HIGHLIGHTS OF SOVIET PHARMACOLOGY[1]

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During the six years which have elapsed since the publication of the first article under this heading in this Review [Ann. Rev. Pharmacology, Vol. 1], Soviet pharmacologists have achieved considerable progress in their work. The main focus has been on the pharmacology of the nervous system. The greater part of the research has dealt with the pharmacology of the central and peripheral synapses.

As noted in our first review of 1961, cholinergic agents are divided in Soviet pharmacology into N- and M-cholinomimetics, and N- and M-cholinolytics, according to their prevalent action upon nicotine-sensitive and muscarine-sensitive cholinoreceptors. The cholinolytics that exert a prevalent central action are, as a rule, classed separately under the general denomination of "central cholinolytics." The central cholinolytic most in favour among Soviet pharmacologists and clinicians is the one synthetized at the Drug-Synthetizing Laboratory of the Institute of Experimental Medicine named metamizil (2-diethylaminopropylic ester of benzoic acid-hydrocholoride) [Torf (1)].

Compared with the closely related benactyzine (amizil), metamizil possesses a superior cholinolytic potency [Denissenko (2); Ilyuchonok (3)]. The structure-activity relationships of several compounds that are closely allied with metamizil have been studied, and it has been found that the substitution of the methyl group in the α-position relative to nitrogen with some other aliphatic radical, or a shift from α to β position diminishes the central as well as the peripheral cholinolytic action of the compound [Lossev (4)].

Soviet pharmacologists have also been engaged in the search for new central N-cholinolytic drugs. They have found that 1,1-diphenyl-5-diphenylaminopeptine-3-chlorhydrate is a central N-cholinolytic agent, which is practically devoid of any M-cholinolytic action [Golikov, Razumova Selivanova (5)]. This drug prevents nicotine-induced convulsions and electroencephalographic troubles, without being antagonistic to the central action of arecoline.

Experimentation with central M- and N-cholinolytics enables us to locate the central M- and N-cholinoreceptors and to ascertain the part they play in intracerebral connections. On the basis of electroencephalographic data obtained during chronic experiments with implanted electrodes as well

[1] The survey of literature pertaining to this review was concluded in June, 1967.

as acute experiments with cerebral sections [Anichkov & Borodkin (6)], it has been shown that M-cholinoreceptors are located in all parts of the cerebrum. However, the greatest M-cholinoreactivity is displayed by the reticular formation synapses, while N-cholinoreactive receptors are chiefly grouped in the formations of the intermediate and frontal parts.

In Soviet Russia, a great deal of attention has been paid to the pharmacology of peripheral cholinergic synapses, and during the last few years a certain advance has been noted in the synthesis of curare-like compounds and in the elucidation of the mechanism of their action. Kharkevich (7) (I Medical Institute, Moscow) has studied the curarimimetic effect of a number of cyclobutane-dicarboxylic acids and their structure-activity relationships. It has been found that certain bis-ammonium derivatives of α-truxillic acid are very potent curare-like agents with anti-depolarizing effect.

Podlesnaya (8, 9) (Institute of Experimental Medicine) has studied the curare-like properties of bis-ammonium, as well as bis-sulphonic derivatives of diphenylhexane and bis-ammonium derivatives of benzidine. While studying the effect of curare-like compounds on the bioelectric activity of denervated skeletal muscles, she discovered that *d*-tubocurarine and other antipolarizers do not influence this activity, while decamethonium and other depolarizers act primarily as intensifiers and secondarily as depressors of this activity. It follows that the compounds of the latter group, unlike those of the first, are able to penetrate through the postsynaptic membrane into the sarcoplastic reticulum [Podlesnaya (10)].

Michelson (Institute of Evolutionary Physiology) and Khromov-Borisov (Institute of Experimental Medicine), after comparing the curare-like action of bis-ammonium compounds with 10 and 16 carbon atoms, have suggested the hypothesis of tetrameric structure of muscular cholinoreceptors, with the ammonium groups located at the four corners of a square, and the esterophilic groups diagonally. A comparative study of relative sensitivity in various classes of animals in their phylogenetic aspect has led the authors to the assumption that sensitivity to C-16 structure appears much earlier than sensitivity to the C-10 structure. It follows then that the dimeric C-16 receptor structure was formed first, and then the C-10 structure added, transforming the C-16 dimeric structure into a tetrameric one. The exposition of the hypothesis of both authors, together with the bibliography on the subject was published in the Pharmacological Review [Khromov-Borisov & Michelson (11)].

Aceclidine, a 3-acetoxynucleidine salicylate synthetized and studied in the USSR, is a stimulant of the peripheral M-cholinoreceptors [Mashkovsky & Zaitseva (12)]. Aceclidine has been successfully used by Soviet ophthalmologists as a myotic drug and in cases where parasympatheticotropic drugs are indicated.

