The XIIIth International Congress of Pharmacology convened in Münich’s Convention Hall from July 26 through July 31. It consisted of nearly 3000 lectures, short presentations, or posters. Nearly 4000 scientists were registered at the Congress. This report covers only posters devoted to the new CNS drugs.

**MEMORY ENHANCING DRUGS**

**M. Csejtei et al.** (Gedeon Richter Ltd., Budapest, Hungary) reported pharmacological studies with RGH-2716 (8-{4,4-bis(4-fluorophenyl)butyl}-3-1,1-dimethylethyl)-4-methylene-1-oxa-3,8-diazaspiro{4,5}decan-2-one), known also as TDN-345. This drug was reported to protect ischemic brain tissue from energy loss in mice at doses ranging from 3 to 30 mg/kg i.p. At 0.1 to 10 μM it blocked veratridine-induced release of [3H]dopamine or [3H]norepinephrine in rat brain slices. It is thought to prevent elevation of intracellular Ca^{2+} levels and inhibit voltage-gated Na^{+} channels in neurons. Gedeon Richter Ltd. is developing RGH-2716 as a memory-enhancing and neuroprotective drug in collaboration with Takeda Chemical Industries of Japan.

**M. Paroczai et al.** (Gedeon Richter Ltd., Budapest, Hungary) reported behavioral effects of RGH 5279 ([–]-transapovincaminic acid-[acetoxy]ethyl ester [3b, 16α]) in rats. RGH-5279 was previously reported to have neuroprotective activity and to inhibit lipid peroxidation in animals. It was now found to antagonize learning and memory deficits induced by diazepam or scopolamine in young rats in the water labyrinth test. It was effective in a retrograde amnesia model at doses as low as 3 mg/kg p.o. It was also effective as a cognition enhancer in rats with basal forebrain lesions.

**K. Iwasaki et al.** (Fukuoka Univ., Japan) reported that the muscarinic (M₁) partial agonist SB202026A ([R-(Z)]-α-(methoxyimino)-1-azabicyclo{2,2,2}octane-acetonitrile monohydrochloride) improved deficits in spatial cognition induced by scopolamine, pilenazepine, or experimental brain ischemia in rats. At doses as low as 1 μg/kg i.p., SB202026A decreased errors in radial maze task. The drug is under development for the treatment of Alzheimer’s disease.

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M. Nanri et al. (Taiho Pharmaceutical Co., Tokushima, Japan) found that GTS-21 (3-[2,4-dimethoxybenzylidene]anabaseine, also known as DMXB), a novel nicotinic agonist, reduced brain damage and cognitive deficits produced by permanent occlusion of bilateral common carotid arteries in rats. The drug was administered at 1 or 10 mg/kg p.o. at 24 h and 30 min before and once a day for 2 months after occlusion of the arteries.

Ma Yong-Xing et al. (Huadong Hospital, Shanghai, China) reported the results of clinical trials with huperzine A, an alkaloid from Huperzia Serrata (Thumb) Trev, a potent anticholinesterase agent, in 314 patients with impaired cognition and/or dementia. Huperzine A, at 0.03 mg i.m., b.i.d. for 15 d, improved cognitive function (memory quotient) in 60% of patients as compared to 35% in the control group.

R. U. Ostrovskaya et al. (Institute of Pharmacology, RAMS, Moscow, Russia) presented two posters on the cognition-restoring activity of GVS-111 (N-phenylacetylprolylglycin), a small peptide, in rats. It antagonized memory deficits caused by scopolamine, frontal lobectomy, and brain compression. It also normalized behavioral disturbances of the offspring caused by prenatal hypoxia, alcohol, or morphine. At doses from 0.1 mg/kg i.p. or p.o. it facilitated learning in the step-through passive avoidance or active avoidance tests in rats. GVS-111 appears to facilitate input of information, consolidation and retrieval processes. It may act as a pro-drug facilitating the formation of cyclo-L-prolylglycine. The effects of GVS-111 in avoidance tests in rats were previously described (Behav Pharmacology 1997;8:261–268) and a US patent was obtained (#5,439,930) in 1995.

