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Effects of *Origanum vulgare* and *Scutellaria baicalensis* on the Physiological Activity and Biochemical Parameters of the Blood in Rats on a High-Fat Diet

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Abstract: The pharmacological effects of medicinal plants play a primary role in the mild correction of body weight in humans and animals, reducing the accumulation of fat in their bodies during a state of obesity. *Origanum vulgare* L. and *Scutellaria baicalensis* Georgi are widely used as food additives and medicinal plants, but their comprehensive physiological evaluation in model animals in a state of obesity has not been carried out. In a 30-day laboratory experiment on male rats which had developed obesity through a hypercaloric diet, the effects of adding the dry crushed grass *O. vulgare* or dry crushed roots of *S. baicalensis* to their feed was evaluated. During the experiment, the rats fed with *O. vulgare* increased in body weight to only 105.5% of their initial weight, while the body weight of the control group increased to 111.5%, and that of animals fed on *S. baicalensis* increased to 124.0% of their initial body weight. The average daily increase in the rats' body weight when *O. vulgare* was added to their diet decreased to 205 mg/day, and when *S. baicalensis* was added, on the contrary, it increased to 1417 mg/day, compared to 700 mg/day among the control group. Under the influence of *O. vulgare*, the lipid metabolism of the rats normalized: the atherogenic index decreased to 33.7%, compared with the values of the control group, due to an increase in the concentration of high-density lipoproteins from cholesterol. The concentration of triglycerides decreased, and the concentration of glucose decreased. The roots of *S. baicalensis* being added into the diet of rats increased the activity of alkaline phosphatase and decreased the concentration of urea. The atherogenic index also decreased (by up to 35.5% in the control group) and the concentration of high-density lipoprotein cholesterol increased, while the concentrations of triglycerides and glucose decreased. The physical activity of the rats showed a slight tendency to decrease when both *O. vulgare* and *S. baicalensis* were added to their diet. Both plant species contributed to a decrease in the emotional status of animals, which was most pronounced when the *O. vulgare* grass was added to the feed. The results of the study demonstrate the potential of the use of *O. vulgare* and *S. baicalensis* as herbal supplementations for the correction of hyperlipidemia and type-2 diabetes mellitus in overweight patients.

Keywords: oregano; Baikal skullcap; relative mass of the organs; bodyweight increase; high-fat diet; phytotherapy; obesity correction

1. Introduction

Origanum vulgare L., or oregano, is a perennial herbaceous plant of the Lamiaceae family. *Origanum* herb (lat. *Herba Origani vulgaris*) is used as a medicinal raw material and is cut during mass flowering. *O. vulgare* L. is referred to in the USSR/Russian *Pharmacopoeia* and is among the popular wild plants of the Russian *Pharmacopoeia* that were traditionally used as food [1–3].

O. vulgare is one of the most famous and economically important culinary herbs due to its essential oil, which is also used for medicinal purposes [4,5]. However, it

must be kept in mind that plant species of the genus *Origanum* have an intraspecific polymorphism and contain different amounts of biologically active substances; therefore, investigations and studies of new varieties and forms of processing of these plants are still ongoing [6]. Pezzani et al. [7] reviewed the biological activities of *O. vulgare* and its main bioactive phytochemicals, considering both preclinical (in vitro and in vivo) and human studies focused on the plant's anticancer, anti-inflammatory, antioxidant and antimicrobial activities. The contents of the active substances in the essential oils varies depending on the growing conditions, and consequently on the storage conditions. Moreover, the amounts of these substances change significantly when passing through the gastrointestinal tract, and their effective concentrations can be significantly reduced at the site of action (the small intestine and colon) [8].

The popularity and importance of *O. vulgare* are associated with its content of essential oil, which, in the dry aerial part of the plant, is 0.3–1.2%. To obtain the essential oil, the aerial mass is processed by hydrodistillation immediately after harvesting, and for the preparation of raw materials, it is dried as a spice in well-ventilated rooms or in a dryer at a temperature of no more than 30–40 °C. It must be taken into account that the chemical composition of oregano is determined by no single drying method that can be effectively used for the dehydration of all herbs. Heat treatment can lead to biochemical changes, which increases the plant's antibacterial activity [9,10]. The main identifying substances in oregano essential oils are thymol—44–50%, carvacrol, bicyclic and tricyclic sesquiterpenes—12.5%, and geranyl acetate—2.6–5.0%. All species of *Origanum* contain carvacrol as the main compound, and other compounds (thymol, gamma-terpinene, p-cymene, linalool, terpinen-4-ol, germacrene-D, beta-caryophyllene, myrcene, etc.) are found in most species as well [11,12]. *Origanum vulgare* is described as one of the sources of vegetable tannins [13], which probably explains the widespread use of its essential oil in treating skin diseases [14]. It is known that plants rich in polyphenols are used to prevent thrombosis, and the antiplatelet activity of *O. vulgare* is associated with the presence of caffeic acid, salvigenin and umbelliferone [15].