In the province of adrenergic-synapse pharmacology, definite success has

been achieved in the study of amphetamine derivatives. It has been found that by substituting an alkylaromatic or a heterocyclic radical for a hydrogen atom in the H–N bond, the hypertensive and analeptic properties of amphetamine disappear. Among similar agents possessing hypotensive properties are certain sedatives antagonistic to amphetamine and adrenoblocking agents.

A number of amphetamine derivatives with carboxylic acids, containing heterocyclic rings in their molecule, have been studied by Arbusov (13). Among the most interesting of these compounds is the condensation product of amphetamine with pyridoxine. This drug possesses sedative and hypotensive properties blocking α-adrenoreceptors [Arbusov & Smirnova (14); Arbusov, Aleksandrova & Smirnova (15)].

The study of amphetamine derivatives with various radicals substituted for the hydrogen atom in the H–N bond has been carried out in the Institute of Experimental Medicine. Most extensively investigated was the amide of amphetamine and paraaminophenylacetic acid. This compound possesses sedative and hypotensive properties and is a direct antagonist of amphetamine [Hsi-Tui Wu & Baibekov (16); Fedyayeva (17)].

Recently much attention has been paid to the action of pharmacological agents upon intracerebral connections. Among neurotropic drugs must be noted particularly the alkyl derivatives of the imidazoldicarboxylic acid diamide, which received the name of antifeines [Borodkin (18)]. One of the characteristic representatives of this group, the 4,5-bis-(methylamide)-1-ethylimidazoldicarboxylic acid, named ethymizol, has been extensively used in our clinical practice as a potent respiratory analeptic [Borodkin & Kostin (19)]. As may be gathered from EEG experiments and conditioned-reflex and behaviour studies, ethymizol and related compounds alter the normal intracerebral connections. While in most cases stimulation of the reticular formation elicits a depression of the diffuse thalamocortical projectional system and the limbic structure, the action of antifeines is characterized by the fact that intense stimulation of the reticular formation is accompanied by a simultaneous stimulation of the diffuse thalamocortical projectional system and some limbic-system formations. At the same time, ethymizol exerts a direct depressing action upon the cerebral cortex.

Such a variety of effects is the cause of dissociation of the EEG picture from the behaviour of the animal. A certain degree of a similar kind of dissociation has also been observed by Burov (Institute of Pharmacology and Chemotherapy) under the action of perphasine, meprobamate, and benactyzine [Burov (20)].

New sedatives have been studied by Zakussov and co-workers (Institute of Pharmacology & Chemotherapy), who experimented with γ-oxybutyric acid. The results obtained were reported in a lecture delivered by Zakussov at the Third International Pharmacological Congress in São Paulo (21).

A number of studies at the Institute of Pharmacology and Chemotherapy are devoted to the action of analgetics upon the transmission and summation of impulses at thalamus level [Sinitsin (22); Kruglov (23)]. The pharmacology of analgetics has long been the subject of studies elected by A. K. Sangailo, who occupies the Chair of Pharmacology in Sverdlovsk. He has evolved original methods of analgetic testing upon volunteers [Sangailo (24)].

Among the central sedatives synthetized and used in the USSR, oxylidine (3-benzol-oxychinucleidine-hydrochloride) ought to be mentioned. This compound was developed and studied at the All-Union Scientific Research Chemo-Pharmaceutical Institute [Mashkovsky & Zaitseva (25)]. Oxylidine is related to aceclidine, the difference residing in the presence of an aromatic radical. It possesses cholinolytic properties, which is often the case when aromatic radicals are introduced into the molecule of a cholinomimetic. Oxylidine has also been successfully used as a sedative.

Mashkovsky & Trubitsina (26) have studied and introduced into clinical practice the antidepressant indopane (α-methyl-tryptamine).

Functional and morphological research in neurotropic action upon the regulation of physiological functions have been carried out at the I Leningrad Medical Institute under the direction of the Head of Pharmacology, A. V. Valdman, Corresponding Member of the USSR Academy of Medical Sciences. The research sought to determine what morphological substrata of subcortical nervous structures, the reticular formation, and the cerebral stem are affected by the action of neurotropic drugs. The effects of these drugs upon the various components of the bulbar, vascular, and respiratory centers, and upon the efferent, facilitating, and inhibiting functions of the reticular formation were studied. New data were obtained with respect to the action of psychotropic drugs on the various cerebral areas related to the integrating of emotions and behavioural manifestations. These studies have been summarized under the title of *Actual Problems in the Pharmacology of the Reticular Formation and Synaptic Transmission* [Valdman (27, 28)].

Pharmacological survey has not been limited to synthetic neurotropic drugs. Certain substances obtained from native plants have undergone similar investigation, and it has been found that a considerable number possess neurotropic properties.

Most fruitful has been the search for medicinal plants in Central Asia, many of which have been found to be alkaloid bearers. Most of the alkaloids extracted were investigated under the direction of I. K. Kamilov at the Institute of Vegetal-Stuff Chemistry of the Uzbek SSR Academy of Sciences at Tashkent, and under the direction of A. D. Turova (29) at the All-Union Medicinal and Aromatic Plants Institute, Moscow. Among these neurotropic alkaloids the following central nervous system stimulators must be noted: securinine (from *Securinega suffrucosa Pall.*); echinopsine (from *Echinops ritro L.*); and evinine (from *Vinca erecta*). Securinine and echinopsine possess a

strychnine-like action and have been used clinically as tonics.

