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STUDY OF THE EFFECT OF AQUEOUS EXTRACTS AND TINCTURES FROM FEIJOA LEAVES AND FRUITS ON BIOCHEMICAL PARAMETERS OF BLOOD IN HYPOTHYROID RATS

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This article presents a study of the effect of aqueous extracts and 30% alcohol tinctures from Feijoa leaves and fresh fruits on biochemical parameters of metabolism in hypothyroidism in rats. Experimental hypothyroidism was induced by 0,05% aqueous solution of merkazolil given to rats instead of drinking water for 30 days. Investigated extracts and tinctures were given to hypothyroid rats at a dose of 1 ml/100 g of body weight for 21 days. The effectiveness of studied substances was assessed by the content of thyroxine, triiodothyronine, alanine aminotransferase, aspartate aminotransferase, creatine kinase, lactate dehydrogenase, total protein, albumin, urea, creatinine, cholesterol, triglycerides and glucose in blood serum. Experimental hypothyroidism led to a decrease of thyroid hormones content, an increase of urea, creatinine, creatine kinase, cholesterol and glucose content. But the levels of alanine aminotransferase, aspartate aminotransferase, lactate dehydrogenase, total protein and albumin weren't significantly changed. As a result of the experiment, it was found that the treatment of hypothyroid rats with the extracts and tinctures from Feijoa leaves and fresh fruits led to a decrease in cholesterol, triglycerides, urea, creatinine, ALT and creatine kinase and an increase in serum glucose levels in animals.

Key words: *Feijoa leaves, Feijoa fruits, experimental hypothyroidism, mercazolil, thyroid hormones.*

Connection of publications with planned research works.

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Introduction.

Pathology of the endocrine system occupies a leading position in the structure of the total morbidity of the population. In recent years, the level of endocrinological diseases has tended to increase both worldwide and, in our country [1-2]. There is an increase in the number of patients with various endocrinopathies, one of the most common of which is thyroid disease. Increased interest in the problems of thyroid pathology in Ukraine in recent years has been caused by its growing prevalence among the adult population, high incidence of temporary and permanent disability [3-4]. Thyroid pathology accounts for 46% of the total endocrinological morbidity, given the fact that thyroid diseases include I-III-degree goiter (18.6%), nodular goiter (9.8%), hypothyroidism (6.4%), thyroiditis (5.9%), thyrotoxicosis (1.7%) and thyroid cancer (4,3%) [5-7].

Disruption of the functional activity of the thyroid gland leads to changes in metabolic processes and, as a result, imbalances in the homeostasis system. A special role in ensuring adaptation is played by hormones synthesized by the thyroid gland – thyroxine and triiodothyronine, which affect a wide range of metabolic and physiological processes. The effects of thyroid hormones on the cardiovascular system are well studied. Thyroid hormones regulate the processes of systolic contraction and diastolic relaxation of the heart muscle, overall peripheral vascular resistance, and the synthesis of myocardial structural proteins. Thyroid hormones regulate the activity of the apoB receptor in hepatocytes by genomic and non-genomic means, thus affecting the catabolism of atherogenic low-density lipoproteins. In the case of hypothyroidism, atherogenic dyslipidaemia, hyperhomocysteinaemia, and insulin resistance are commonly detected. Thus, thyroid dysfunction is one of the endocrine pathologies that is associated with metabolic disorders in most cases [8-12].

It should be noted that to date, the treatment of hypothyroid conditions has mainly involved replacement therapy – thyroid hormone preparations, or therapy aimed at restoring iodine deficiency – iodine preparations [13, 14]. Correction of biochemical parameters in thyroid dysfunction may be associated with the intake of thyroid hormones and biologically active substances into the bloodstream from drugs used to treat metabolic disorders [15]. Medicinal plants are the most promising source of biologically active substances. The expediency of studying medicinal plants in this area is determined by the wide range of their pharmacological effects and relative safety during long-term use [15, 16].

