, 37 (1965).
(473) Benet, L. Z., and Goyan, J. E., *J. Pharm. Sci.*, **54**, 983(1965).
(474) Bolton, S., *ibid.*, **54**, 373(1965).
(475) *Ibid.*, **54**, 583(1965).
(476) Jameson, R. F., and Neillie, W. F. S., *J. Chem. Soc.*, **1965**, 2391.
(477) Kaplan, M. A., Lannon, J. H., and Buckwalter, F. H., *J. Pharm. Sci.*, **54**, 163(1965).
(478) Ricketts, C. R., *et al.*, *Nature*, **208**, 237(1965).
(479) Goebert, H., *Z. Ges. Inn. Med. Ihre Grenzgebiete*, **20** (2), 250(1965); through *Chem. Abstr.*, **63**, 18855(1965).
(480) Von Ruiz-Torres, A., and Meinig, K.-H., *Arzneimittel-Forsch.*, **15**, 443(1965).
(481) Chen, P. S., Jr., and Lane, K., *Arch. Biochem. Biophys.*, **112**, 70(1965).
(482) Brunkhorst, W. K., and Hess, E. L., *ibid.*, **111**, 54 (1965).
(483) Stafford, W. L., *Salicylates, Intern. Symp., London*, **1962**, 74; through *Chem. Abstr.*, **62**, 4478(1965).
(484) Gadzala, A. E., *Dissertation Abstr.*, **25**, 6549(1965).
(485) Kapadia, A. J., *ibid.*, **26**, 1087(1965).
(486) Breuninger, W. B., and Goettsch, R. W., *J. Pharm. Sci.*, **54**, 1487(1965).
(487) Platt, D., and Rawlings, N. C., *Arch. Biochem. Biophys.*, **109**, 20(1965).
(488) Blaug, S. M., and Rick, A. G., *J. Pharm. Sci.*, **54**, 30(1965).
(489) Goudah, M. W., and Guth, E. P., *ibid.*, **54**, 298 (1965).
(490) Patel, N. K., and Foss, N. E., *ibid.*, **54**, 1495(1965).
(491) Storz, G. V., DeKay, H. G., and Banker, G. S., *ibid.*, **54**, 92(1965).
(492) Ansel, H. C., *ibid.*, **54**, 1159(1965).
(493) Aliev, A. M., and Gasanov, A. S., *Dokl. Akad. Nauk. Azerb. SSR*, **20** (8), 79(1964); through *Chem. Abstr.*, **62**, 5142(1965).
(494) Pauli, W. A., and Lach, J. L., *J. Pharm. Sci.*, **54**, 1745(1965).
(495) Chae, D. K., *Yakhak Hoeji*, **7** (1), 1(1963); through *Chem. Abstr.*, **62**, 9645(1965).
(496) Fleischman, D. E., *Dissertation Abstr.*, **25**, 6194 (1965).
(497) Meier, J., and Higuchi, T., *J. Pharm. Sci.*, **54**, 1183(1965).
(498) Sawardeker, J. S., *Dissertation Abstr.*, **25**, 5224 (1965).
(499) Teller, D. N., *ibid.*, **25**, 5542(1965).
(500) Roze, U., *ibid.*, **26**, 1927(1965).
(501) Wadke, D. A., and Guttman, D. E., *J. Pharm. Sci.*, **54**, 1293(1965).
(502) Blei, I., *Arch. Biochem. Biophys.*, **109**, 321(1963).
(503) Rao, V. S. R., and Foster, J. F., *J. Phys. Chem.*, **69**, 656(1965).
(504) Knox, W. J., Jr., and Wright, J. F., *J. Colloid Sci.*, **20**, 177(1965).
(505) Strickland, W. A., Jr., and Robertson, L., *J. Pharm. Sci.*, **54**, 452(1965).
(506) Bakore, V. G. V., and Mathur, M. A., *Naturwissenschaften*, **52**, 159(1965).
(507) Rodgers, D. H., *J. Pharm. Sci.*, **54**, 459(1965).
(508) Prakash, V. S., Ichhaporia, F. M., and Pandey, J. D., *Naturwissenschaften*, **52**, 11(1965).
(509) Gray, V. R., *Chem. Ind. (London)*, **1965**, 969.
(510) Hidy, G. M., *J. Colloid Sci.*, **20**, 123(1965).
(511) Sennett, P., and Oliver, J. P., *Ind. Eng. Chem.*, **57** (8), 32(1965); through *Chem. Abstr.*, **63**, 7677(1965).
(512) Watanabe, A., *Funtai Oyobi Funmatsuyakin*, **11** (2), 73(1964); through *Chem. Abstr.*, **63**, 14099(1965).
(513) Higuchi, W. I., Rhee, T. O., and Flanagan, D. R., *J. Pharm. Sci.*, **54**, 510(1965).
(514) Hidy, G. M., and Lilly, D. K., *J. Colloid Sci.*, **20**, 867(1965).
(515) Makino, R. C., and Rogers, E., *Arch. Biochem. Biophys.*, **109**, 499(1965).
(516) Rigole, W., and Van der Wee, P., *J. Colloid Sci.*, **20**, 115(1965).
(517) Nakagaki, M., and Kawamura, S., *Yakugaku Zasshi*, **85**, 894(1965).

(518) Elworthy, P. H., and MacFarlane, C. B., *J. Pharm. Pharmacol.*, **17**, 65(1965).
(519) *Ibid.*, **17**, 129(1965).
(520) Rozhdestvenskii, D. A., and Pugacheva, L. A., *Maslozhir. Prom.*, 31 (6), 17(1965); through *Chem. Abstr.*, **63**, 7212(1965).
(521) Weiner, N. D., and Zografi, G., *J. Pharm. Sci.*, **54**, 436(1965).
(522) Becher, P., *J. Colloid Sci.*, **20**, 728(1965).
(523) Mysels, E. K., and Mysels, K. J., *ibid.*, **20**, 315 (1965).
(524) Phares, R. E., Jr., *J. Pharm. Sci.*, **54**, 408(1965).
(525) Zwierzykowski, W., *Chem. Stosowana, Ser. A*, **9** (1), 91(1965); through *Chem. Abstr.*, **63**, 17179(1965).
(526) Suwalska, W., and Kujkowa, E., *Prace Inst. Wiokiennictwa, Ser. B*, **1965** (1), 3; through *Chem. Abstr.*, **63**, 6346(1965).
(527) Goette, E., *Fette, Seifen, Anstrichmittel*, **66** (7), 502 (1964); through *Chem. Abstr.*, **62**, 735(1965).
(528) Elworthy, P. H., and Florence, A. T., *Kolloid-Z.*, **204**, 105(1965).
(529) Graham, J., *Rev. Pure Appl. Chem.*, **14** (3), 31 (1964); through *Chem. Abstr.*, **62**, 3438(1965).
(530) Fripiat, J. J., *et al., J. Phys. Chem.*, **69**, 2185(1965).
(531) du Basty, W., Jacquin, C., and Simandoux, P., *Bull. Groupe Franc. Argiles*, **14** (9), 105(1964); through *Chem. Abstr.*, **62**, 2274(1965).
(532) Mocik, S., *Chem. Zvesti*, **18** (10), 777(1964); through *Chem. Abstr.*, **62**, 54(1965).
(533) Oleinik, M. I., and Yurchakevich, Ya. M., *Tr. Ukr. Nauchn.-Issled. Geol.-Razved. Inst.*, **1963** (7), 136(1963); through *Chem. Abstr.*, **62**, 5926(1965).
(534) Packham, R. F., *J. Colloid Sci.*, **20**, 81(1965).
(535) Ovcharenko, F. D., and Tarasevich, Yu. I., *Ukr. Khim. Zh.*, **30** (10), 1039(1964); through *Chem. Abstr.*, **62**, 4651(1965).
(536) Prilipko, L. T., and Kurilenko, O. D., *ibid.*, **31**, 376(1965); through *Chem. Abstr.*, **63**, 3654(1965).
(537) Edwards, D. G., Posner, A. M., and Quirk, J. P., *Nature*, **206**, 168(1965).
(538) Popova, Ya. G., Usheva, V., and Tenov, R., *Nauchni Tr., Nauchnoizsled. Inst. Konserona Prom., Plovdiv*, **2**, 79(1964); through *Chem. Abstr.*, **63**, 2853(1965).
(539) Nose, K., Suzuki, T., and Fukunaga, K., *Nippon Dojo-Hiryogaku Zasshi*, **35** (2), 57(1964); through *Chem. Abstr.*, **62**, 53(1965).
(540) Zapior, B., and Wozniakiewicz, M., *Zeszyty Nauk. Uniw. Jagiel., Prace Chem.*, **8**, 41(1963); through *Chem. Abstr.*, **62**, 5923(1965).
(541) Hockey, J. A., *Chem. Ind. (London)*, **1965**, 57.
(542) Waksmundski, A., Wawrzynowicz, T., and Wolski, T., *Ann. Univ. Mariae Curie-Sklodowska, Lublin Polonia Sect. AA*, **17**, 27(1962); through *Chem. Abstr.*, **62**, 5148(1965).
(543) Krotikov, V. A., Kharitonov, N. P., and Nilova, G. P., *Izv. Akad. Nauk SSSR, Ser. Khim.*, **1964** (9), 1689; through *Chem. Abstr.*, **62**, 54(1965).
(544) Rohdewald, P., *Kongr. Pharm. Wiss., Votr. Originalmitt, 23, Muenster (Westfalen), Ger.*, **1963**, 687; through *Chem. Abstr.*, **62**, 5928(1965).
(545) Blaug, S. M., and Gross, M. R., *J. Pharm. Sci.*, **54**, 289(1965).
(546) Levin, J., Fredrick, E. H., and Lobotsky, J., *J. Clin. Endocrinol. Metab.*, **25**, 1519(1965).
(547) Saski, W., and Shah, S. G., *J. Pharm. Sci.*, **54**, 71 (1965).
(548) Samsonov, G. V., *et al., Kolloidn. Zh.*, **27** (1), 101 (1965).
(549) Mitsui, T., *Am. Perfumer Cosmet.*, **80** (8), 23(1965).
(550) Nemoto, Y., *et al., Yukagaku*, **14** (5), 247(1965); through *Chem. Abstr.*, **63**, 18486(1965).
(551) Tawashi, R., and Lindenwald, H. V. C., *Am. Perfumer Cosmet.*, **80** (9), 31(1965).
(552) Morris, R. M., and Morris, A., *Chem. Ind. (London)*, **1965**, 1902.