The alkaloids perforine (from various species of *Happlophyllum*), vincamine (from *Vinca erecta*), hippeasterine and ungerine (from various species of *Ungernia*), and thaleosonine (from *Thalietrum isopyroides*) possess sedative properties. Vincamine has been adopted in clinical practice. The pharmacological properties of the aforementioned, as well as certain other alkaloids extracted from home-growing plants, have been described in *Alkaloid Pharmacology*, a book published in 1965 in Tashkent. The alkaloid, galantamine, possessing anticholinesterasic properties, first extracted in the USSR from *Galantus voronovi*, and now found in other plants as well, has been extensively adopted in clinical practice.

Medical treatment in the USSR has had recourse to some plants growing in the far-eastern section of our country. Special attention has been directed to the root, ginseng (*Radix ginseng*), of the plant *Panax Shin-seng*. According to experimental data obtained by Prof. I. I. Brekhman and co-workers (30) in Vladivostok, the glycosides extracted from ginseng which have received the general appellation, panaxosides, possess stimulating and gonadotropic properties. A stimulating action upon the central nervous system is also exerted by the roots of the Far-Eastern plants *Aralia Manshurica Prupp et Maxim* and *Echinopenax elatum*. Both these plants belong to the same family of *Araliaceae* as the ginseng. The fruit of *Schizandre chinensis Baill* and the root of leusea (*Leusea carthamoides DC*) have also been used as stimulants. These plants are also natives of the far-eastern USSR. [Mashkovsky (31)].

Soviet pharmacologists carry out their research work on neurotropic agents along the lines of Pavlov's physiology, according to which the activity of all organs depends upon the nervous system. On the basis of this theory, which Pavlov himself named nervism, Soviet pharmacologists study the effect of neurotropic drugs acting on various organs through the nervous system. Recently, therapy has been adopted by several investigators of neurotropic drug-effect upon the endocrine glands, and the tropic functions of the hypophysis, in particular. Investigating the action of central neurotropic drugs stimulating the hypophysis-adrenal system, Ryzhenkov and co-workers endeavoured to find pharmacological agents capable of obviating the secondary insufficiency of the adrenal cortex due to prolonged administration of glycocorticoids. These requirements are best met by agents belonging to the group of antifeines, ethymizol in particular, of which mention was made earlier. Even in small doses, ethymizol heightens the level of corticosteroids in the blood by stimulating the hypothalamo-hypophyseo-adrenal system. Unlike cortisone or ACTH, cessation of ethymizol administration does not cause abatement in the activity of the adrenal cortex. This makes ethymizol a valuable drug in treatment of rheumatoid arthritis and other allergic diseases [Ryzhenkov (32); Ryzhenkov, Pitkovskaya & Livshitz (33)].

Research has also been carried out in order to find agents preserving the

hypothalamus from excessive stimulation. The most effective in this respect is the central cholinolytic metamizil which prevents the increase of the corticosteroid level in the blood caused by certain stresses. These properties of metamizil are turned to account in surgical practice and premedication [Ryzhenkov et al. (34)].

When studying the action of neurotropic drugs on gastricointestinal secretion, Soviet pharmacologists mainly avail themselves of Palvov's practice of chronic experiments on dogs, allying them with up-to-date biochemical methods. When analyzing the central mechanism of drug action on gastric secretion, the agents are introduced into the cerebral arteries through polyethylene catheters implanted into the common carotid of a dog. The results obtained are compared with the action of the same drugs after intravenous introduction [Anichkov & Grechishkin (35)]. Thus, it has been shown that inhibition of the gastric secretion by central cholinolytics, benactyzine in particular, is to be attributed to the blocking of not only peripheral, but central cholinergic synapses as well [Anichkov & Grechishkin (36)]. In order to investigate the action of neurotropic drugs upon the gastric contractions, Soviet pharmacologists make use of the periodical hunger contractions of the stomach, discovered by one of Pavlov's disciples, Boldyrev. According to his views, the periodicity of these contractions is controlled by subcortical centers of the cerebrum, and its fluctuations may, therefore, be used as an index not only of the peripheral action of the neurotropic drugs, such as epinephrine, atropine, and the gangliolytics, but of neurotropic drugs of central action as well. Thus, it has been shown that such neurotropic agents as barbiturates, morphine, and metamizil exert the most spectacular action on the periodic activities of the hungry stomach when they are introduced into the staminal parts of the cerebrum through a catheter implanted into the arteria vertebralis. This shows that the central effects of these drugs influence the motor activities of the stomach [Grechishkin (37)].

