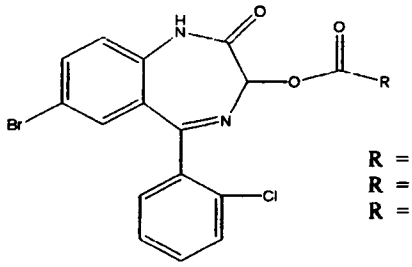

$R = C_5H_{11}$ $R = C_{13}H_{27}$
$R = C_8H_{17}$ $R = C_{15}H_{31}$
$R = C_{11}H_{23}$ $R = C_{17}H_{35}$

Anticonvulsive activity according to DCTC and DTE values is higher than control at 1.8–2.8 and 1.8–2.4 times, respectively. The maximal activity of studied esters is detected 3 hours after administration.

P.3.035 The profile of anti-anxiety action of tofisopam in the treatment of generalized anxiety disorder

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Statement of the study: Tofisopam, which belongs to 2,3-benzodiazepines, i.e., homophtalazines, seems to have different mechanisms of action than other benzodiazepines, although they still remain unrevealed. Their anxiolytic properties are related to their specific binding to the basal ganglia (Horvath et al. 2000). Results of multicenter, randomized, double blind comparison of tofisopam (150 mg/d) and hydroxyzine (75 mg/d) in a group of 51 patients, with generalized anxiety disorder, indicated the same reduction of anxiety symptoms measured by Hamilton Anxiety Rating Scale after 2 weeks and after 6 weeks of treatment. In the study of Kokoszka and Bryła (2004) 66 patients, aged 19–74 M = 41.4 DS 13.2 with generalized anxiety disorders were randomized for two weeks of the treatment of tofisopam (50 mg three times a day), diazepam (5 mg three times a day), or placebo group. The mean decrease in Hamilton Anxiety Rating Scale score was significantly higher than in placebo group both in tofisopam ($p < 0.001$) and diazepam group ($p < 0.001$). This paper is aiming at the presentation of the data on profile of the action of tofisopam found in this study.

Methods: The anxiety symptoms were measured with items of Hamilton Anxiety Rating Scale, whereas other neurotic symptoms were measured with the self-rating symptoms check list S-II (Aleksandrowicz, 2000), a Polish derivate of Derogatis SCL-90, that measures subjective experiencing of symptoms by patients.

Results: The mean decrease of symptoms in S-II list was statistically significantly higher in the tofisopam than placebo group (M = 87.6 versus 38.6; $t = -2.16$, $p < 0.005$) and there was no statistically significant difference between tofisopam and diazepam groups (M = 87.6 versus 81.7; $t = 0.22$, $p > 0.80$).

After two weeks of treatment with tofisopam statistically significant changes in Wilcoxon's test were found in:
Items of HARS
- At $p < 0.001$: anxiety, tension, intellectual, respiratory, cardiovascular symptoms
- At $p < 0.004$: depressed mood
- At $p < 0.005$: fears, insomnia
- At $p < 0.002$: autonomic symptoms and behavior at interview
- At $p < 0.05$: gastrointestinal symptoms

Items of S-II
- At $p < 0.001$: dystymia
- At $p < 0.002$: anxiety, insomnia
- At $p < 0.003$: somatic, intellectual dysfunctions
- At $p < 0.05$: social dysfunctions, dissociatio

Conclusions: Tofisopam is effective in the treatment of a wide variety of symptoms related to anxiety. In the self-report scale tofisopam was similarly effective as diazepam and statistically more effective than placebo.