(553) Stauffer, C. E., *J. Phys. Chem.*, **69**, 1933(1965).
(554) Racz, I., and Orban, E., *J. Colloid Sci.*, **20**, 99 (1965).
(555) Jannke, P. J., and Friedenberg, R., *J. Chem. Educ.*, **42**, 157(1965).
(556) Nikolics, K., Bidlo, G., and Nikolics, K., *Acta Pharm. Hung.*, **35** (4), 152(1965); through *Chem. Abstr.*, **63**, 17804(1965).
(557) Brown, G. M., and Levy, H. A., *Science*, **147**, 1038 (1965).
(558) Shefter, E., and Wolf, W., *J. Pharm. Sci.*, **54**, 104 (1965).
(559) Majumdar, A. J., and Roy, R., *J. Phys. Chem.*, **69**, 1684(1965).
(560) Austin, K. W. B., Marshall, A. C., and Smith, H., *Nature*, **208**, 999(1965).
(561) Allen, D. J., Milosovich, G., and Mattocks, A. M., *J. Pharm. Sci.*, **54**, 383(1965).
(562) Meleshko, L. O., *Mekhanizm i Kinetika Kristallizatsii, Nauchn. Sov. Akad. Nauk. Belorussk. SSR po Fiz. Tverd. Tela*, **1964**, 113; through *Chem. Abstr.*, **62**, 15991 (1965).
(563) Cross, M. M., *J. Colloid Sci.*, **20**, 417(1965).
(564) Hoffmann, W., *Rheol. Acta*, **3** (3), 172(1964); through *Chem. Abstr.*, **62**, 7153(1965).
(565) Bianchi, U., Patrone, E., and Babini, M., *J. Polymer Sci.*, **3B**, 609(1965).
(566) Frisman, E. V., Shchagina, L. V., and Vorob'ev, V. I., *Kolloidn. Zh.*, **27** (1), 130(1965).
(567) Hiller, K. H., *Rheol. Acta*, **3** (3), 132(1964); through *Chem. Abstr.*, **62**, 7152(1965).
(568) Greenberg, S. A., Jarnutowski, R., and Chang, T. N., *J. Colloid Sci.*, **20**, 20(1965).
(569) Schulge, H. J., *Bergakademie*, **17** (4), 226(1965); through *Chem. Abstr.*, **63**, 7679(1965).
(570) Singhal, J. P., and Malik, W. V., *Rheol. Acta*, 3 (3), 127(1964); through *Chem. Abstr.*, **62**, 7153(1965).
(571) Komskaya, M. S., *Dokl. Akad. Nauk SSSR*, **162**, 1112(1965); through *Chem. Abstr.*, **63**, 6349(1965).
(572) Storz, G. K., DeKay, H. G., and Banker, G. S., *J. Pharm. Sci.*, **54**, 85(1965).
(573) Haas, H. C., and Eloranta, P. J., *J. Polymer Sci.*, **3A**, 411(1965).
(574) Hermans, J., Jr., *ibid.*, **3A**,, 1859(1965).
(575) Charm, S. E., and McComis, W., *Food Technol.*, **19** (6), 58(1965).
(576) Carlson, W. A., and Ziegenfuss, E. M., *ibid.*, **19** (6), 64(1965).
(577) Smith, H. L., and Goyan, J. E., *J. Pharm. Sci.*, **54**, 545(1965).
(578) Nixon, J. R., and Chawla, B. P. S., *J. Pharm. Pharmacol.*, **17**, 558(1965).
(579) Bujake, J. E., Jr., *J. Pharm. Sci.*, **54**, 1599(1965).
(580) Dintenfass, L., *Proc. Intern. Congr. Rheol., 4th, 1963*, Pt. 3, 621; through *Chem. Abstr.*, **63**, 14079(1965).
(581) Higuchi, W. I., and Stehle, R. G., *J. Pharm. Sci.*, **54**, 265(1965).
(582) Matsumoto, S., *Bull. Chem. Soc. (Japan)*, **38**, 553 (1965); through *Chem. Abstr.*, **63**, 3648(1965).
(583) Horsch, W., *Pharmazie*, **20**, 265(1965).
(584) Wachelko, T., *Przeglad Odlewnictwa*, **14** (7), 199 (1964); through *Chem. Abstr.*, **62**, 53(1965).
(585) Rodrigues, L. D., and Barrosa, M. T., *Rev. Port. Farm.*, **14**, 425(1964); through *Chem. Abstr.*, **62**, 11625(1965).
(586) Tung, L. H., *J. Polymer Sci.*, **3A**, 1045(1965).
(587) Robertson, R. E., *J. Phys. Chem.*, **69**, 1575(1965).
(588) Bruck, S. D., *J. Chem. Educ.*, **42**, 18(1965).
(589) Kawai, T., *Kolloid-Z.*, **201**, 15(1965).
(590) Price, C. C., *J. Chem. Educ.*, **42**, 13(1965).
(591) Cooper, P., *W. African Pharmacist*, **6** (1), 2, 24 (1964); through *Chem. Abstr.*, **62**, 12987(1965).
(592) Dmitryenko, L. V., and Hale, D. K., *J. Chem. Soc.*, **1965**, 5570.
(593) Freeman, D. H., Patel, V. C., and Smith, M. E., *J. Polymer Sci.*, **3A**, 2893(1965).
(594) Lappas, L. C., and McKeehan, W., *J. Pharm. Sci.*, **54**, 176(1965).
(595) Lenkevich, M. N., and Yakovlev, A. A., *Nachr. Ophthalmol.* (USSR), **75** (5), 81(1962); through *Chem. Abstr.*, **63**, 16137(1965).
(596) Grosz, I., and Nagy, G. T., *Gyogyszeresset*, **9**, 342 (1965); through *Chem. Abstr.*, **63**, 16126(1965).
(597) Tachihana, T., and Nakamura, A., *Kolloid-Z.*, **203**, 130(1965).
(598) Fernandez, J. M. T., *Medicamenta Madrid*, **29** (15), 260(1963); through *Chem. Abstr.*, **63**, 16127(1965).
(599) Kiviman, G. Ya., and Rudzit, E. A., *Antibiotiki*, **10** (4), 369(1965); through *Chem. Abstr.*, **62**, 1678(1965).
(600) Muggleton, P. W., O'Callaghan, C. H., and Stevens, W. K., *Brit. Med. J.*, **2**, 1234(1964); through *Chem. Abstr.*, **62**, 6994(1965).
(601) Umezawa, H., *et al., J. Antibiotics (Tokyo)*, **18**, 101 (1965).
(602) Arai, T., *et al., ibid.*, **18**, 63(1965).
(603) Shtol'ts, M. G., Shtamm, L. K., and Bednyagina, N. P., *Med. Prom. SSSR*, **19** (2), 35(1965); through *Chem. Abstr.*, **62**, 11635(1965).
(604) Soong, P.-N., Au, A. A., and Hsu, J.-S., *Hua Hsueh*, **3**, 127(1964); through *Chem. Abstr.*, **62**, 11626(1965).
(605) Yamamoto, H., *et al., Agr. Biol. Chem. (Tokyo)*, **29**, 360(1965); through *Chem. Abstr.*, **63**, 1653(1965).
(606) Whaley, H. A., *et al., Antimicrobial Agents Chemotherapy*, **1964**, 83; through *Chem. Abstr.*, **63**, 4093(1965).
(607) Godtfredsen, W. O., and Vangedal, S., *Acta Chem. Scand.*, **19**, 1088(1965); through *Chem. Abstr.*, **63**, 12970 (1965).
(608) Furész, S., Arioli, V., and Scotti, R., *Arzneimittel-Forsch.*, **15**, 802(1965).
(609) Klein, J., *et al., Am. J. Med. Sci.*, **248** (6), 640 (1964); through *Chem. Abstr.*, **62**, 5782(1965).
(610) Garrett, E. R., and Miller, G. H., *J. Pharm. Sci.*, **54**, 427(1965).
(611) Anon., *Federal Register*, **29**, 16911(1964); through *Chem. Abstr.*, **62**, 3883(1965).
(612) Severinets, L. Ya., *Materialy 2 oi* [*Vtoroi*] *Konf. Molodykh Uchenykh Leningr. Inst. Antibiotikov, Leningrad, Sb*, **1964**, 80; through *Chem. Abstr.*, **63**, 6785(1965).
(613) Klein, J. O., Eickhoff, T. C., and Finland, M., *Am. J. Med. Sci.*, **248**, 528(1964); through *Chem. Abstr.*, **62**, 4475 (1965).
(614) Sarsunova, M., *Cesk. Farm.*, **13** (9), 470(1964); through *Chem. Abstr.*, **62**, 2665(1965).
(615) Kjensi, O., *Svensk Farm. Tidskr.*, **68**, 899(1964); through *Chem. Abstr.*, **62**, 8933(1965).
(616) Bigeleisen, J., *Science*, **147**, 463(1965).
(617) Vukcevic-Kovacevic, V., *Farm. Glasnik*, **21**, 273 (1964); through *Chem. Abstr.*, **63**, 9742(1965).
(618) Mikheev, N. B., Abdaullah, E., and El Garhy, M., *Kernenergie*, **7** (9), 664(1964); through *Chem. Abstr.*, **62**, 5147(1965).
(619) Quazi, A. H., *Naturwissenschaften*, **52**, 490(1965).
(620) Evans, H. D., and Mubarak, M. A., *Intern. J. Appl. Radiation Isotopes*, **16**, 387(1965).

(621) Stillstrom, J., *ibid.*, **16**, 357(1965).
(622) Mann, D. E., Jr., *J. Pharm. Sci.*, **54**, 499(1965).
(623) Valette, G., *Harokach Haivri*, **10**, 161(1964); through *Chem. Abstr.*, **63**, 2847(1965).
(624) Vogt, W., *Arch. Exptl. Pathol. Pharmakol.*, **250** (2), 210(1965); through *Chem. Abstr.*, **62**, 12973(1965).
(625) Lakshminarayanaiah, N., *Chem. Rev.*, **65**, 491 (1965).
(626) Doluisio, J. T., and Swintosky, J. V., *Am. J. Pharm.*, **137**, 144(1965).
(627) *Ibid.*, **137**, 175(1965).
(628) Smith, H. J., and Williams, H., *J. Pharm. Pharmacol.*, **17**, 601(1965).
(629) Papalexiov, Ph., *Schweiz. Apotheker Ztg.*, **102**, 775, 822(1964); through *Chem. Abstr.*, **62**, 6339(1965).
(630) Doluisio, J. T., and Swintosky, J. V., *J. Pharm. Sci.*, **54**, 1594(1965).