Soviet pharmacologists engaged in gastroenterology hold the opinion that neurotropic agents act through the nervous system not only upon the secretory and motor activities of the stomach, but upon all coordinated metabolic processes of the gastric mucosa, which are usually called trophic processes. Intense irritation in an animal causes ulceration of the gastric mucosa, which, according to the ideas developed by Zavodskaya, is the result of neurogenic dystrophy.

In order to obtain neurogenic dystrophies in the gastric wall of the rat, the laboratory headed by Zavodskaya at the Institute of Experimental Medicine employs either mechanical traumatizing of the duodenum, or a three-hour electrization of the anterior limbs of immobilized animals. Pharmacological analysis has led to the determination of the paths followed by the reflexes altering the trophic processes in the gastric wall. The efferent paths of these reflexes are the sympathetic nerves, as neurogenic dystrophy is

prevented by gangliolytics, presynaptic symphatholytics and postsynaptic adrenolytics, while peripheral M-cholinolytics are, in this respect, ineffective [Anichkov & Zavodskaya (38)]. That the sympathetic nerves take part in impulse transmission causing gastric wall dystrophy is corroborated, moreover, by the fact that the appearance of dystrophy is preceded in the gastric wall tissues by an abrupt fall, in some cases almost down to zero, of the level of catecholamines, especially norepinephrine [Zavodskaya (39)]. In the course of development of a reflex-induced dystrophy, the level of norepinephrine and bound acetylcholine in the subcortical formations of the cerebrum falls, too, which points to the fact that the central links of the reflexes which impair the trophic processes are located precisely there.

Stimulation of the posterior hypothalamus of the rabbit by means of implanted electrodes causes ulcers in the gastric mucosa similar to reflex ulcerations. These centrally induced ulcerations, as well as those obtained by means of reflexes, are prevented or weakened by barbiturates, gangliolytics and adrenolytics [Moreva (40, 41)], which confirms the hypothesis of the sympathetic path followed by the impulses impairing the trophic processes.

Zavodskaya's laboratory has also shown that catecholamines do not only participate in trophic alterations, but when administered in small doses, may cause a beneficial action on trophic processes by restoring the functions of the gastric glands when they are exhausted by prolonged secretion [Grechishkin (42)]. Most effective in this respect is the adrenolytic dichloroisoproterenol, whose action is neutralized by β-blockers. The conclusion is that sympathetic impulses and catecholamines exert, on the gastric glands, an influence similar to the one they have on an exhausted skeletal muscle (Orbeli-Ghinetsinsky phenomenon), which Orbeli construed as their action upon trophic processes. By comparing all data obtained in this series of investigations, one is brought to the conclusion that, in normal cases, norepinephrine, as a mediator, regulates trophic processes, but in cases of its excessive mobilization, is the cause of their disturbance, i.e. dystrophy.

Electrical stimulation of immobilized rats brings about, together with reflex-induced gastric-wall dystrophy, destructive lesions in the liver. The lesions are preceded by an abrupt fall in the glycogen level, a decrease in proteins, and as in the gastric wall, a change in the structure and in the optic density of mitochondria, and an exhaustion of norepinephrine stocks. This form of neurogenic dystrophy of the liver was also subjected to the action of neurotropic agents. It was shown that barbiturates, gangliolytics, and adrenolytics prevent, to a certain extent, liver lesions induced in the animal by excessive irritation [Korkhov & Levin (43)].

As seen from pharmacological analysis, destructive lesions developing in the animal after excessive irritation are reflex in origin, but are accompanied by alterations in the function of endocrine glands. This leads to the investigation of the part played by hormones in the development of neurogenic dys-

trophies. Preliminary extirpation of the adrenals or the hypophysis [Anichkov & Zavodskaya (38); Korkhov & Levin (43)], as well as the administration of cortisone and ACTH to intact animals [Kachanov (44)], intensified the development of neurogenic dystrophies of the stomach and liver. Resistance of the gastric wall to the development of neurogenic dystrophy is, in a definite degree, conditioned by the function of genital glands. In male rats the lesions of the stomach, induced by electrical stimulation and immobilization, are far more pronounced than in females. Preliminary castration heightens the intensity of reflex dystrophies in females, as well as in males, and sex differences are abolished. Reflex dystrophies are similarly aggravated by preliminary administration of sex hormones [Botsolin (45, 46)]. It follows that in the case of corticosteroids, as well as in that of gonadotropic hormones, normal hormonal level ensures maximum resistance to neurogenic dystrophies in the gastric mucosa.

Hormones of the thyroid exert a definite influence on neurogenic dystrophy. Preliminary administration of thyroxine intensifies the development of reflex-induced gastric wall dystrophy, while extirpation of the thyroid lessens it [Denissenko & Poskalenko (47)]. This is probably attributable to the fact that the hormones of the thyroid enhance the action of the norepinephrine mediator.