One of the promising plants containing a complex of biologically active substances is Feijoa (*Feijoa sellowiana Berg.*). As a result of phytochemical studies, the presence of iodine and 14 other elements (calcium, potassium, silicon, sodium, etc.) was found in the leaves and fresh fruits of Feijoa. We have identified 32 biologically active substances of various chemical groups (phytosterols, saturated hydrocarbons, aldehydes and ketones, fatty acids, etc. The results of our preliminary screening studies on healthy rats showed the presence of thyroid-stimulating effects of Feijoa fruits and leaves in the form of aqueous extracts and alcohol tinctures [17].

The aim of the study.

To investigate the effect of aqueous extracts and alcoholic tinctures from Feijoa leaves and fresh fruits on biochemical parameters in the blood serum of rats with experimental hypothyroidism.

Object and methods of research.

The experiments were conducted on white nonlinear male rats weighing 120-150 g in accordance with the requirements of the NUPh Bioethics Committee and the General Ethical Principles for Animal Experiments (Kyiv, 2001), which are consistent with the provisions of the

European Convention for the Protection of Vertebrate Animals Used for Experimental or Other Scientific Purposes (Strasbourg, 1986). The rats were kept in standard vivarium conditions under natural light and diet recommended for this species.

The objects of the study were aqueous extract from Feijoa leaves (AEFL), 30% alcoholic tincture from Feijoa leaves (TFL), aqueous extract from fresh Feijoa fruits (AEFF) and 30% alcoholic tincture from fresh Feijoa fruits (TFF), obtained at the Department of Quality, Standardization and Certification of Medicines of the National University of Pharmacy and standardized in accordance with the requirements of the State Pharmacopoeia of Ukraine and the European Pharmacopoeia. Experimental hypothyroidism was induced by daily administration of an aqueous solution of mercazolil (500 mg per 1 l) provided by FC "Zdorovye LLC" instead of drinking water for 30 days [18]. The experimental animals were divided into 6 groups of 10 rats each: Group 1 – intact control (IC), Group 2 – rats treated with the thyrostatic mercazolil (control pathology (CP), Group 3 – hypothyroid rats treated with AEFL, Group 4 – hypothyroid rats treated with TFL, Group 5 – hypothyroid rats treated with AEFF, Group 6 – hypothyroid rats treated with TFF. The studied objects were administered intragastrically to animals of the 3rd – 6th experimental groups for 21 days, starting from the 13th day of mercazolil administration, at a dose of 1 ml/100 g of body weight.

At the end of the experiment, the animals were surgically sacrificed and autopsied. Functional activity of the thyroid gland was assessed by the content of thyroid hormones in the blood serum – triiodothyronine (T3) and thyroxine (T4) by enzyme-linked immunosorbent assay using test systems (Granum LLC). Among the biochemical parameters in the blood serum, the content of alanine aminotransferase (ALT), aspartate aminotransferase (AST), creatine kinase (CK), lactate dehydrogenase (LDH), total protein, albumin, urea, creatinine, cholesterol (CHO), triglycerides (TG) was determined using Biosystems test kits (Spain). Glucose content was determined using a One Touch Ultra glucometer.

Statistical analysis of the results was performed using the standard statistical software package "Statistica 6.0". The obtained experimental data are presented as the arithmetic mean ($\bar{x}$), its error (±S). Statistical processing of the results was performed using a nonparametric analogue of one-factor analysis of variance – the Kruskal-Wallis test, followed by the Mann-Whitney test. Differences between the groups were considered significant at the accepted level of statistical significance $p<0.05$ [19].

Research results and their discussion.

Mercazolil is a well-known thyrostatic whose mechanism of action is to block the synthesis of thyroid hormones at the level of interaction of mono- and diiodotyrosine, as well as to inhibit the process of iodination of tyrosine fragments of thyroglobulin [11].

The results of our study showed that mercazolil administration led to a decrease in the synthetic function of the thyroid gland in experimental animals, which was manifested in a decrease in the level of thyroid hormones. In hypothyroidism, the concentrations of both thyroxine and triiodothyronine were statistically significantly lower than in intact animals by 2.3 and 1.6 times, respectively **(fig.)**. The results obtained indicate the development of hypothyroidism in experimental animals with characteristic clinical signs: apathy, lethargy, decreased appetite, loss of attention, decreased motor activity, which were recorded in rats of all experimental groups and which persisted until the end of the experiment in animals of the control group.