(631) Vaidhyanathan, V. S., Perkins, W. H., and Towbin, E. J., *J. Theoret. Biol.*, **7** (2), 339(1964); through *Chem. Abstr.*, **62**, 3445(1965).
(632) Ariens, E. J., *Med. Arhiv Sarajevo*, **18** (4), 21(1964); through *Chem. Abstr.*, **62**, 15242(1965).
(633) Schnaare, R. S., and Martin, A. N., *J. Pharm. Sci.*, **54**, 1707(1965).
(634) Burmeister, W., *Science*, **148**, 1336(1965).
(635) Milne, M. D., *Proc. Roy. Soc. Med.*, **57** (9), 809 (1964); through *Chem. Abstr.*, **62**, 5753(1965).
(636) Wagner, J. G., *et al.*, *Nature*, **207**, 1301(1965).
(637) Levy, G., and Nelson, E., *J. Pharm. Sci.*, **54**, 812 (1965).
(638) Duchene-Marullaz, P., and Vacher, J., *Compt. Rend. Soc. Biol.*, **158**, 1008(1964); through *Chem. Abstr.*, **62**, 4488(1965).
(639) Schmank, H. W., Holbert, J. M., and Beekman, S. M., *J. Pharm. Sci.*, **54**, 1285(1965).
(640) Nakagaki, M., *Yakuzaigaku*, **24** (4), 278(1964); through *Chem. Abstr.*, **63**, 3477(1965).
(641) Gressel, Y., *Dissertation Abstr.*, **26**, 2262(1965).
(642) Lewis, C., Stern, K. F., and Grady, J. E., *Antimicrobial Agents Chemotherapy*, **1964** (Oct.), 13; through *Chem. Abstr.*, **63**, 3495(1965).
(643) Poole, J. W., Zeigler, L. A., and Dugan, M. A., *J. Pharm. Sci.*, **54**, 651(1965).
(644) Remmers, E. G., *et al.*, *ibid.*, **54**, 49(1965).
(645) Dare, J. G., *Australasian J. Pharm.*, **45**, S58(1964); through *Chem. Abstr.*, **62**, 8944(1965).
(646) Ivanov, N. M., *Antibiotiki*, **8** (10), 943(1963); through *Chem. Abstr.*, **62**, 981(1965).
(647) Higuchi, K., *Intern. Congr. Chemotherapy, Proc., 3rd, Stuttgart*, **1963** (1), 732; through *Chem. Abstr.*, **63** 18912(1965).
(648) Anghileri, L. J., *Intern. J. Appl. Radiation Isotopes*, **16**, 623(1965).
(649) Fincher, J. H., *Dissertation Abstr.*, **25**, 4661(1965).
(650) Katz, M., and Shaikh, Z. I., *J. Pharm. Sci.*, **54**, 591(1965).
(651) Marcus, A. D., *et al.*, *ibid.*, **54**, 495(1965).
(652) Von Gladtke, E., and Schmalz, G., *Arzneimittel-Forsch.*, **15**, 927(1965).
(653) Kjellman, H., *Farm. Revy*, **64**, 85(1965); through *Chem. Abstr.*, **62**, 15989(1965).
(654) Benthe, H. F., and Chenpanich, K., *Arch. Exptl. Pathol. Pharmakol.*, **250** (2), 233(1965); through *Chem. Abstr.*, **63**, 1097(1965).
(655) Wurster, D. E., *Am. Perfumer Cosmet.*, **80** (1), 21 (1965).
(656) Morrison, A. B., and Campbell, J. A., *J. Pharm. Sci.*, **54**, 1(1965).
(657) Levy, G., *Harokeach Haivri*, **10**, 182(1964); through *Chem. Abstr.*, **63**, 8889(1965).
(658) Levy, G., *Arch. Intern. Pharmacodyn.*, **152** (1–2), 59(1964); through *Chem. Abstr.*, **62**, 13708(1965).
(659) Calesnick, B., Katchen, B., and Black, J., *J. Pharm. Sci.*, **54**, 1277(1965).
(660) Saski, W., and Shah, S. C., *ibid.*, **54**, 277(1965).
(661) Yamada, H., and Yamamoto, R., *Chem. Pharm. Bull. (Tokyo)*, **13**, 1279(1965).
(662) Sorby, D. L., *J. Pharm Sci.*, **54**, 677(1965).
(663) Mellinger, T. J., Mellinger, E. M., and Smith, W. T., *Clin. Pharmacol. Therap.*, **6**, 486(1965).
(664) Von Dimmling, Th., and Wagner, W. H., *Arzneimittel-Forsch.*, **15**, 1288(1965).
(665) Moore, W. E., *et al.*, *J. Pharm. Sci.*, **54**, 36(1965).
(666) Von Hackenthal, E., *Arzneimittel-Forsch.*, **15**, 1075(1965).
(667) Wood, J. H., *J. Pharm. Sci.*, **54**, 1207(1965).
(668) McGinn, J. T., *Current Therap. Res.*, **7**, 110(1965).
(669) Levy, G., and Jusko, W. J., *J. Pharm. Sci.*, **54**, 219(1965).
(670) Holt, L. P. J., and Hawkins, C. F., *Brit. Med. J.*, **1**, 1354(1965); through *Chem. Abstr.*, **63**, 7539(1965).
(671) Lowenthal, W., and Borzelleca, J. F., *J. Pharm. Sci.*, **54**, 1790(1965).
(672) Swarbrick, J., and Farthing, C. P., *Experientia*, **19** (8), 407(1963); through *Chem. Abstr.*, **63**, 12149(1965).
(673) Von Diller, W., and Bunger, P., *Arzneimittel-Forsch.*, **15**, 1274(1965).
(674) Kakemi, K., Arita, T., and Muranishi, S., *Chem. Pharm. Bull. (Tokyo)*, **13**, 969(1965).
(675) *Ibid.*, **13**, 976(1965).
(676) Neuwald, F., and Kunze, F., *Arzneimittel-Forsch.*, **14** (10), 1162(1965); through *Chem. Abstr.*, **62**, 5148(1965).
(677) Daskel, L., and Raik, I., *Harokeach Haivri*, **10**, 178(1964); through *Chem. Abstr.*, **63**, 2857(1965).
(678) Vasil'ev, V. K., Lazareva, E. N., and Pochapinskii, V. I., *Antibiotiki*, **10**, 442(1965); through *Chem. Abstr.*, **63**, 4850(1965).
(679) Fredriksson, T., *Arzneimittel-Forsch.*, **15**, 1070 (1965).
(680) Takenouchi, K., *et al.*, *Bitamin*, **31**, 315(1965); through *Chem. Abstr.*, **63**, 2264(1965).
(681) Whitworth, C. W., and Becker, C. H., *J. Pharm. Sci.*, **54**, 569(1965).
(682) Dempski, R. E., DeMarco, J. D., and Marcus, A. D., *J. Invest. Dermatol.*, **44**, 361(1965).
(683) Konttinen, Y., *Ann. Med. Exptl. Biol. Fenniae Helsinki*, **43** (1), 43(1965); through *Chem. Abstr.*, **63**, 1095 (1965).
(684) Billups, N. F., and Sager, R. W., *Am. J. Pharm.*, **137**, 57(1965).
(685) Shell, J. W., *J. Pharm. Sci.*, **54**, 1392(1965).
(686) Homrowska, H., Myszkorowska, H., and Paszek, T., *Acta Polon. Pharm.*, **20** (2), 205(1963); through *Chem. Abstr.*, **62**, 3273(1965).
(687) Yousef, R. T., *Sci. Pharm.*, **33** (1), 1(1965); through *Chem. Abstr.*, **63**, 2857(1965).
(688) Gstirner, F., *Kongr. Pharm. Wiss., Vortr. Originalmitt., 23, Muenster Westfalen, Ger.*, **1963**, 533; through *Chem. Abstr.*, **62**, 6347(1965).
(689) Alyushin, M. T., *Aptechn. Delo*, **14** (2), 21(1965); through *Chem. Abstr.*, **63**, 4098(1965).
(690) Schulze, W., *Fette, Seifen, Anstrichmittel*, **66**, 531 (1964); through *Chem. Abstr.*, **62**, 2114(1965).
(691) Blaug, S. M., and Canada, A. T., Jr., *Am. J. Hosp. Pharm.*, **22**, 662(1965).
(692) Levy, G., and Matsuzawa, T., *J. Pharm. Sci.*, **54**, 1003(1965)
(693) Wolfson, B. B., and Banker, G. S., *ibid.*, **54**, 195 (1965).
(694) Israels, M. C. G., and Cook, T. A., *Lancet*, **1965**, 654.
(695) Gewant, W. C., and Lare, H. K., *Proc. Penn. Acad. Sci.*, **38** (2), 111(1965); through *Chem. Abstr.*, **63**, 17805 (1965).
(696) Horita, A., and Weber, L. J., *Life Sci.*, **3**, 1389 (1964); through *Chem. Abstr.*, **62**, 12348(1965).
(697) Levy, G., Leonards, J. R., and Procknal, J. A., *J. Pharm. Sci.*, **54**, 1719(1965).
(698) Randeri, K. J., *Dissertation Abstr.*, **25**, 7212(1965).
(699) Tikkanen, R., and Strandman, D., *Farm. Aikakauslehti*, **74** (2), 59(1965); through *Chem. Abstr.*, **62**, 11639 (1965).
(700) Leonards, J. R., and Levy, G., *J. Am. Med. Assoc.*, **193** (2), 99(1965); through *Chem. Abstr.*, **63**, 8938(1965).
(701) Clark, R. L., and Lasagna, L., *Clin. Pharmacol. Therap.*, **6**, 568(1965).
(702) Hollister, L. E., and Kanter, S. L., *ibid.*, **6**, 5(1965).
(703) Crosland-Taylor, P., *et al.*, *Current Therap. Res.*, **7**, 244(1965).
(704) Srivastava, L. K., and Maney, P. V., *Mfg. Chemist Aerosol News*, **36** (3), 55(1965).
(705) Silson, J. E., *Drug Cosmetic Ind.*, **96**, 632(1965).
(706) Frederik, W. S., and Cass, L. J., *J. New Drugs*, **5**, 138(1965).
(707) Khomyakov, K. P., *et al.*, *Vysokomolekul Soedin.*, **7**, 1035(1965); through *Chem. Abstr.*, **63**, 16134(1965).
(708) Levy, G., and Hollister, L. E., *J. Pharm. Sci.*, **54**, 1121(1965).