N. Hamaue et al. (Dept. of Pharmacology, Hokkaido Univ., Japan) found that isatin, an endogenous monoamine oxidase (MAO) inhibitor, increases dopamine and acetylcholine levels in rat brain. It has a higher affinity for MAO than for acetylcholinesterase (AChE), although it inhibits both enzymes. Isatin increases acetylcholine release in the rat brain at concentrations lower than required for the inhibition of AChE. It was, therefore, proposed that isatin increases acetylcholine concentrations indirectly through dopamine acting on D₁ or D₂ receptors.

Zhang Juntian et al. (Institute of Materia Medica, Chinese Academy of Medical Sciences, Beijing, China) submitted an abstract on the nootropic activity of (–)clausenamide, an alkaloid isolated from Clausena lansium. This substance was reported to increase intracellular calcium and to promote glutamate release LTP production, and protein expression in hippocampus. It was claimed to ameliorate amnesia. It was suggested that it may even improve intelligence in normal adults.

T. L. Garibova et al. (Institute of Pharmacology, RAMS, Moscow, Russia) reported that nooglutil (N-5[hydroxynicotinoyl]-L-glutamic acid) antagonizes benzodiazepine withdrawal syndrome. Nooglutil was previously described by the same group to improve learning and memory in a variety of behavioral tests. Its antiamnesic effect is apparently mediated through AMPA receptors. Nooglutil is currently in clinical trials as an antiamnesic agent.

**NEUROPROTECTIVE AND ANTICONVULSANT DRUGS**

G. Gigler et al. (Egis Pharmaceuticals Ltd., Budapest, Hungary) found that selective AMPA/kainate antagonists (benzodiazepines, 3-N-substituted 3,4-reduced analogs of GYKI-52466 (1-[4-aminophenyl]-4-methyl-7,8-methylenedioxy-5H-2,3-benzodiazepine))
have neuroprotective and anticonvulsant effects. These drugs had antiischemic effects in
ergibils subjected to bilateral carotid artery occlusion and in mice with MgCl₂-induced
global cerebral ischemia. In this respect, the analogs were more potent than GYKI-52466
(PD₅₀ = 8 vs. 24 mg/kg i.p.). They also protected mice from electroshock- or sound-in-
duced convulsions at doses three times lower than GYKI-52466.

M. Niva et al. (Gifu Univ., Japan) found that N-tosyl-L-phenylalanine chloromethyl
ketone (TCPK) protects hippocampal neurons from delayed death (48 to 72 h after ische-
mic insult) induced in gerbils by forebrain ischemia. In the surviving neurons, TCPK in-
duced formation of Bel-2, an apoptosis-regulating protein.

A. Rostock et al. (Asta Medica AG, Radebeul, Germany) described broad-spectrum
anticonvulsant and anxiolytic effects of AWD 131-138 (1-[4-chlorophenyl]-4-morpho-
lino-2H,5H-imidazole-2-one). In anticonflict test in rats it was effective at doses as low as
3 mg/kg p.o. At 10 mg/kg p.o. it was also effective in the elevated maze test. Unlike di-
azepam, AWD 131-138 produced no ataxia in rats at doses up to 500 mg/kg, and at doses
up to 200 mg/kg it did not potentiate ethanol. It had only a weak affinity for the benzo-
diazepine binding site of the GABAₐ receptor complex. In kindled rats, AWD 131-138,
10 mg/kg p.o. elevated the seizure threshold. It was effective in all conventional models
of chemically induced seizures as well as in the genetic model of epilepsy. The therapeutic
index of AWD 131-138 was better than that for standard anticonvulsants.

ANTIDEPRESSANT DRUGS

J. Maj et al. (Polish Academy of Sciences, Krakow, Poland) reported that repeatedly
given pramipexole (PRA; 2-amino-4,5,6,7-tetrahydro-6-propyl-aminobenzthiazole dihyd-
rochloride) enhanced the responsiveness of D₂ and D₃ receptors in rats. It increased the
binding of [³H]spiperone to D₂ receptors in the mesolimbic system but not in caudate pu-
tamen. It also increased the binding to receptors in Calleja islands. PRA increased ð-am-
phetamine-induced hypermotility and reduced immobility of rats in the forced swimming
test. PRA appears to be useful in the treatment of depression as well as of Parkinson’s
disease.