The use of the studied extracts and tinctures contributed to the restoration of the functional state of the thyroid gland in rats with experimental hypothyroidism. When hypothyroid animals were administered aqueous extracts from Feijoa leaves and fresh fruits, the level of thyroxine and triiodothyronine increased by 1.6 and 1.3 times, respectively, when TFL was administered – by 1.8 and 1.4 times, when TFF was administered – by 1.7 and 1.3 times **(fig.)**.

Analysis of the dynamics of biochemical parameters in the blood serum of experimental rats showed that both in the group of animals with hypothyroidism (group 2) and in animals that were administered the test substances against the background of hypothyroidism, there were no significant changes in the level of total protein and albumin. Their values remained within the range of values of rats of the IC group **(table)**.

Mercazolil administration led to an increase in serum creatinine and urea levels in hypothyroid rats by 1.3 and 1.7 times, respectively, compared with those in the IC group **(table)**. Increased serum urea levels may indicate impaired glomerular filtration on the one hand, and impaired urea-forming function of the liver on the other. Also, the increase in this indicator may be due to increased protein catabolism. The introduction of AEFL in the setting of hypothyroidism significantly reduced the urea

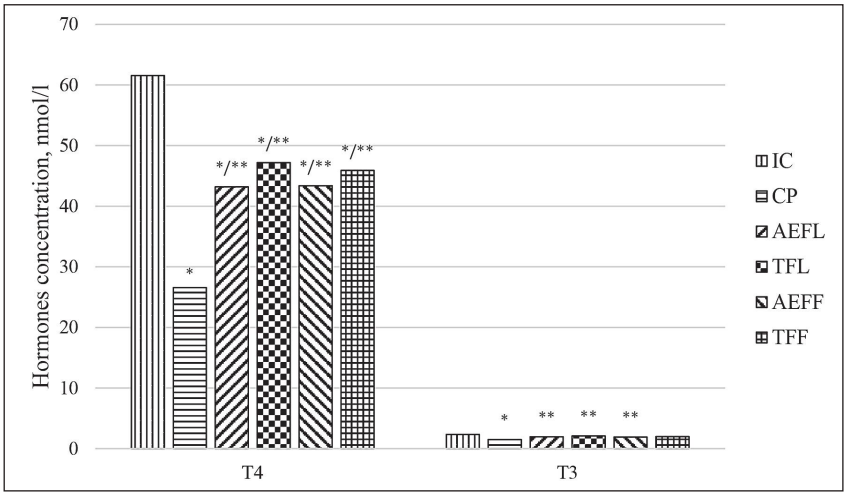

Figure – Hormone levels in the blood serum of rats of experimental groups (n=10).

Notes: * – differences are statistically significant relative to the IC group, $p<0.05$; ** – differences are statistically significant relative to the CP group, $p<0.05$; n – number of animals in each group; IC – intact control; CP – control pathology; AEFL – aqueous extract from Feijoa leaves; TFL – 30% tincture from Feijoa leaves, AEFF – aqueous extract from fresh Feijoa fruits, TFF – 30% tincture from fresh Feijoa fruits.

and creatinine content by 1.41 and 1.17 times, respectively, compared to the animals of the control group. Similar changes were observed in the case of administration of TFL, AEFF and TFF. The urea content in the blood serum of hypothyroid animals decreased by 1.44 times after administration of TFF and AEFF, and by 1.36 times after administration of TFF. The creatinine level decreased by 1.14 times with the use of TFL, and 1.1 times with the use of AEFF and TFF compared to the animals of the control group **(table)**.