Among the research studies carried on in the USSR in cardiovascular pharmacology, an important place is occupied by investigation of drug action upon cardiac neuroregulation. Intense work has been done during the last few years by Kaverina and co-workers at the Institute of Pharmacology and Chemotherapy in working out methods of pharmacological action upon the coronary flow. The basic method has been the resistography of the coronary vessels. Recording of the cardiac oxygen absorption has been carried on simultaneously, and in some experiments, the recording of the electric activity of extracardiac nerves has been added. Kaverina published, in 1963, in Moscow, the results of her investigations upon the action of various agents supposed to possess vasodilating properties. Her book entitled, *Pharmacology of the Coronary Circulation*, was published, with additions, in English by Pergamon Press (48).

One of the lines followed in the work of her laboratory is the investigation of possibility of controlling the central tonus regulation of the coronary vessels pharmacologically. After a series of experiments, the conclusion arrived at was that the positive effect of certain drugs, notably analgetics and inhibitors of monoaminoxydases, on the blood supply of the heart was a result of their ability to inhibit reflexes constricting the coronary vessels. Such mechanism of action, according to Kaverina, is also peculiar to nitrites. The analysis carried out in her laboratory of pharmacological actions upon the central processes conducive to the forming of coronary vasoconstrictive reflexes has led to the affirmation that nitrites, analgetics, and MAO-inhibi-

tors depress the spontaneous and reflex activity of the cardiac sympathetic nerves. Data have also been obtained indicative of connections existing between these effects and alterations in the monoamine metabolism in the central nervous system [Kaverina, Mirzoyan & Rozanov (49)].

A number of Soviet investigations have been devoted to the action of neurotropic agents upon the neurogenic affections of the heart. Vedeneyeva (Institute of Experimental Medicine) studied the pharmacology of neurogenic myocardial dystrophies. In order to obtain them, she developed a method of eliciting reflex-originated myocardial lesions in rats by submitting the aortic arch to an electric current, the electrodes being introduced into the lumen of the arch through the right carotid. Forty-eight hours after a three-hour stimulation in the majority of cases, destructive lesions developed in the myocardium, which produce multiple minute necrotic foci. These destructive changes caused by the irritation of the arch may be prevented by gangliolytics, presynaptic sympatholytics, and postsynaptic adrenolytics. The conclusion drawn is that myocardial dystrophy caused by extreme irritation of the aortic arch is the result of an excessive flow of sympathetic impulses [Vedeneyeva (50)]. This hypothesis is corroborated by the striking similarity of the cardiac lesions caused by aortic electrical stimulation and those following the administration of toxic doses of epinephrine, norepinephrine, and isoproterenol, the latter causing the most lesions. These facts are considered as arguments in favour of the thesis that myocardial lesions caused by exogenous catecholamines, and consequently, the lesions caused by an excessive flow of sympathetic impulses, are not the result of coronary vasoconstriction, but of metabolic disturbances in the myocardium [Vedeneyeva (51)].

In order to obtain neurogenic lesions in the myocardium Bendikov (Institute of Pharmacology & Chemotherapy) introduced a solution of potassium chloride into the lateral ventricle of the cerebrum. He considers the lesions obtained to be a result of an acute disturbance of coronary circulation. These lesions are prevented by nitrites, amizil and iproniazid, whose action the author considers to be central [Bendikov (52)].

Among the agents exerting a direct action upon the myocardium, those which have attracted the most attention of our pharmacologists are the cardiac glycosides of plants growing in the USSR. Particularly active work in this field is being done at the laboratory of M. A. Angarskaya (Kharkov Scientific Research Chemo-Pharmaceutical Institute). The treacle mustard (*Erysimum*), a most common weed, is one of the plants used in the USSR as a cardiac agent. Its chief glycoside, erysimin, was known previously, but now, another glycoside, erychroside, has been extracted from the same plant [Angarskaya, Bezruk & Lubetskaya (53); Lubetskaya, Bezruk & Angarskaya (54)]. The individual glycoside, homphotine, has been isolated from the plant, *Gomphocarpus fruticosus*; pharmacologically, it has very much in com-

mon with strophanthin [Angarskaya, Bezruk & Krivolutskaya (55)]. *Bowiea volubilis* is the source of the individual glycoside, bovaside A. Pharmacologically, it is related to the glycoside group of digitoxin [Angarskaya, Bezruk & Tkachenko (56)]. From the Far-Eastern variety of the lily of the valley (*Convallaria majalis var. manshurica Kom.*), several glycosides related to the glycoside convallatoxin have been obtained, viz, desglycoheirotoxin, convallatoxol, and locundiesid [Angarskaya, Lubartseva & Sokolova (57); Lubartseva, Angarskaya & Sokolova (58)].

The action of cardiac glycosides on certain enzymes of carbohydrate-phosphate metabolism has been studied at the Kiev Medical Institute by N. M. Dmitrieva (59), who is continuing the work initiated by her teacher, A. I. Cherkes, a member of the USSR Academy of Medical Sciences. Experiments were carried out on intact rats, as well as rats with experimental cardiac disorders. Increased phosphorylase activity, observed after administration of toxic doses of epinephrine ("energetic heart failure") was returned to normal under the action of cardiac glycosides. Equally corrected was the reduced phosphorylase activity of the myocardium accompanying heart failure, caused by methemoglobinemic anoxia of haemodynamic stress, after constriction of the abdominal aorta by means of a copper ring.