(709) Cass, L. J., and Frederik, W. S., *Current Therap. Res.*, **7**, 673(1965).
(710) *Ibid.*, **7**, 683(1965).
(711) Tomasini, L., and Sheikova, G., *Farmatsiya (Sofia)*, **14** (5), 31(1964); through *Chem. Abstr.*, **62**, 7593(1965).
(712) Gledhill, W. S., and Westwood, A. P., *Australasian J. Pharm.*, **45**, S12(1964); through *Chem. Abstr.*, **62**, 8946 (1965).
(713) Bliuder, S., *Current Therap. Res.*, **7**, 769(1965).
(714) Kaplan, L. L., *J. Pharm. Sci.*, **54**, 457(1965).
(715) Sjogren, J., and Ervik, M., *Acta Pharm. Suecica*, **1** (6), 219(1964); through *Chem. Abstr.*, **62**, 12985(1965).
(716) Noerby, P., *Dansk Tidsskr. Farm.*, **39** (5), 171 (1965); through *Chem. Abstr.*, **63**, 9753(1965).
(717) Adamczewski, B., and Lutomski, J., *Biul. Inst. Roslin Leczniczych*, **10** (4), 205(1965); through *Chem. Abstr.*, **63**, 11258(1965).
(718) Arita, T., *Kagaku No Ryoiki*, **19** (2), 123(1965); through *Chem. Abstr.*, **63**, 16960(1965).
(719) Brinkmann, R., and Schoenenberger, H., *Pharm. Ztg.*, **110** (2), 40(1965); through *Chem. Abstr.*, **62**, 15246 (1965).
(720) Hart, S. L., and Nissim, J. A., *Nature*, **208**, 145 (1965).
(721) Finholt, P., *Kongr. Pharm. Wiss., Vortr. Originalmitt., 23, Muensler Westfalen, Ger.*, **1963**, 145; through *Chem. Abstr.*, **62**, 8262(1965).
(722) Martin, B. K., *Nature*, **207**, 274(1965).
(723) Kakemi, K., Arita, T., and Muranishi, S., *Chem. Pharm. Bull. (Tokyo)*, **13**, 861(1965).
(724) Wurster, D. E., and Munies, R., *J. Pharm. Sci.*, **54**, 554(1965).
(725) Munies, R., and Wurster, D. E., *ibid.*, **54**, 1281 (1965).
(726) Okuda, K., and Sasayma, K., *Am. J. Physiol.*, **208**, 14(1965).
(727) Heinrich, H. C., and Gabbe, E. E., *Klin. Wochschr.*, **43** (4), 196(1965); through *Chem. Abstr.*, **62**, 16859(1965).
(728) Heinivaara, O., *et al.*, *Ann. Med. Interrae Fenniae*, **53** (3), 75(1964); through *Chem. Abstr.*, **62**, 16874(1965).

(729) Adams, J. F., Love, W. C., and Kennedy, E. H., *Scot. Med. J.*, **10** (1), 24(1965); through *Chem. Abstr.*, **63**, 1133(1965).
(730) Bianco, G., *et al.*, *Boll. Soc. Ital. Biol. Sper.*, **41** (1), 1(1965); through *Chem. Abstr.*, **62**, 13743(1965).
(731) Angelino, P. F., Vacca, G., and Ferro, G. F., *Minerva Med.*, **56** (6), 197(1965); through *Chem. Abstr.*, **62**, 16792(1965).
(732) Green, V. A., *J. Pharm. Sci.*, **54**, 314(1965).
(733) Kimura, S., *et al.*, *Shika Igaku*, **26** (3), 304(1963); through *Chem. Abstr.*, **62**, 987(1965).
(734) Beckett, A. H., and Rowland, M., *J. Pharm. Pharmacol.*, **17**, 628(1965).
(735) McColl, I., and Nissim, J. A., *Nature*, **207**, 949 (1965).
(736) Gibaldi, M., and Kanig, J. L., *J. Pharm. Sci.*, **54**, 599(1965).
(737) Bahal, S. M., *Dissertation Abstr.*, **26**, 1602(1965).
(738) Reed, D. J., *et al.*, *Am. J. Physiol.*, **209**, 757(1965).
(739) Mornex, R., *et al.*, *Compt. Rend. Soc. Biol.*, **157**, 823 (1963); through *Chem. Abstr.*, **63**, 15402(1965).
(740) Samperez, S., Jouan, P., and Duthil, J., *Therapie*, **20** (2), 453(1965); through *Chem. Abstr.*, **63**, 6182(1965).
(741) MacDonald, H., *et al.*, *Antimicrobial Agents Chemotherapy*, **1964** (Oct.), 173; through *Chem. Abstr.*, **63**, 3518(1965).
(742) Buclon, M., Favre, H., and Peres, G., *Compt. Rend. Soc., Biol.*, **158** (8–9), 1643(1964); through *Chem. Abstr.*, **62**, 13725(1965).
(743) Tidwell, H. C., Moore, W. T., and McPherson, J. C., *Proc. Soc. Exptl. Biol Med.*, **118** (4), 986(1965); through *Chem. Abstr.*, **63**, 1119(1965).
(744) Sanchez, F. S., *Arch. Inst. Farmacol. Exptl. Madrid*, **16** (2), 149(1964); through *Chem. Abstr.*, **63**, 12139(1965).
(745) Martin, B. K., *Nature*, **207**, 959(1965).
(746) Azhgikhin, T. S., and Sal'nikov, E. T., *Aptechn. Delo*, **14** (2), 17(1965); through *Chem. Abstr.*, **63**, 4098 (1965).
(747) Heuneberg, M., *Acta Polon. Pharm.*, **20**, 236(1963); through *Chem. Abstr.*, **62**, 2112(1965).
(748) Stelmach, H., Robinson, J. R., and Eriksen, S. P., *J. Pharm. Sci.*, **54**, 1453(1965).
(749) Wilbrandt, W., *Schweiz. Med. Wochschr.*, **94**, 737(1964); through *Chem. Abstr.*, **62**, 6339(1965).
(750) Forist, A. A., *J. Pharm. Sci.*, **54**, 927(1965).
(751) Nayak, K. P. Brochmann-Haussen, E., and Leong Way, E., *ibid.*, **54**, 191(1965).
(752) Hollister, L. E., and Levy, G., *Chemotherapia*, **9** (1), 20(1964); through *Chem. Abstr.*, **62**, 15249(1965).
(753) Hollister, L. E., and Levy, G., *J. Pharm. Sci.*, **54**, 1126(1965).
(754) Levy, G., *ibid.*, **54**, 959(1965).
(755) Bedford, C., Cummings, A. J., and Martin, B. K., *Brit. J. Pharmacol.*, **24** (2), 418(1965); through *Chem. Abstr.*, **63**, 1082(1965).
(756) Levy, G., and Miller, K. E., *J. Pharm. Sci.*, **54**, 1319(1965).
(757) Bruce, R. B., *et al.*, *J. Med. Chem.*, **8**, 157(1965).
(758) Nelson, E., *J. Pharm. Sci.*, **54**, 1075(1965).
(759) Levy, G., *Brit. J. Anaesthesia*, **36**, 694(1964); through *Chem. Abstr.*, **62**, 15249(1965).
(760) Kakemi, K., *Yakuzaigaku*, **24** (4), 263(1965); through *Chem. Abstr.*, **63**, 3477(1965).
(761) Matsuzawa, E., *Yakuzaigaku*, **24** (4), 273(1964); through *Chem. Abstr.*, **63**, 3477(1965).
(762) Schlagel, C. A., *J. Pharm. Sci.*, **54**, 335(1965).
(763) Hug, C. C., Jr., and Mellett, L. B., *J. Pharmacol. Exptl. Therap.*, **149**, 446(1965).
(764) Born, G. S., *et al.*, *J. Pharm. Sci.*, **54**, 1646(1965).
(765) Menachenoff, E., *Harokeach Haivri*, **10**, 189(1965); through *Chem. Abstr.*, **63**, 6180(1965).
(766) Prochazka, J., Havelka, J., and Hejzlar, M., *Casopis Lekaru Ceskych*, **103** (14), 378(1964); through *Chem. Abstr.*, **63**, 6180(1965).
(767) Lagert, I. K., *Materialy III-ei (Trel'ei) Nauchn. Sessii Leningr. Inst. Antibiotikov, Leningrad, Sb. 1963*, 50; through *Chem. Abstr.*, **62**, 985(1965).
(768) Fischer, L. J., and Riegelman, S., *J. Pharm. Sci.*, **54**, 1571(1965).
(769) Medina, A., *et al.*, *Antimicrobial Agents Chemotherapy*, **1963**, 189; through *Chem. Abstr.*, **62**, 6976(1965).
(770) Kinney, V. R., Tauxe, W. N., and Dearing, W. H., *J. Lab. Clin. Med.*, **66**, 187(1965).
(771) DeGrazia, J. A., *et al.*, *ibid.*, **66**, 822(1965).
(772) Goldberg, L., and Martin, L. E., *Life Sci.*, **3**, 1465 (1964); through *Chem. Abstr.*, **62**, 12325(1965).
(773) Bannerman, R. M., *J. Lab. Clin. Med.*, **65**, 944 (1965).
(774) Schedl, H. P., *J. Clin. Endocrinol. Metab.*, **25**, 1309 (1965).
(775) Cummings, A. J., *Salicylates, Intern. Symp., London*, **1962**, 28; through *Chem. Abstr.*, **62**, 4475(1965).
(776) Cotty, V., *et al.*, *J. Pharm. Sci.*, **54**, 868(1965).
(777) Conklin, J. D., Buzard, J. A., and Hoetis, J. P., *Arch. Intern. Pharmacodyn.*, **155** (1), 105(1965); through *Chem. Abstr.*, **63**, 12147(1965).
(778) Conklin, J. D., and Buzard, J. A., *J. Pharm. Sci.*, **54**, 1766(1965).
(779) Doyle, A. E., and Morley, A., *Brit. J. Pharmacol.*, **24** (3), 701(1965); through *Chem. Abstr.*, **63**, 6180(1965).
(780) Ferlemann, G., and Vogt, W., *Arch. Exptl. Pathol. Pharmakol.*, **250** (4), 479(1965); through *Chem. Abstr.*, **63**, 6178(1965).
(781) Gold, O., and Stormann, H., *Arzneimittel-Forsch.* **14**, 1108(1964); through *Chem. Abstr.*, **62**, 5752(1965).
(782) Peets, E. A., *et al.*, *Am. Rev. Respirat. Diseases*, **91** (1), 51(1965); through *Chem. Abstr.*, **63**, 1081(1965).