When studying the activity of the enzymes CK and LDH, it was found that the development of experimental hypothyroidism is accompanied by an increase in the activity of CK in the blood serum of experimental animals by 33% compared to the group of IC animals. The activity of LDH remained at the level of intact animals. Creatine kinase and LDH are enzymes involved in the formation of energy and its breakdown, and their release into the bloodstream indicates damage to muscle integrity. In the case of hypothyroidism, an increase in the activity of CK may be a consequence of increased catabolic processes in skeletal muscle. Also, it should be taken into account that thyroxine inhibits the activity of CK. The administration of all the studied substances to hypothyroid rats led to a decrease in the content of CK in the serum of the experimental animals by an average of 12.6% **(table)**.

Table – Biochemical parameters in the blood serum of hypothyroid rats with the use of aqueous extracts and tinctures from leaves and fruits of Feijoa

Indicator	Group (n=10)					
	1	2	3	4	5	6
ALT, µcat/l	0.380± 0.013	0.424± 0.019	0.373± 0.019	0.359± 0.023	0.406± 0.022	0.400± 0.022
AST, µcat/l	0.525± 0.03	0.621± 0.05	0.534± 0.03	0.529± 0.03	0.544± 0.02	0.536± 0.03
CK, U/l	286.74± 0.29	381.49± 30.13*	333.26± 27.23	335.75± 27.54	309.10± 10.50	337.64± 25.23
LDH, µcat/l	3.80± 0.14	3.84± 0.14	3.91± 0.22	3.87± 0.16	3.75± 0.17	3.86± 0.14
Total protein, g/l	55.41± 0.50	54.65± 1.17	55.72± 1.25	56.74± 1.09	57.71± 1.84	53.19± 1.95
Albumin, g/l	34.45± 0.54	32.42± 1.35	32.63± 0.68	33.85± 1.49	34.86± 0.59	34.12± 0.89
Urea, mmol/l	6.75± 0.39	11.65± 0.66*	8.26± 0.47*/**	8.08± 0.81**	8.11± 0.39*/**	8.54± 0.47*/**
Creatinine, µmol/l	84.6± 2.86	108.29± 4.33*	92.55± 3.54**	94.67± 4.58	103.40± 5.10*	97.23± 5.11
CHO, mmol/l	2.96± 0.17	3.92± 0.16*	3.01± 0.16**	2.90± 0.12**	2.94± 0.19**	2.81± 0.10**
TG, mmol/l	0.51± 0.26	0.85± 0.25*	0.66± 0.32*/**	0.66± 0.47**	0.56± 0.04**	0.64± 0.03*/**
Glucose, mmol/l	5.85± 0.19	4.90± 0.15*	5.65± 0.26**	5.75± 0.14**	5.83± 0.13**	6.18± 0.17**

Notes: * – differences are statistically significant relative to the IC group, $p<0.05$; ** – differences are statistically significant relative to the CP group, $p<0.05$; n – number of animals in each group; 1 – intact control; 2 – control pathology; 3 – aqueous extract from Feijoa leaves; 4 – 30% tincture from Feijoa leaves, 5 – aqueous extract from fresh Feijoa fruits, 6 – 30% tincture from fresh Feijoa fruits.

In the study of lipid metabolism, it was found that the hypothyroid state induced by mercazolil administration was also accompanied by corresponding changes **(table)**. The cholesterol content in the second experimental group of animals increased by 32.4%, and TG – by 66.7%. Hypercholesterolaemia associated with hypothyroidism in humans and animals is largely due to an increase in the content of cholesterol in low-density lipoprotein and very low-density lipoprotein, although there is evidence of an increase in the concentration of high-density lipoprotein. After 21 days of administration of the studied extracts and tinctures, positive changes were observed in rats with experimental hypothyroidism. Thus, compared to the animals of the CP group, the cholesterol content in the blood serum of the experimental animals significantly decreased by an average of 25.6%, and the TG content significantly decreased and reached the levels of the IC group **(table)**.