A. S. Saratikov (Tomsk Medical Institute) has been engaged in a comprehensive study of camphor, which is even now very extensively used as a heart tonic by Soviet physicians. Through investigation of the cardiotoxic effects of camphor on rabbits, cats, and rats, Saratikov has shown that subcutaneous administration of camphor corrects the metabolism of carbohydrates affected by experimental cardiac disorders, and increases cardiac sensitivity to the activating effect of the cardiac sympathetic nerve. These observations were summed up in a monograph, published by the author in 1966 (60).

In studying the direct action of pharmacological agents on the vascular wall, our pharmacologists have focused their attention on the biochemical aspect of this effect. The Ukrainian pharmacologist, F. P. Trinus, Head of Pharmacology at the Donetsk Medical Institute, has been investigating the constrictive effect of some vasomotor agents on strips of vessels recording tissue respiration simultaneously. He has reached the conclusion that norepinephrine and epinephrine which, at sufficiently high concentrations, cause intense constriction of the aorta, increase its tissue respiration, diminish the incorporation of labelled phosphorus in its tissues, and lower the level of ATP acid. On the contrary, acetylcholine and serotonin, which do not cause a full contraction of the smooth vascular muscles, have practically no effect upon the aforementioned aspects of vascular-wall metabolism [Trinus (61)].

In another work, F. P. Trinus, together with his teacher, A. I. Cherkes, has studied the importance of free thiol groups for the reactivity of vascular

α- and β-adrenoreceptors [Cherkes & Trinus (62)]. In order to bind thiol groups, they used salts of cadmium, and for their liberation, unithiol (potassium dithiopropane-sulphonate). They concluded that thiol groups participate in the interaction of α-receptors and catecholamines. No participation of thiol groups in the reactions of β-receptors with epinephrine has been detected.

Khadjai (Kharkov Scientific Research Chemo-Pharmaceutical Institute) has systematically studied the action of flavocoumarol and coumarins upon the smooth muscles of organs and vessels. He has investigated more than 30 materials of this class, extracted from various plants, whose preparations have medicinal value, and has established their structure-spasmolytic activity relationships [Khadjai & Kuznetsova (63); Khadjai, Obolentseva & Prokopenko (64); Obolentseva & Khadjai (65)].

A. A. Belous (Volgograd Medical Institute) has been engaged for many years in the study of vascular hypertension pharmacotherapy. She has worked out a simple and effective method of obtaining experimental hypertension in animals by means of repeated intravenous injections of posterior pituitary solutions. Such injections given every day for a period of two or three weeks produces in dogs and rabbits a steady hypertension which lasts several months, despite the cessation of injections. This simple experimental model of hypertension is being successfully used by Soviet pharmacologists [Belous & Hofman (66)].

During the last quinquennium, our pharmacologists have continued their investigation of agents capable of controlling cholesterolaemia and lipid concentration in the aorta of rabbits affected with experimental cholesterol atherosclerosis (N. N. Anichkov's artificial atherosclerosis). Several compounds, synthetized by I. B. Simon at the Ukrainian Scientific Research Institute of Endocrinology, possess anticholesterolaemic properties. Such are the aminoethanol salts of nicotine acid [Klebanov (67)], and of phenylacetic acid [Kozlovskaya (68)]. In the Department of Pharmacology at the Leningrad Chemo-Pharmaceutical Institute headed by T. A. Melnikova sodium-N_1-malonyl-bis-paraamino-benzoate has been tested and found efficient. According to data published by Turova, Gladkikh & Yatsin (29) positive results in the treatment of experimental atherosclerosis are obtained by using certain saponins.

Since the publication of the first article on Soviet pharmacology in the present Review many new pharmacological research units have appeared in the USSR, including: in Kiev, the Institute of Pharmacology and Toxicology; the newly formed Department of Gerontic Pharmacology at the Institute of Gerontology; and the Laboratory of Biochemical Pharmacology at the Ukrainian Academy of Sciences; in Leningrad, at the Institute of Evolutionary Physiology and Biochemistry, a pharmacological laboratory of corresponding profile; in Tashkent—a pharmacological laboratory at the Institute

of Chemistry of Vegetable Stuffs (Uzbek Academy of Sciences).

Soviet pharmacologists are members of the All-Union Pharmacological Society which has branches in all university cities. At present their number amounts to more than 600. The members take an active part in all international pharmacological congresses, reading papers and delivering lectures in various countries of the East and West. On the other hand, they receive with traditional Russian hospitality their numerous foreign colleagues, who come to the Soviet Union to take part in symposia or to make reports and communications.

In May 1967 on the initiative of the President of the Finnish Pharmacological Society, Prof. Vartiainen, and the Board of Administration of the Leningrad Pharmacological Society, there took place, in Leningrad, a joint meeting of both societies, at which the Finnish pharmacologists reported their achievements.