(783) Polyak, M. S., *Materialz 2-oi(Vtoroi) Konf. Molodykh Uchenykh Lenigr. Inst. Antibiotikov, Leningrad, Sb.*, **1964**, 66; through *Chem. Abstr.*, **63**, 6181(1965).
(784) Stripp, B., *Acta Pharmacol. Toxicol.*, **22** (4), 353 (1965); through *Chem. Abstr.*, **63**, 15383(1965).
(785) Gibaldi, M., *Dissertation Abstr.*, **26**, 1086(1965).
(786) Kakemi, K., *et al.*, *Chem. Pharm. Bull. (Tokyo)*, **13**, 551(1965).
(787) Tocco, D. J., *et al.*, *J. Pharmacol. Exptl Therap.*, **149**, 263(1965).
(788) Chew, W. H., Kaplan, K., and Weinstein, L., *Clin. Pharmacol. Therap.*, **6**, 307(1965).
(789) Kaplan, K., Chew, W. H., and Weinstein, L., *ibid.*, **6**, 316(1965).
(790) Amundson, M. E., Johnson, M. L., and Manthey, J. A., *J. Pharm. Sci.*, **54**, 684(1965).
(791) Minatoya, H., Lands, A. M., and Portmann, G. A., *ibid.*, **54**, 968(1965).
(792) Portmann, G. A., Minatoya, H., and Lands, A. M., *ibid.*, **54**, 973(1965).
(793) Bleidner, W. E., *et al.*, *J. Pharmacol. Exptl. Therap.*, **150**, 484(1965).
(794) Hoshi, A., and Kuretani, K., *Yakugaku Zasshi*, **85**, 905(1965).
(795) McChesney, E. W., and Banks, W. F., Jr., *Proc. Soc. Exptl. Biol. Med.*, **119**, 1027(1965).
(796) Proft, Von D., *Arzneimittel-Forsch.*, **15**, 214(1965).
(797) Nowacki, E., *Postepy Nauk Rolniczych*, **11** (4), 19 (1964); through *Chem. Abstr.*, **62**, 6339(1965).
(798) Akacic, B., and Kustrak, D., *Farm. Glasnik*, **21**, 99 (1965); through *Chem. Abstr.*, **63**, 9741(1965).
(799) Farkas, L., and Pallos, L., *Planta Med.*, **12**, 296 (1964); through *Chem. Abstr.*, **62**, 6337(1965).
(800) Hiller, K., *Pharm. Praxis, Beilage Pharmazie*, **1965** (6), 138.
(801) Pakrashi, S. C., and Bhattacharyya, J., *J. Sci. Ind. Res. (India)*, **24**, 293(1965); through *Chem. Abstr.*, **63**, 9741(1965).
(802) Schultz, O. E., *Planta Med.*, **12**, 371(1964); through *Chem. Abstr.*, **62**, 3883(1965).
(803) Carew, D. P., and Staba, E. J., *Lloydia*, **28**, 1(1965).
(804) Zaman, M. B., and Imam, S. M., *Proc. Pan Indian Ocean Sci., Congr., Sect. D*, **1960**, 387; through *Chem. Abstr.*, **62**, 14419(1965).
(805) Zatula, E. I., and Bugrim, N. A., *Med. Prom. SSSR*, **18** (12), 35(1964); through *Chem. Abstr.*, **62**, 8944(1965).
(806) Sciuchetti, L. A., and Born, A. E., *J. Pharm. Sci.*, **54**, 285(1965).
(807) Schenck, G., Froemming, K. H., and Kluge, H. J., *Pharm. Ztg. Ver. Apotheker-Ztg.*, **107**, 1777(1962); through *Chem. Abstr.*, **62**, 3889(1965).
(808) Lindemann, G., *Riechstoffe, Aromen, Koerperflegemittel*, **15**, 13(1965); through *Chem. Abstr.*, **62**, 14419(1965).
(809) Hofmann, A., *Planta Med.*, **12** (3), 341(1964); through *Chem. Abstr.*, **62**, 2665(1965).
(810) Pelt, J. M., *Bull. Soc. Pharm. Nancy*, **62**, 18(1964); through *Chem. Abstr.*, **62**, 1511(1965).
(811) Uphaus, R. A., *et al.*, *J. Pharm. Sci.*, **54**, 202(1965).
(812) Mooijman, J. G. J. M., *Dissertation Abstr.*, **25**, 4390 (1965).
(813) Döepke, V. W., *Naturwissenschaften*, **52**, 133(1965).
(814) Oudtshoorn, V., and Gerrtisma, K. W., *ibid.*, **52**, 35(1965).
(815) Sciuchetti, L. A., and Mingis, N. C., *Lloydia*, **28**, 230(1965).
(816) Householder, D. E., and Camp, B. J., *J. Pharm. Sci.*, **54**, 1676(1965).
(817) Bhattacharjee, S. S., and Timell, T. E., *Can. J. Chem.*, **43**, 758(1965).
(818) Hammer, R. H., and Cole, J. R., *J. Pharm. Sci.*, **54**, 235(1965).
(819) Lou, V., Koo, W.-Y., and Ramstad, E., *Lloydia*, **28**, 207(1965).
(820) Iwasa, J. and Naruto, S., *Yakugaku Zasshi*, **85**, 469(1965).
(821) Sakan, T., *et al.*, *Bull. Chem. Soc. (Japan)*, **37** (12), 1888(1964); through *Chem. Abstr.*, **62**, 7582(1965).
(822) Gakhniyan, R., Nikolova, M., and Drumev, D., *Izv. Inst. po Fiziol., Bulgar. Akad. Nauk.*, **5**, 307(1962); through *Chem. Abstr.*, **62**, 3885(1965).
(823) Dean, F. M., Mongkolsuk, S., and Podimuang, V., *J. Chem. Soc.*, **1965**, 828.
(824) Albright, J. D., Van Meter, J. C., and Goldman, L., *Lloydia*, **28**, 212(1965).
(825) Dasgupta, B., *J. Pharm. Sci.*, **54**, 481(1965).
(826) Bowden, K., and Drysdale, A. C., *Tetrahedron Letters*, **1965**, 727.
(827) Mueller, G. F. R., and Eugster, C. H., *Helv. Chim. Acta*, **48**, 910(1965); through *Chem. Abstr.* **63**, 6786(1965).
(828) Köhler, K.-H., *Naturwissenschaften*, **52**, 561(1965).
(829) Döpke, V. M., and Dalmer, H., *ibid.*, **52**, 60(1965).
(830) *Ibid.*, **52**, 61(1965).
(831) Kohlmuenzer, S., and Waclaw-Rozkrutowa, B., *Acta Polon. Pharm.*, **20** (4), 321(1963); through *Chem. Abstr.*, **62**, 399(1965).
(832) Brutko, L. I., and Utkin, L. M., *Med. Prom. SSSR*, **19** (1), 30(1965); through *Chem. Abstr.*, **62**, 11626(1965).
(833) Hata, K., *et al.*, *Yakugaku Zasshi*, **85**, 656(1965).
(834) Nitta, A., *ibid.*, **85**, 55(1965).

(835) *Ibid.*, **85**, 173(1965).
(836) Hata, K., and Kozawa, M., *Tetrahedron Letters*, **1965**, 4557.
(837) Boissier, J. R., *et al.*, *Lloydia*, **28**, 191(1965).
(838) Taylor-Smith, R. E., *Tetrahedron*, **21**, 3721(1965).
(839) Gerlach, H., Grundmann, W., and Giessner, R., *Pharmazie*, **20**, 450(1965).
(840) Weissmann, G., Bruns, K., and Grutzmacher, H. Fr., *Tetrahedron Letters*, **1965**, 4623.
(841) Foldeak, S., and Dombradi, G. A., *Acta Univ. Szeged., Acta Phys. Chem.*, **10**, 91(1964); through *Chem. Abstr.*, **62**, 6339(1965).
(842) Venkateswarlu, V., *Current Sci. (India)*, **34** (1), 16(1965); through *Chem. Abstr.*, **62**, 7581(1965).
(843) Hylin, J. W., and Watson, D. P., *Science*, **148**, 499 (1965).
(844) Murakami, T., *et al.*, *Yakugaku Zasshi*, **85**, 832 (1965).
(845) Sommer, L., Stenescu, M., and Geleceanu-Baltazar, G., *Izuch. i Ispol'z. Lekarstv. Rastit. Resursov SSSR Sb.*, **1964**, 72; through *Chem. Abstr.*, **63**, 1655(1965).
(846) Rybalko, K. S., *Khim. Prirodn. Soedin., Akad. Nauk Uz. SSR*, **1965** (2), 142; through *Chem. Abstr.*, **63**, 6786(1965).
(847) Radhakrishman, P. V., Rama Ras, A. V., and Venkataraman, K., *Tetrahedron Letters*, **1965**, 663.
(848) Gracza, L., *Planta Med.*, **12**, 440(1964); through *Chem. Abstr.*, **62**, 11626(1965).
(849) Punyarajun, S., *Dissertation Abstr.*, **26**, 1361(1965).
(850) Tomita, M., and Kozuka, M., *Yakugaku Zasshi*, **85**, 77(1965).
(851) Joule, J. A., *et al.*, *Tetrahedron*, **21**, 1717(1965).
(852) Gilbert, B., *et al.*, *ibid.*, **21**, 1141(1965).
(853) Ivanov, V., *et al.*, *Farmatsiya (Sofia)*, **15** (2), 99 (1965); through *Chem. Abstr.*, **63**, 11249(1965).
(854) Montes, A. L., *Anales Soc. Cienti. Arg.*, **176**, 71 (1963); through *Chem. Abstr.*, **62**, 8929(1965).
(855) Petcu, P., *Arch. Pharm.*, **298**, 73(1965).
(856) Santamaria, L., Martinez, M. L., and Asenjo, C. F., *J. Agr., Univ. Puerto Rico*, **49**, 259(1965); through *Chem. Abstr.*, **63**, 12971(1965).
(857) Schneider, W. P., Caron, E. L., and Hinman, J. W., *J. Org. Chem.*, **30**, 2856(1965).
(858) Worthen, L. R., Snell, W. H., and Dick, E. A., *Lloydia*, **28**, 44(1965).
(859) Karsten, V. U., *Naturwissenschaften*, **52**, 84(1965).
(860) Nakano, T., Terao, S., and Lee, K. H., *J. Pharm. Sci.*, **54**, 1201(1965).
(861) Döpke, V. W., and Müeller, B., *Naturwissenschaften*, **52**, 61(1965).