The development of hypothyroidism was also accompanied by a 1.2-fold decrease in serum glucose concentration **(table)**. One of the reasons for the observed decrease in glucose levels may be a decrease in its absorption in the intestine as a result of a decrease in hexokinase activity and impaired blood transport. The analysis of the experimental data obtained on the serum glucose content in rats showed that in the group of animals treated with AEFL, TFL and AEFF, its concentration significantly increased to the level of the IC group of animals. In rats treated with TFF, the glucose level also increased significantly and slightly exceeded that of the IC group.

Conclusions.

Mercazolyl-induced hypothyroidism is characterized by a decrease in the functional activity of the thyroid gland, which is manifested in a decrease in the content of thyroid hormones in the blood serum of experimental animals. Hypothyroidism contributed to the development of negative manifestations of biochemical reactions in the body in the form of increased serum cholesterol, triglycerides, urea, creatinine, ALT, AST and CK enzymes, and decreased glucose levels, indicating a violation of lipid, protein and carbohydrate metabolism in the setting of hypothyroidism.

The use of AEFL, TFL, AEFF and TFF contributed to the restoration of biochemical parameters in the blood serum, as well as the level of thyroid hormones. In the experimental group receiving the studied extracts and tinctures against the background of hypothyroidism, the level of thyroxine and triiodothyronine increased, and positive changes in biochemical parameters occurred, which can be regarded as a sign of the restoration of metabolic processes.

Prospects for further research.

The experimental data obtained make it possible to assert the expediency of further studies of the effect of aqueous extracts and 30% alcohol tinctures from Feijoa leaves and fresh fruits as promising objects for the development of drugs intended for the prevention and treatment of hypothyroidism.

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ДОСЛІДЖЕННЯ ВПЛИВУ ВОДНИХ ЕКСТРАКТІВ І НАСТОЙОК З ЛИСТЯ ТА ПЛОДІВ ФЕЙХОА НА БІОХІМІЧНІ ПОКАЗНИКИ КРОВІ У ГІПОТИРЕОЇДНИХ ЩУРІВ

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Резюме. За даними ВООЗ, захворювання щитовидної залози є другим за поширеністю ендокринним розладом після цукрового діабету. За статистикою, щорічний приріст кількості захворювань щитоподібної залози у світі становить 5%. Пошук і вдосконалення методів профілактики та лікування залишаються завжди актуальними. На думку експертів, фітотерапія є перспективним напрямком. Тому, метою дослідження стало вивчення впливу водних екстрактів і спиртових настойок з листя та свіжих плодів фейхоа на біохімічні параметри у сироватці крові щурів в умовах експериментального гіпотиреозу. Експериментальний гіпотиреоз відтворювали щоденним введенням 0,05% водного розчину мерказолілу щурам замість питної води протягом 30 днів. Досліджувані засоби гіпотиреоїдним тваринам вводили внутрішньошлунково в дозі 1 мл/100 г маси тіла протягом 21-го дня. В сироватці крові оцінювали вміст тиреоїдних T_3 і T_4, також визначали вміст аланінамінотрансферази (АЛТ), аспартатамінотрансферази (АСТ), креатинкінази (КК), лактатдегідрогенази (ЛДГ), загального білку, альбуміну, сечовини, креатиніну, холестерину (ХС) і тригліцеридів (ТГ). Мерказоліл-індукований гіпотиреоз характеризується зниженням функціональної активності ЩЗ, що проявляється у зменшенні вмісту тиреоїдних гормонів у сироватці крові дослідних тварин. Результати дослідження показали, що гіпофункція щитоподібної залози сприяла підвищенню у сироватці крові вмісту холестерину, тригліцеридів, сечовини, креатиніну, активності ферментів АЛТ, АсАТ та КК і зниженню рівня глюкози, що свідчить про порушення ліпідного, білкового та вуглеводного обмінів на тлі гіпотиреозу. Застосування досліджуваних екстрактів і настойок сприяло відновленню біохімічних показників у сироватці крові, а також рівня гормонів щитоподібної залози. У дослідних групи, що отримували досліджувані композиції на тлі гіпотиреозу, підвищувався рівень T_4 та T_3, відбувалися позитивні зміни в біохімічних показниках, що можливо розцінювати як ознаку відновлення обмінних процесів. Таким чином, було зроблено висновок про доцільність подальших досліджень впливу водних екстрактів та 30% спиртових настойок з листя та свіжих плодів фейхоа як перспективних об'єктів для створення препаратів, призначених для профілактики та лікування гіпотиреозу.