Soviet pharmacologists are ardent partisans of international friendship uniting all scientists, regardless of race, religion and social system, and are eagerly striving for peace in the whole world.

LITERATURE CITED

1. Torf, S. F., *Med. promyshl. SSSR*, **7**, 26–29 (1965)
2. Denissenko, P. P., *Central Cholinolytics* (Meditsina, Moscow, 279 pp., 1965)
3. Ilyuchonok, R. Y., *Neurohumoral Mechanisms of Brain-stem Reticular Formation* (Nauka, Moscow, 258 pp., 1965)
4. Lossev, N. A., *XXI Conf. Problems of Higher Nervous Activity*, 185 (Leningrad, 1966)
5. Golikov, S. N., Razumova, M. A., Selivanova, A. T., *Farmakol. i Toksikol.*, **28**, 1, 20–23 (1965)
6. Anichkov, S. V., Borodkin, Y. S., *X Cong. Physiol. USSR*, 62–63 (Erevan, 1964)
7. Kharkevich, D. A., *Farmakol. i Toksikol.*, **29**, 6, 715–20 (1966)
8. Podlesnaya, A. I., *1960 Year-Book Inst. Exptl. Med.*, 262–66 (Medgiz, Leningrad, 1961)
9. Podlesnaya, A. I., *Farmakol. l Toksikol.*, **25**, 5, 538–43 (1962)
10. Podlesnaya, A. I., *Farmakol. i Toksikol.*, **29**, 4, 409–12 (1966)
11. Khromov-Borisov, N. V., Michelson, M. J., *Pharmacol. Rev.*, **18**, 3, 1051–90 (1967)
12. Mashkovsky, M. D., Zaitseva, K. A., *Farmakol. i Toksikol.*, **23**, 5, 398–406 (1960)
13. Arbusov, S. Y., In *Present Problems of Pharmacology*, 206–17 (Meditsina, Moscow, 1963)
14. Arbusov, S. Y., Smirnova, S. M., *Farmakol. i Toksikol.*, **27**, 4, 420–23 (1964)
15. Arbusov, S. Y., Aleksandrova, A. E., Smirnova, S. M., *Farmakol. i Toksikol.*, **29**, 5, 521 (1966)
16. Wu, Hsi-Tui Baibekov, E. B., *Farmakol. i Toksikol.*, **24**, 1, 22–30 (1961)
17. Fedyayeva, L. P., *Farmakol. i Toksikol.*, **28**, 5, 515–17 (1965)
18. Borodkin, Y. S., *Antifeines* (Meditsina, Moscow, 205 pp., 1966)
19. Borodkin, Y. S., Kostin, E. D., *Vestn. khirurg. im. Grekova*, **8**, 84–88 (1963)
20. Burov, Y. V., *J. Nevropatol. Psikhiat.*, **1**, 129–34 (1966)