(862) Kupchan, S. M., and Abushanab, E., *J. Org. Chem.*, **30**, 3931(1965).
(863) Alves, A. C., *Anais Fac. Farm. Porto*, **24**, 65(1964); through *Chem. Abstr.*, **63**, 17797(1965).
(864) Maloney, E. M., *et al.*, *J. Pharm. Sci.*, **54**, 1166 (1965).
(865) Gröger, V. D., Stolle, K., and Falshaw, C. P., *Naturwissenschaften*, **52**, 132(1965).
(866) Moza, B. K., and Trojanek, J., *Chem. Ind. (London)*, **1965**, 1260.
(867) Richter, V. I., *et al.*, *Naturwissenschaften*, **52**, 305 (1965).
(868) Warnhoff, E. W., Pradhan, S. K., and Ma, J. C. N., *Can. J. Chem.*, **43**, 2594(1965).
(869) Adinarayan, D., and Seshadri, T. R., *Tetrahedron*, **21**, 3727(1965).
(870) Atkinson, R. E., and Curtis, R. F., *Tetrahedron Letters*, **1965**, 297.
(871) Lavenir, R., and Paris, R. R., *Ann. Pharm. Franc.*, **23**, 307(1965).
(872) Takeda, K., *et al.*, *Chem. Pharm. Bull. (Tokyo)*, **13**, 691(1965).
(873) Takemoto, T., Daigo, K., and Sai, T., *Yakugaku Zasshi*, **85**, 83(1965).
(874) Takemoto, T., and Sai, T., *ibid.*, **85**, 33(1965).
(875) Tsai, Y., Ting, C.-K., and Nieh, S.-L., *Yao Hsueh Hsueh Pao*, **11**, 801(1964); through *Chem. Abstr.*, **62**, 6337 (1965).
(876) Tsai, H.-Y., *et al.*, *ibid.*, **12** (1), 23(1965); through *Chem. Abstr.*, **62**, 11623(1965).
(877) Kupchan, S. M., Patel, A. C., and Fujita, E., *J. Pharm. Sci.*, **54**, 580(1965).
(878) Talalaj, S., *W. African Pharmacist*, **7** (3), 44(1965); through *Chem. Abstr.*, **63**, 16123(1965).
(879) Manzoor-I Khuda, M., and Sarela, S., *Tetrahedron*, **21**, 797(1965).
(880) Aspinall, G. O., Fraser, R. N., and Sanderson, G. R., *J. Chem. Soc.*, **1965**, 4325.
(881) Wakayama, S., and Namba, S., *Bull. Chem. Soc. Japan*, **38**, 860(1965); through *Chem. Abstr.*, **63**, 4091(1965).
(882) Bleier, W., *et al.*, *Pharm. Acta Helv.*, **40**, 554(1965).
(883) Wang, H.-K., Yang, P.-C., and Chen, H.-M., *Yao Hsueh Hsueh Pao*, **11** (6), 382(1964); through *Chem. Abstr.*, **62**, 10291(1965).
(884) Wang, H.-K., Yang, P.-C., and Chen, H.-M., *Yao Hsueh Hsueh Pao*, 11 (6), 389(1964); through *Chem. Abstr.*, **62**, 10291(1965).
(885) Kondo, K., Kondo, Y., and Takemoto, T., *Yakugaku Zasshi*, **85**, 664(1965).
(886) Sharma, R. K., *et al.*, *Lloydia*, **28**, 209(1965).
(887) Tomita, M., Lee, K.-H., and Nakamo, T., *Yakugaku Zasshi*, **85**, 276(1965).
(888) Nigam, M. C., Nigam, I. C., and Levi, L., *Can. J. Chem.*, **43**, 521(1965).
(889) Sadgopal, D., *France Parfums*, **4** (21), 179(1961); through *Chem. Abstr.*, **62**, 1509(1965).
(890) Dranik, L. I., *Med. Prom. SSSR*, **19** (5), 13(1965); through *Chem. Abstr.*, **63**, 6786(1965).
(891) Malhotra, A., Murti, V. V. S., and Seshadri, T. R., *Tetrahedron Letters*, **1965**, 3191.
(892) Chen, C.-L., and Tseng, K. F., *Yao Hsueh Hsueh Pao*, **12** (2), 119(1965); through *Chem. Abstr.*, **63**, 1654 (1965).
(893) Basu, N. K., and Nasipuri, R. N., *Current Sci. (India)*, **31**, 463(1963); through *Chem. Abstr.*, **63**, 2850(1965).
(894) Chan, W., and Staba, E. J., *Lloydia*, **28**, 55(1965).
(895) Gibson, M. R., and Danquist, C. A., *J. Pharm. Sci.*, **54**, 1526(1965).
(896) Shah, C. S., and Khanna, P. N., *J. Pharm. Pharmacol.*, **17**, 115(1965).
(897) Evans, W. C., and Woolley, J. G., *J. Chem. Soc.*, **1965**, 4936.
(898) Evans, W. C., Major, W. V., and PeThan, M., *Planta Med.*, **13** (3), 353(1965); through *Chem. Abstr.*, **63**, 14637(1965).
(899) Sciuchetti, L. A., Hisatomi, A., and Masoud, A. N., *J. Pharm. Sci.*, **54**, 403(1965).
(900) Pigulevskii, G. V., Kovaleva, V. I., and Motskus, D. V., *Rast. Resursy*, **1**, 227(1965); through *Chem. Abstr.*, **63**, 9739(1965).
(901) Gubanov, I. A., *Planta Med.*, **13** (2), 200(1965); through *Chem. Abstr.*, **63**, 4093(1965).
(902) Yeh, P. Y., Lin, L.-C., and Yang, S.-S., *J. Chinese Chem. Soc. (Taiwan)*, **12** (1–2), 61(1965); through *Chem. Abstr.*, **63**, 9745(1965).
(903) Kemerteludze, E. P., *Med. Prom. SSSR*, **19** (4), 22 (1965); through *Chem. Abstr.*, **63**, 1653(1965).
(904) Amato, H., *New Istanbul Contrib. Clin. Sci.*, **7** (1/2), 33(1964); through *Chem. Abstr.*, **62**, 6341(1965).
(905) Kaiser, V. F., and Voigtlander, W., *Naturwissenschaften*, **52**, 108(1965).
(906) Libizov, N. I., and Gulyi, E. V., *Izuch. i Is'polz. Lekarstv. Ratstit. Resursov SSSR Sb.*, **1964**, 250; through *Chem. Abstr.*, **62**, 10293(1965).
(907) Abdel-Wahab, S. M., Ahmed, Z. F., and El Keiy, M. A., *J. Chem. U.A.R.*, **7** (2), 165(1964); through *Chem. Abstr.*, **63**, 11250(1965).
(908) Ionescu-Stoian, P., *et al.*, *Farmacia (Bucharest)*, **12** (9), 529(1964); through *Chem. Abstr.*, **62**, 10292(1965).
(909) Betts, T. J., *Lloydia*, **28**, 181(1965).
(910) Kroszczynski, W., *et al.*, *Acta Polon. Pharm.*, **21** (3), 257(1964); through *Chem. Abstr.*, **63**, 432(1965).
(911) Sato, D., *Shionogi Kenkyusho Nempo*, **14**, 14(1964); through *Chem. Abstr.*, **62**, 3883(1965).
(912) Turowska, I., *et al.*, *Dissertationes Pharm.*, **17** (2), 251(1965); through *Chem. Abstr.*, **63**, 16128(1965).
(913) Zurkowska, J., Budzynska, M., and Ozarowski, A., *Acta Polon. Pharm.*, **20**, 109(1963); through *Chem. Abstr.*, **62**, 1513(1965).
(914) Calcandi, V., Lungeanu, I., and Calcandi, I., *Ann. Pharm. Franc.*, **23**, 99(1965).
(915) Gharbo, S. A., *et al.*, *Lloydia*, **28**, 237(1965).
(916) Kaiser, E., *Sci. Pharm.*, **32**, 265(1964); through *Chem. Abstr.*, **62**, 8932(1965).
(917) Padmanabha Rao, T. V., and Venkateswarlu, V., *Tetrahedron*, **21**, 389(1965).
(918) Buzas, A., and Egnell, C., *Ann. Pharm. Franc.*, **23**, 351(1965).
(919) Loshkarev, P. M., and Bordachuk, L. S., *Med. Prom. SSSR*, **18** (10), 16(1964); through *Chem. Abstr.*, **62**, 3884(1965).
(920) Kapadi, A. H., Sobti, R. R., and Dev, S., *Tetrahedron Letters*, **1965**, 2729.
(921) Manske, R. H. F., and Shin, K. H., *Can. J. Chem.*, **43**, 2180(1965)
(922) Porsch, F., Farnow, H., and Winkler, H., *Dragoco Rept.*, **12** (3), 47(1965); through *Chem. Abstr.*, **63**, 1650(1965).
(923) Kupchan, S. M., Knox, J. R., and Udayamurthy, M. S., *J. Pharm. Sci.*, **54**, 929(1965).
(924) Tariverdieva, S. A., *Izuch. i Is'polz. Lekarstv. Rastit. Resursov SSSR Sb.*, **1964**, 359; through *Chem. Abstr.*, **62**, 11627(1965).
(925) Kupchan, S. M., *et al.*, *J. Pharm. Sci.*, **54**, 1703 (1965).
(926) Steinegger, E., and Wicky, K., *Pharm. Acta Helv.*, **40**, 610(1965).
(927) Markham, K. R., *Tetrahedron*, **21**, 3687(1965).
(928) Pakrashi, S. C., Roy, S. K., and Bhattacharyya, J., *J. Indian Chem. Soc.*, **41** (10), 651(1964); through *Chem. Abstr.*, **62**, 7587(1965).
(929) Weisser, W., and Blome, J., *Deut. Apotheker-Ztg.*, **105**, 644(1965); through *Chem. Abstr.*, **63**, 6784(1965).
(930) Harris, W. M., and Geissman, T. A., *J. Org. Chem.*, **30**, 432(1965).
(931) Harris, W. M., *Dissertation Abstr.*, **25**, 6231(1965).
(932) Ulubelen, A., Caldwell, M. E., and Cole, J. R., *J. Pharm. Sci.*, **54**, 1214(1965).
(933) Manni, P. E., and Sinsheimer, J. E., *ibid.*, **54**, 1541(1965).
(934) Appel, H., Rother, A., and Schwarting, A. E., *Lloydia*, **28**, 84(1965).
(935) Rother, A., *et al.*, *ibid.*, **28**, 90(1965).