Ключові слова: листя фейхоа, плоди фейхоа, експериментальний гіпотиреоз, мерказоліл, тиреоїдні гормони.

A STUDY OF THE EFFECT OF AQUEOUS EXTRACTS AND TINCTURES FROM FEIJOA LEAVES AND FRUITS ON BIOCHEMICAL PARAMETERS OF BLOOD IN HYPOTHYROID RATS

Kononenko A. H., Kravchenko V. M.

Abstract. According to the WHO, thyroid disease is the second most common endocrine disorder after diabetes mellitus. According to statistics, the annual increase in the number of thyroid diseases in the world is 5%. The search

for and improvement of methods of prevention and treatment remain always relevant. According to experts, herbal medicine is a promising area. Therefore, the aim of the study was to investigate the effect of aqueous extracts and alcoholic tinctures from Feijoa leaves and fresh fruits on biochemical parameters in the blood serum of rats with experimental hypothyroidism. Experimental hypothyroidism was induced by daily administration of a 0.05% aqueous solution of mercazolil to rats instead of drinking water for 30 days. The study substances were administered to hypothyroid animals intragastrically at a dose of 1 ml/100 g of body weight for 21 days. Serum levels of thyroid T3 and T4 were assessed, and alanine aminotransferase (ALT), aspartate aminotransferase (AST), creatine kinase (CK), lactate dehydrogenase (LDH), total protein, albumin, urea, creatinine, cholesterol (CHO) and triglycerides (TG) were also determined. Mercazolyl-induced hypothyroidism is characterized by a decrease in the functional activity of the thyroid gland, which is manifested in a decrease in the content of thyroid hormones in the blood serum of experimental animals. The results of the study showed that hypothyroidism contributed to an increase in serum cholesterol, triglycerides, urea, creatinine, ALT, AST and CK enzymes, and a decrease in glucose levels, indicating a violation of lipid, protein and carbohydrate metabolism in the setting of hypothyroidism. The use of the studied extracts and tinctures contributed to the restoration of biochemical parameters in the blood serum, as well as the level of thyroid hormones. In the experimental group receiving the studied compositions against the background of hypothyroidism, the level of T4 and T3 increased, positive changes in biochemical parameters occurred, which can be regarded as a sign of restoration of metabolic processes. Thus, it was concluded that further studies of the effect of aqueous extracts and 30% alcohol tinctures of feijoa leaves and fresh fruits as promising objects for the development of drugs intended for the prevention and treatment of hypothyroidism are advisable.

Key words: Feijoa leaves, Feijoa fruits, experimental hypothyroidism, mercazolil, thyroid hormones.

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The Authors declare no conflict of interest.

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CURRENT CLINICAL AND EPIDEMIOLOGICAL FEATURES OF MEASLES: A RETROSPECTIVE COHORT STUDY COMPARING THE 2006 AND 2018 OUTBREAKS

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The article is dedicated to defining the clinical and epidemiological features of the current course of measles when comparing the outbreaks of the disease between 2006 and 2018.

The medical records of 218 patients who were in hospital in a communal enterprise of the Poltava Regional Clinical Infectious Diseases Hospital of the Poltava Regional Council with the diagnosis "Measles" for the periods of epidemic outbreaks of measles epidemic outbreaks between January and May 2006 and between January and December 2018.

The analysis showed that in general, among both groups, persons of young age from 18 to 39 years prevailed, however, during the outbreak of 2018, the age structure of patients was registered in more patients older than 30 years than during the outbreak of 2006. According to gender analysis, men were significantly more prevalent among those hospitalized during the 2018 outbreak when compared to data from 2006.

A comparative analysis of the clinical course of the disease depending on the year of the epidemic outbreak showed that among those hospitalized in 2018, such clinical symptoms as general weakness, runny nose, enlarge-