21. Zakussov, V. V., *Intern. Cong. Pharmacol., III*, 104 (São Paulo, 1966)
22. Sinitsin, L. N., *Intern. J. Neuropharmacol.*, **3**, 325–26 (1964)
23. Kruglov, N. A., *Intern. J. Neuropharmacol.*, **3**, 197–203 (1964)
24. Sangailo, A. K., *Farmakol. i Toksikol.*, **26**, 2, 138–44 (1963)
25. Mashkovsky, M. D., Zaitseva, K. A., *Farmakol. i Toksikol.*, **25**, 1, 32–37 (1962)
26. Mashkovsky, M. D., Trubitsina, G. K., *J. Nevropatol. Psikhiat.*, **1**, 72–79 (1963)
27. Valdman, A. V., *Actual Problems in the Pharmacology of the Reticular Formation and Synaptic Transmission* (Meditsina, Leningrad, 415 pp., 1963)
28. Valdman, A. V., Pharmacology and Physiology of the Reticular Formation, 1–92. In *Progress in Brain Research*, Vol. **20** (Valdman, A. V., Ed., Elsevier, Amsterdam, 1967)
29. Turova, A. D., Gladkikh, A. S., Yatsin, A. J., In *Pharmacology of Cardiac Drugs*, 198–204 (Zdorovya, Kiev, 1965)
30. Brekhman, I. I., Dardymov, I. V., Dobriakov, Y. I., *Farmakol. i Toksikol.*, **29**, 2, 167–71 (1966)
31. Mashkovsky, M. D., *Medicinal Remedies* (Meditsina, Moscow, vol. I—706 pp., vol. II—462 pp., 1967)
32. Ryzhenkov, V. E., *1961–62 Year-Book Inst. Exptl. Med.*, **7–8**, 2, 179–82 (1963)
33. Ryzhenkov, V. E., Pitkovskaya, E. N., Livshitz, R. S., *Sovetsk. Med.*, **4**, 127–31 (1967)
34. Ryzhenkov, V. E., Romankova, M. P., Grekh, I. F., Bognibov, E. A., *Khirurgia*, **8**, 103–8 (1966)
35. Anichkov, S. V., Grechishkin, L. L., *Farmakol. i Toksikol.*, **28**, 5, 587–90 (1965)
36. Anichkov, S. V., Grechishkin, L. L., *Arch. Intern. Pharmacodyn.*, 166, 2, 417–23 (1967)
37. Grechishkin, L. L., *Farmakol. i Toksikol.*, 26, 1, 36–40 (1963)
38. Anichkov, S. V., Zavodskaya, I. S., *Pharmacotherapy of Gastric Ulcer* (Meditsina, Leningrad, 188 pp., 1965)
39. Zavodskaya, I. S., *Symp. Action of Neurotropic Drugs on Trophic Processes and Tissue Metabolism*, 38 (Leningrad, 1966)
40. Moreva, E. V., *Symp. Action of Neurotropic Drugs on Trophic Processes and Tissue Metabolism*, 62–63 (Leningrad, 1966)
41. Moreva, E. V., In *Problems of Pharmacology and Experimental Therapy*, 26–28 (Meditsina, Leningrad, 1966)
42. Grechishkin, L. L., *Symp. Action of Neurotropic Drugs on Trophic Processes and Tissue Metabolism*, 29–30 (Leningrad, 1966)
43. Korkhov, V. V., Levin, V. N., In *Problems of Surgical Pathology*, 78–82 (Med. Pediatric Inst., Leningrad, 1965)
44. Kachanov, A. D., *Symp. Gastric Ulcer*, 12–13 (Leningrad, 1965)
45. Botsolin, P. S., *Zhurn. Zdravoökhranenie*, **5**, 39–40 (Kishinev, 1966)
46. Botsolin, P. S., In *Problems of Pharmacology and Experimental Therapy*, 31 (Meditsina, Leningrad, 1966)
47. Denissenko, P. P., Poskalenko, A. N., *Symp. Action of Neurotropic Drugs on Trophic Processes and Tissue Metabolism*, **35** (Leningrad, 1966)
48. Kaverina, N. N., *Pharmacology of Coronary Circulation* (Pergamon Press, Oxford, 1965)
49. Kaverina, N. N., Mirzoyan, R. S., Rozanov, Y. B., *Farmakol. i Toksikol.*, **28**, 6, 689–94 (1965)
50. Vedeneyeva, Z. I., *Symp. Action of Neurotropic Drugs on Trophic Processes and Tissue Metabolism*, 18–19 (Leningrad, 1966)
51. Vedeneyeva, Z. I., *Farmakol. i Toksikol.*, **25**, 3, 286–91 (1962)
52. Bendikov, E. A., *Farmakol. i Toksikol.*, **27**, 6, 695–99 (1964)
53. Angarskaya, M. A., Bezruk, P. I., Lubetskaya, J. A., *Farmakol. i Toksikol.*, **29**, 1, 39–43 (1966)
54. Lubetskaya, J. A., Bezruk, P. I., Angarskaya, M. A., *Farmakol. i Toksikol.*, **29**, 2, 80–83 (1966)
55. Angarskaya, M. A., Bezruk, P. I., Krivolutskaya, S. A., *Soviet. Meditsina*, **11**, 28–31 (1966)
56. Angarskaya, M. A., Bezruk, P. I., Tkachenko, D. A., *Farmatsevt. Zhurn.*, **1**, 77–79 (1965)
57. Angarskaya, M. A., Liubartseva, L. A., Sokolova, V. E., *Farmakol. i Toksikol.*, **26**, 6, 687–93 (1963)
58. Liubartseva, L. A., Angarskaya, M. A., Sokolova, V. E., *Farmakol. i Toksikol.*, **28**, 6, 653–56 (1965)

59. Dmitrieva, N. M., In *Pharmacology of Cardiac Drugs*. 28–33 (Zdorovya, Kiev, 1965)
60. Saratikov, A. S., *Kamphara* (Tomsk Univ., Tomsk, 272 pp., 1966)
61. Trinus, F. P., In *Pharmacology of Cardiac Drugs*, 87–94 (Zdorovya, Kiev, 1965)
62. Cherkes, A. I., Trinus, F. P., In *Problems of General and Age Pharmacology*, 170–76 (Meditsina, Leningrad, 1965)
63. Khadjai, J. I., Kuznetsova, V. V., *Farmatsevt. Zhurn.*, **1**, 77–79 (1966)
64. Khadjai, J. I., Obolentseva, G. V., Prokopenko, A. P., *Farmakol. i Toksikol.*, **29**, 2, 156–62 (1966)
65. Obolentseva, G. V., Khadjai, J. I., *Farmakol. i Toksikol.*, **29**, 4, 469–72 (1966)
66. Belous, A. A., Hofman, S. M., *Farmakol. i Toksikol.*, **27**, 5, 584–86 (1964)
67. Klebanov, B. M., In *Pharmacology of Cardiac Drugs*, 193–94 (Zdorovya, Kiev, 1965)
68. Kozlovskaya, O. I., In *Pharmacology of Cardiac Drugs*, 189–92 (Zdorovya, Kiev, 1965)

CONTENTS