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P.3.036 Novel anxiolytic Selank: results of the Phase II clinical trials

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One of the recent trends in the design of novel psychotropic medicines is creation of anxiolytics on the basis of an endogenous neuropeptide structure. During long-term fundamental research at Zakusov State Institute of Pharmacology and the Institute of Molecular Genetics an original synthetic heptapeptide derivate of taftsin, Selank, was developed. Experimental study of Selank

activity revealed anxiolytic, activating and stimulatory effects on mnestic and cognitive functions. Effects of the drug are realized through catecholamine and serotonin systems modulation, influence on the activity of enzymes of monoamine biosynthesis and inhibition of encephaline-degradating enzymes. Clinical trials of Selank drops for intranasal administration (0.15%) were carried out on 21 patients aged 18–45 years with psychogenic anxiety disorders, who did not previously respond to placebo administration. The state of patients was examined with standardized clinical scales, psychological methods and pharmaco-EEG. Single dose of Selank was 900 μg, course dose was 2700 μg. Analysis of clinical pharmacological data showed that action of the single dose of Selank started 30–40 min after intranasal administration and lasted during a period of 6–12 hours. Initial tranquilo-activating effect was found in 67% of patients. It was manifested as reduction of anxiety, emotional and muscular tension, restlessness and fatigability, and improvement of activity and ability to work. Tranquilizing and tranquilo-sedative reactions after drug administration, that are typical for benzodiazepines, were rare. Continuous administration of Selank was characterized by harmonic association of anxiolytic and stimulatory effects. Anxiety, irritability, affective liability reduced rapidly after 1–3 days of therapy. At the same time, significant decrease in fatigue, apathy, psychomotor retardation and somnolence were observed. These changes reflex both anxiolytic and antiasthenic effects. Positive influence on hypothymia was also observed. At the same time administration of Selank was associated with normalization of sleep and decrease of vegetative disorders. It is interesting that in 15 (71%) patients the psychopathological symptoms reduced critically in the initial days of therapy. In another 29% of patients the improvement was gradual. It was found that Selank was effective in case of a 5-days course therapy: significantly marked improvement was observed in 81% of patients, mild improvement – in 19% of patients. Selank was well tolerated with no adverse effects. During the EEG-analysis of Selank action most significant changes were observed in the frontal part of the brain cortex. These EEG data indicate that Selank action is characterized by the following: tranquilizing (because of increase in frequencies of beta-1-rhythm typical for anxiolytics) and nonspecific activating effect, which is characterized by the direction of changes in delta-rhythm. These findings of alpha-rhythm (with its overall amplitude increase) are typical for nootrops and psychostimulators. The data of these clinical trials suggest that Selank could be employed as a medicine for correction of anxious and anxious-asthenic disorders.

P.3.037 Results of clinical study of ladasten, a drug with stimulatory and anxiolytic activity

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Phase II of clinical trials of a new drug ladasten (N-(2-adamantyl)-N-(n-bromophenyl)amine), whose spectrum of activity combines psychostimulatory and anxiolytic action, is carried out. Research is carried out on 30 patients aging from 18 to 50 years and having psychogenic asthenic disorders with the diagnosis "Neurasthenia F48.0" according to ICD-10. The drug was applied as monotherapy. The design of the study included a preliminary placebo-control stage. To estimate the drug action the study employed clinical dynamic symptomatic scale, Hamilton's anxiety rating scale, Spielberger's rating scale, scale of Clinical General Impression, self-estimation test, psychophysiological testing and pharmaco-EEG analysis. The results of the study supported presence of psychostimulatory and anxiolytic properties of ladasten, with prevalence of psychostimulatory effect. In contrast to typical psychostimulants ladasten possessed harmonious rather "balanced" action and only rarely expressed superfluous stimulation. Ladasten improved psychophysiological parameters of attention, success of operation performance and complex senso-motor functions and worsened the quality of choice performance. Ladasten increased alpha-rhythm power within the range of 10–12.5 Hz, typical for psychostimulant action. Less prominent was an increase in power of beta-1-rhythm in the range of 15–17 Hz, which is a typical EEG-pattern for anxiolytics. There was no significant change in delta and theta rhythms after ladasten as compared with placebo. Ladasten was found highly efficient in patients with asthenic disorders. The drug was well tolerated and safe. These data prove that this drug has perspective for medical use.

P.3.038 Peculiarities of action of anxiolytic afobazole in patients from different typological groups

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One current aspect of modern clinical psychopharmacology is research on individual differences in effects of psychotropic drugs. This problem is especially important in