ANTIPSYCHOTIC DRUGS

Laszlovszky et al. (Gedeon Richter Ltd., Budapest, Hungary) described the pharma-
cology of a potential atypical antipsychotic, RGH-1756 (1-(2-methoxy-phenyl)-4-
{4[6-imidazo-[2,1-b]thiazolyl]-phenoxy|butyl|piperazine). In binding studies this drug
had a very high affinity for human D₃ receptors (IC₅₀ = 0.2 nM) and lesser affinity for
human D₂L or 5-HT₂A receptors. It increased dopamine turnover in mouse forebrain (ED₃₀
= 15.7 µmol/kg p.o.) and reduced 5-HT turnover (ED₃₀ = 52.4 µmol/kg p.o.). The effects
of RGH-1756 were more pronounced in mice than rats. The in vivo profile of RGH-1756
resembled more D₂ than D₃ antagonists. At antipsychotic doses, RGH-1756 had no
prolactin-releasing activity and is expected to have little or no Parkinsonian side effects.
ANTIEMETIC DRUGS

T. Yoshikawa et al. (Dainippon Pharmaceutical Co., Osaka, Japan) discovered a new broad spectrum antiemetic, AS-8112, with fewer CNS side effects than currently available antiemetic agents. It had high affinity for D₂, D₃, and 5-HT₃ receptors. It was as potent as ondansetron in inhibiting emesis induced by cytotoxic agents and as effective as domperidone in antagonizing apomorphine-induced emesis. At antiemetic doses it had little or no CNS depressant effects. AS-8112 is (R)-(−)-5-bromo-N-(1-ethyl-4-methyl-hexahydro-1H-1,4-diazepin-6-yl)-2-methoxy-6-methylamino-3-pyridine-carboxamide • 2 fumarate.

ANTINOCICEPTIVE DRUGS

Kaori Inoue et al. (Faculty of Pharmaceutical Sciences, Meijo University, Nagoya, Japan) reported antinociceptive effects of a novel dynorphin analog, SK-9709, Tyr-D-Ala-Phe-Leu-Arg (GHD₂NH)Arg-NH₂. It was administered by subcutaneous, intracerebroventricular, and intrathecal injections to mice and found effective in hot plate and acetic acid writhing tests. It was less potent than morphine, but its effects were long lasting. The effects of SK-9709 appeared to be mediated by spinal and supraspinal κ-opioid receptors.

ANTIMIGRAINE DRUGS

J. M. Novalbos et al. (Universidad Autonoma de Madrid, Spain) studied the pharmacology of dotarizine, a flunarizine-like Ca²⁺ antagonist, that was found effective in clinical trials in prophylaxis of migraine. In bovine adrenal chromaffin cell cultures, dotarizine was less cytotoxic than flunarizine. At 3 to 30 μM, dotarizine blocked P/Q type Ca²⁺ channels in these cells. The authors suggested that the antimigraine effects of dotarizine may represent the consequence of blockade of P/Q type Ca²⁺ currents, leading to reduction of neuropeptide release. According to V. D. Petkov et al. (Bulgarian Academy of Sciences, Sofia, Bulgaria), dotarizine is also an antagonist at 5-HT₁A and 5-HTD₂ receptors and blocks K⁺-induced 5-HT release in rat hippocampal slices. Unlike flunarizine, dotarizine reduces prolactin release. It is less likely than flunarizine to produce extrapyramidal side effects. Dotarizine is 1-(diphenylmethyl)-4-[3-(2-phenyl-1,3-dioxalan-2-yl)propyl]piperazine.

G. W. John et al. (Centre de Recherche Pierre Fabre, Castres Cedex, France) described, pharmacological effects of a new 5-HT₁B/₁D antagonist, F 11356. It has a subnanomolar affinity and high selectivity for human 5-HT₁B and 5-HT₁D receptors. In functional assays, F 11356 acted as an agonist at the same receptors. F 11356 was found to selectively constrict carotid arteries in dogs and was active orally at 0.16 to 2.5 mg/kg p.o.. F 11356 is 4-(4-{2-[3-(2-aminoethyl)-1H-indol-5-ytoxy]-acetyl}-piperazine-1-yl)-benzonitrile HCl.