(936) Herz, W., and Lakshmikanthan, M. V., *Tetrahedron*, **21**, 1711(1965).
(937) Charma, M. L., Nigam, M. C., and Handa, K. L., *Riechstoffe Aromen*, **13**, 325(1963); through *Chem. Abstr.*, **62**, 6335(1965).

(938) Beyrich, Th., *Arch. Pharm.*, **298,** 672(1965).
(939) Misra, G., and Mitra, C. R., *Res. Ind.*, **9,** 325(1964); through *Chem. Abstr.*, **62,** 14418(1965).
(940) Grigorescu, E., *Farmacia (Bucharest)*, **12** (11), 655 (1964); through *Chem. Abstr.*, **62,** 7587(1965).
(941) Euler, K. L., *et al.*, *Lloydia*, **28,** 203(1965).
(942) Khanna, J. M., *et al.*, *J. Pharm. Sci.*, **54,** 1016 (1965).
(943) Khafagy, S. M., Mnajed, H. K., and Haddad, D. Y., *Lloydia*, **28,** 101(1965).
(944) Boichinov, A., *et al.*, *Farmatsiya (Sofia)*, **15** (2), 92(1965); through *Chem. Abstr.*, **63,** 11250(1965).
(945) Finnegan, R. A., and Mueller, W. H., *J. Pharm. Sci.*, **54,** 1136(1965).
(946) Mishra, S. S., Tewari, J. P., and Matin, M. A., *ibid.*, **54,** 471(1965).
(947) Graf, E., and Dahlke, E., *Planta Med.*, **12,** 293 (1964); through *Chem. Abstr.*, **62,** 3885(1965).
(948) Der Marderosian, A. H., *Dissertation Abstr.*, **25,** 6548(1965).
(949) Kupchan, S. M., Hemingway, J. C., and Knox, J. R., *J. Pharm. Sci.*, **54,** 659(1965).
(950) Huneck, S., *Naturwissenschaften*, **52,** 477(1965).
(951) Datta, D. D., and Bami, H. L., *Sci. Cult. (Calcutta)*, **28,** 283(1962); through *Chem. Abstr.*, **62,** 8928(1965).
(952) Tyler, J. M., *J. Chem. Soc.*, **1965,** 5288, 5300.
(953) Korotaeva, M. M., *Tr. Tsentr. Sibirsk. Botan. Sada*, **1964,** 161; through *Chem. Abstr.*, **63,** 1649(1965).
(954) Gulati, B. C., and Duhan, S. P. S., *Indian Oil Soap J.*, **30,** 233(1965); through *Chem. Abstr.*, **63,** 12965(1965).
(955) Tomita, M., *et al.*, *Yakugaku Zasshi*, **85,** 593(1965).
(956) McLaughlin, J. L., and Paul, A. G., *J. Pharm. Sci.*, **54,** 661(1965).
(957) Bonzani da Silva, J., *Rev. Fac. Farm. Bioquim., Univ. Sao Paulo*, **2** (2), 15(1964); through *Chem. Abstr.*, **63,** 12969(1965).
(958) Pizarroso, B., Gamir, A., and Ferdandez, O., *Farm. Nueva Madrid*, **30** (339), 155(1965); through *Chem. Abstr.*, **63,** 14637(1965).
(959) Tulloch, A. P., *Can. J. Chem.*, **43,** 415(1965).
(960) Tomita, M., Lu, S. T., and Lan, P.-K., *Yakugaku Zasshi*, **85,** 588(1965).
(961) Finnegan, R. A., and Bachman, P. L., *J. Pharm. Sci.*, **54,** 633(1965).
(962) El Sissi, H. T., and Saleh, N. A. M., *Planta Med.*, **13** (3), 346(1965); through *Chem. Abstr.*, **63,** 14637(1965).
(963) Norri, R., *Farm. Aikakauslehti*, **74** (3), 108(1965); through *Chem. Abstr.*, **63,** 1651(1965).
(964) Chopra, M. M., Vashist, V. N., and Handa, K. L., *Indian Oil Soap J.*, **30** (2), 41(1964); through *Chem. Abstr.*, **62,** 8928(1965).
(965) Shimizu, S., and Ikeda, N., *Nippon Nogei Kagaku Kaishi*, **36,** 907(1962); through *Chem. Abstr.*, **62,** 6335(1965).
(966) Mitsuhashi, H., and Nomura, T., *Chem. Pharm. Bull. (Tokyo)*, **13,** 274(1965).
(967) Retamar, J. A., and Mazzola, E. B., *Rev. Fac. Ing. Quim., Univ. Nacl. Litoral, Sante Fe, Arg.*, **32,** 49(1963); through *Chem. Abstr.*, **62,** 11623(1965).
(968) Beckett, A. H., *et al.*, *J. Pharm. Pharmacol.*, **17,** 753(1965).
(969) Talalaj, S., *W. African Pharmacist*, **7** (4), 64(1965); through *Chem. Abstr.*, **63,** 16123(1965).
(970) Tomita, M., *et al.*, *Yakugaku Zasshi*, **85,** 662(1965).
(971) Hui, W. H., Loo, S. N., and Arthur, H. R., *J. Chem. Soc.*, **1965,** 2285.
(972) Gulati, B. C., and Shah, N. C., *Perfumery Essent. Oil Record*, **56,** 578(1965); through *Chem. Abstr.*, **63,** 16123 (1965).
(973) Alworth, W. L., and Rapaport, H., *Arch. Biochem. Biophys.*, **112,** 45(1965).
(974) Arata, Y., and Ohashi, T., *Chem. Pharm. Bull. (Tokyo)*, **13,** 392(1965).
(975) Schutte, H. R., and Lehfeld, T. J., *Arch. Pharm.*, **298,** 461(1965).
(976) Jordan, W., and Scheuer, P. J., *Tetrahedron*, **21,** 3731(1965).
(977) Dwivedi, U. N., Chandra, G., and Gupta, G. N., *Indian Perfumer*, **7** (2), 101(1963); through *Chem. Abstr.*, **63,** 12966(1965).
(978) Kostecka-Madalska, O., Bankowski, C., and Kuduk, J., *Acta Polon. Pharm.*, **21,** 387(1964); through *Chem. Abstr.*, **62,** 8927(1965).
(979) Pfeifer, S., and Kühn, L., *Pharmazie*, **20,** 394(1965).
(980) Bhown, A. S., Shah, D. K., and Nath, S., *Naturwissenschaften*, **52,** 516(1965).
(981) Brochmann-Hanssen, E., and Nielsen, B., *Tetrahedron Letters*, **1965,** 1271.
(982) Preininger, VL., Vrublovsky, P., and Stastny, VL., *Pharmazie*, **20,** 439(1965).
(983) Kühn, L., and Pfeifer, S., *ibid.*, **20,** 520(1965).
(984) Pfeifer, S., and Mann, I., *ibid.*, **20,** 643(1965).
(985) Culberson, C. F., *J. Pharm. Sci.*, **54,** 1815(1965).
(986) Ivanov, V., Nikolov, N., and Tonev, Iv., *Farmatsiya (Sofia)*, **15** (3), 164(1965); through *Chem. Abstr.*, **63,** 16127 (1965).
(987) Scheuer, P. J., and Hudgins, W. R., *Perfumery Essent. Oil Record*, **55,** 723(1964); through *Chem. Abstr.*, **62,** 14418(1965).
(988) Novotny, L., and Herout, V., *Collection Czech. Chem. Commun.*, **30,** 3579(1965); through *Chem. Abstr.*, **63,** 16129(1965).
(989) Kostomarova, V. L., *Zh. Prikl. Khim.*, **38,** 2121 (1965); through *Chem. Abstr.*, **63,** 16123(1965).
(990) Krug, V. H., and Borkowski, B., *Naturwissenschaften*, **52,** 161(1965).
(991) Yamaguchi, H., and Nishimoto, K., *Chem. Pharm. Bull. (Tokyo)*, **13,** 217(1965).
(992) O'Hara, M. J., Kinnard, W. J., and Buckley, J. P., *J. Pharm. Sci.*, **54,** 1021(1965).
(993) Takahashi, K., Tanabe, Y., and Hosoda, N., *Yakugaku Zasshi*, **85,** 854(1965).
(994) Aurousseau, M., Berny, C., and Albert, O., *Ann. Pharm. Franc.*, **23,** 251(1965).
(995) Torigoe, Y., *Yakugaku Zasshi*, **85,** 176(1965).
(996) Ahmed, Z. F., Rizk, A. M., and Hammouda, F. M., *J. Pharm. Sci.*, **54,** 1060(1965).
(997) Yaakob, M. S., *Dissertation Abstr.*, **25,** 6550(1965).
(998) El-Dakhakhny, M., *Planta Med.*, **12,** 181(1964); through *Chem. Abstr.*, **62,** 1514(1965).
(999) Gaind, K. N., *et al.*, *Indian J. Pharm.*, **27** (7), 198 (1965); through *Chem. Abstr.*, **63,** 11248(1965).
(1000) Steinmetz, E. F., and Lindermann, G., *Riechstoffe, Aromen, Koerpepflegemittel*, **14,** 409(1964); through *Chem. Abstr.*, **62,** 14419(1965).
(1001) Eickholt, T. H., and Box, R. H., *J. Pharm. Sci.*, **54,** 1071(1965).
(1002) Patel, M. B., *et al.*, *J. Pharm. Pharmacol.*, **17,** 323 (1965).
(1003) Cardoso do Vale, J., *Garcia Orta*, **11,** 107(1963); through *Chem. Abstr.*, **62,** 8933(1965).
(1004) Dabrowski, B., and Malek, B., *Acta Polon. Pharm.*, **21** (3), 281(1964); through *Chem. Abstr.*, **62,** 15990(1965).
(1005) Lemli, J., *Lloydia*, **28,** 63(1965).
(1006) Longo, R., *Boll. Chim. Farm.*, **104** (6), 369(1965); through *Chem. Abstr.*, **63,** 11251(1965).
(1007) Murakami, T., *et al.*, *Yakugaku Zasshi*, **85,** 845 (1965).
(1008) Pigulevskii, G. V., and Belova, N. V., *Zh. Prikl. Khim.*, **37,** 2772(1964); through *Chem. Abstr.*, **62,** 8929 (1965).
(1009) Marczal, G., *Herba Hung.*, **2,** 343(1963); through *Chem. Abstr.*, **63,** 6787(1965).
(1010) Cole, J. R., and Buchalter, L., *J. Pharm. Sci.*, **54,** 1376(1965).
(1011) Novak, I., *et al.*, *Pharmazie*, **20,** 654(1965).
(1012) Novak, I., *et al.*, *Planta Med.*, **13** (2), 226(1965); through *Chem. Abstr.*, **63,** 5446(1965).
(1013) Borkowski, B., and Drost, K., *Pharmazie*, **20,** 390 (1965).
(1014) Kolodziejski, J., *et al.*, *Acta Polon. Pharm.*, **20,** 269 (1963); through *Chem. Abstr.*, **62,** 1509(1965).
(1015) Winstersteiner, O., Krakower, G., and Moore, M., *J. Org. Chem.*, **30,** 2847(1965).
(1016) Jennings, W. G., Creveling, R. K., and Heinz, D. E., *J. Food Sci.*, **29,** 730(1964); through *Chem. Abstr.*, **62,** 6336(1965).
(1017) Chatterjee, A., *et al.*, *Tetrahedron Letters*, **1965,** 67.
(1018) *Ibid.*, **1965,** 952.
(1019) Horii, Z., *et al.*, *Chem. Pharm. Bull. (Tokyo)*, **13,** 1307(1965).
(1020) Madhav, R., Seshadri, T. R., and Subramanian, G. B. V., *Tetrahedron Letters*, **1965,** 2713.
(1021) Okanishi, T., Akahori, A., and Yasuda, F., *Chem. Pharm. Bull. (Tokyo)*, **13,** 545(1965).
(1022) Saber, A. H., Balboa, S. I., and Zaky, A. Y., *Planta Med.*, **13** (1), 104(1965); through *Chem. Abstr.*, **63,** 2849 (1965).
(1023) Maiti, P. C., Mookerjea, S., and Mathew, R., *J. Pharm. Sci.*, **54,** 1828(1965).
(1024) Okuda, S., *et al.*, *Chem. Pharm. Bull. (Tokyo)*, **13,** 482(1965).
(1025) Aspinall, G. O., and Fraser, R. N., *J. Chem. Soc.*, **1965,** 4318.
(1026) Aspinall, G. O., Fraser, R. N., and Sanderson, G. R., *ibid.*, **1965,** 4325.
(1027) Aspinall, G. O., and Nasir-ud-din, *ibid.*, **1965,** 2716.
(1028) Grossert, J. S., *et al.*, *ibid.*, **1965,** 2812.
(1029) Quivin, M., Levy, J., and LeMen, J., *Ann. Pharm. Franc.*, **23,** 93(1965).
(1030) Cava, M. P., Mowdood, S. K., and Beal, J. L., *Chem. Ind. (London)*, **1965,** 2064.
(1031) Markman, A. L., and Freiman, R. E., *Khim. Prirodn., Soedin., Akad. Nauk. Uz. SSR*, **1965** (2), 123; through *Chem. Abstr.*, **63,** 9738(1965).
(1032) Jarvi, M., *Farm. Aikakauslehti*, **74** (1), 11(1965); through *Chem. Abstr.*, **62,** 11624(1965).
(1033) Preuss, Fr. R., and Orth, H., *Planta Med.*, **13,** 261(1965); through *Chem. Abstr.*, **63,** 16123(1965).
(1034) Gheorghiu, A., Ionescu-Matiu, E., and Calcandi, V., *Studii Cercetari Biochim.*, **8,** 193(1965); through *Chem. Abstr.*, **63,** 9745(1965).
(1035) Patil, P. N., *et al.*, *J. Pharm. Sci.*, **54,** 1387(1965).
(1036) Tomimatsu, T., *et al.*, *ibid.*, **54,** 1389(1965).
(1037) Tomimatsu, T., Gharbo, C. R., and Beal, J. L., *ibid.*, **54,** 1390(1965).
(1038) Ivars, L., *Farm. Aikakauslehti*, **73,** 324(1964); through *Chem. Abstr.*, **62,** 11623(1965).
(1039) Kolodziejski, J., Gill, S., and Mruk-Luczkiewicz, A., *Acta Polon. Pharm.*, **20,** 349(1963); through *Chem. Abstr.*, **62,** 1509(1965).
(1040) Tucakov, J., *Riv. Ital. Essenze-Profumi, Piante Offic. Aromi Saponi Cosmet.*, **46,** 376(1964); through *Chem. Abstr.*, **62,** 6335(1965).
(1041) Aguilar Santos, G., *Chem. Ind. (London)*, **1965,** 1074.
(1042) Suzuki, Y., Uda, Y., and Okui, S., *Yakugaku Zasshi*, **85,** 72(1965).
(1043) Kachukhashvili, T. N., *Med. Prom. SSSR*, **19** (3) 46(1965); through *Chem. Abstr.*, **63,** 1654(1965).

(1044) Gill, S., *Acta Polon. Pharm.*, **21** (3), 287(1964); through *Chem. Abstr.*, **63**, 433(1965).
(1045) Yasue, M., *et al.*, *Yakugaku Zasshi*, **85**, 553(1965).
(1046) Volk, O. H., and Schunk, R., *Deut. Apotheker Z.*, **104**, 187(1964); through *Chem. Abstr.*, **63**, 5448(1965).
(1047) Hikino, H., *et al.*, *Yakugaku Zasshi*, **85**, 179(1965).
(1048) Tomko, J., and Vassova, A., *Pharmazie*, **20**, 385 (1965).
(1049) Bobbitt, J. M., and Rao, K. V., *J. Pharm. Sci.*, **54**, 924(1965).
(1050) Höerhammer, V. L., Wagner, H., and Reinhardt, H., *Naturwissenschaften*, **52**, 161(1965).
(1051) Potier, P., *et al.*, *Ann. Pharm. Franc.*, **23**, 61(1965).
(1052) Ciulei, I., *et al.*, *Farmacia (Bucharest)*, **13**, 273 (1965); through *Chem. Abstr.*, **63**, 6784(1965).
(1053) Puisieux, F., *et al.*, *Ann. Pharm. Franc.*, **23**, 33 (1965).
(1054) Santos, A. C., and Aguilar-Santos, G., *Arales Real Acad. Farm.*, **30** (3), 173(1964); through *Chem. Abstr.*, **62**, 397(1965).
(1055) Leary, J. D., *Dissertation Abstr.*, **25**, 4388(1965).
(1056) Lavie, D., Glotter, E., and Shvo, Y., *J. Org. Chem.*, **30**, 1774(1965).
(1057) Blunden, G., Hardman, R., and Wensley, W. R., *J. Pharm. Pharmacol.*, **17**, 274(1965).
(1058) Sharma, M. L., Vashist, V. N., and Handa, K. L., *Perfumery Essent. Oil Record.*, **55**, 720(1964); through *Chem. Abstr.*, **62**, 14417(1965).
(1059) Kramarenko, V. F., *Materialy l-go (Pervogo) Vseros. S'ezda Farmatsevtov Sb.*, **1962**, 240; through *Chem. Abstr.*, **62**, 11625(1965).
(1060) Stivic, I., and Senjkovic, R., *Acta Pharm. Jugoslav.*, **14**, 59(1964); through *Chem. Abstr.*, **63**, 9742(1965).
(1061) Gluzman, M. Kh., and Dashevskaya, B. I., *Med. Prom. SSSR*, **18** (9), 38(1964); through *Chem. Abstr.*, **62**, 2666(1965).
(1062) Vlasova, V. F., *et al.*, *Materialy l-go (Pervogo) Vseros. S'ezda Farmatsevtov*, **1962**, 154; through *Chem. Abstr.*, **63**, 1653(1965).
(1063) Ovadia, M. E., and Skauen, D. M., *J. Pharm. Sci.*, **54**, 1013(1965).
(1064) Novikov, F. I., *Izuch. i Is'polz. Lekarstv. Rastit. Resursov SSSR, Sb.*, **1964**, 347; through *Chem. Abstr.*, **62**, 11625(1965).
(1065) Ionescu-Stoian, P., *et al.*, *Farmacia (Bucharest)*, **13**, 291(1965); through *Chem. Abstr.*, **63**, 6785(1965).
(1066) Belcher, W. F. M., *Perfumery Essent. Oil Record*, **56**, 148(1965); through *Chem. Abstr.*, **62**, 14418(1965).
(1067) Plyashkevich, A. M., and Antoshina, V. A., *Med. Prom. SSSR*, **18** (10), 25(1964); through *Chem. Abstr.*, **62**, 7587(1965).
(1068) Rao, A. V., and Mody, I. C., *Indian J. Technol.*, **3** (8), 261(1965); through *Chem. Abstr.*, **63**, 16129(1965).
(1069) Swaleh, M., *Indian Perfumer*, **7** (2), 93(1963); through *Chem. Abstr.*, **63**, 9739(1965).
(1070) Atal, C. K., and Shah, K. C., *Indian J. Pharm.*, **26**, 265(1964); through *Chem. Abstr.*, **62**, 6343(1965).

Research Articles

In Vivo Pharmacodynamic Evaluation of Oral Dosage Forms by Whole Body Liquid Scintillometry

By GERALD HECHT*, JOHN E. CHRISTIAN, and GILBERT S. BANKER

A large volume liquid scintillation detector was used to determine rates of excretion, absorption, and intercompartmental clearance in ambulatory dogs. A γ-emitting test substance was administered intravenously, orally in aqueous solution, and orally in sustained and delayed-release dosage forms. Unanesthetized female dogs were partially restricted, catheterized, and fasted prior to dosing. Where applicable, plots of log per cent whole body retention as a function of time were resolved into linear components following apparent first-order kinetics. The rate constants of these components were calculated and compared. Sustained-release forms were prepared which exhibited zero-order release characteristics *in vitro* and *in vivo*, and the characteristics of an enteric coated dosage form were compared after *in vitro* and *in vivo* testing. The procedure provided such parameters as absorption, excretion, release, and the effect of formulation techniques and formula variation on the biological availability of the test substance employed without the necessity of excreta and blood sampling and analysis.

THE PROBLEM of evaluating the biological availability and pharmacodynamic properties of any drug, new or old, in a new dosage form, is of increasing importance due to the greater potency and specificity of drugs, the greater complexity of dosage forms, and the increasing demands of the drug laws and new drug application requirements.

Several authors (1–9) have attempted to standardize the *in vitro* testing of various oral dosage forms, not necessarily as a means of simulating the characteristics which would be expected *in vivo*, but rather as a means of insuring control and correlation with data collected *in vivo*.

Many methods for the *in vivo* evaluation of oral dosage forms have been devised, but undoubtedly, those supplying the most pertinent information are concerned with the evaluation of absorption,

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