A possible dose-dependent effect of the biomolecules present in *O. vulgare* on the secretion of male steroids that play a role in the regulation of testicular spermatogenesis was also identified by Tvrdá et al. [16]. In an in vitro experiment, testicular fragments from mature mice were incubated with different concentrations of oregano extract for 24 h. The results showed that the oregano extract significantly reduced the mice's cholesterol and androstenedione (but not dehydroepiandrosterone and testosterone) [16].

Extracts of the *Origanum* genus species exhibit antibacterial, antifungal and microorganism-inhibiting effects. Essential oils with a high content of carvacrol among their bactericidal and antihistamine properties can reflect the activity of some antibiotics. It is with carvacrol and thymol that the antimicrobial and antioxidant activity is associated, which is achieved by increasing the permeability of the cell membrane due to these substances' impregnation in the hydrophobic domains, and this effect is more pronounced in relation to gram-positive bacteria [10,17–19]. Marchese et al. [20] studied the mechanism of the antimicrobial action of carvacrol and its synergy with antibiotics and established its activity against the formation of biofilms, which is an important aspect of the fight against fungi and gram-positive and gram-negative bacteria.

Waller et al. [21] described estragole, 1,8-cineole, terpineol-4 and gamma-terpinene isolated from plant species of the Lamiaceae family that exhibit a pronounced fungicidal activity against the pathogenic fungi *Aspergillus* spp., *Candida* spp., *Malassezia* spp., *Cryptococcus* spp., *Sporothrix* spp., *Microsporum* spp., *Trichophyton* spp. and *Epidermophyton* spp., and highlighted their potential use as antifungal agents for mycoses. In addition to being antimicrobial, oregano essential oils have both antidiabetic and anticancer activities [22,23]. Mahmoudian-Sani et al. [24] found that *O. vulgare* can stimulate the function of the T_{reg} cells (defined as CD4+CD25+Foxp3+), which play an important role in maintaining self-tolerance and preventing autoimmune diseases. The anticancer properties of carvacrol

through its effects on proapoptotic processes have been reported in preclinical models of breast, liver and lung carcinomas [18].

The genus *Scutellaria* includes about 350 plant species, which contain over 295 different compounds. Among them, flavonoids and diterpenes are the most interesting for pharmacology [25–27]. *Scutellaria baicalensis* Georgi (Baikal skullcap or Chinese skullcap) is a perennial species of the Lamiaceae family, growing up to 60 cm high. The species is distributed across China, Korea, Mongolia and the Russian Far East and Siberia [28]. The phytochemistry and pharmacology of plants of the genus *Scutellaria*, particularly the species *S. baicalensis*, *S. barbata* and *S. lateriflora*, have been attracted the interest of many researchers in recent decades. However, so far, many of the results of traditional and clinical research on these plants have not been systematized and summarized [29,30]. *Scutellaria baicalensis* is referred to in the *American Herbal Pharmacopoeia* and regarded as an adaptogen [31].

The root of *S. baicalensis* has long been widely used in traditional Chinese medicine and contains several major biologically active compounds, including wogonin, scutellarein, baicalein and baicalin [32–34]. Qing Fei Pai Du Tang (QFPDT), a Chinese medical formula composed of 21 herb from five classical formulae, was effective against COVID-19 in 10 provinces of mainland China [35]. According to the report, QFPDT prevented the progression of mild cases and decreased the average duration of symptoms and hospital stays. Therefore, it is recommended in the 6th and 7th editions of the Clinical Practice Guidelines for the Treatment of COVID-19 in China. QFPDT and its constituent herbs, including *S. baicalensis*, were reviewed by Zhong et al. [35]. The roots of *S. baicalensis* are used to prevent and treat type-2 diabetes, atherosclerosis, hypertension, hyperlipidemia, dysentery and respiratory diseases [36].

The review of Li et al. [37] provides an overview of the different separation, detection and identification methods employed for the quantitative and qualitative determination of the active components of *S. baicalensis*. *Scutellaria baicalensis* contains around 53 polyphenols in total, including 50 flavonoids and 3 stilbenes. As the active chemicals of the *S. baicalensis* root, 18 polyphenols showed apparent anticancer activities [38–40].

The main bioactive flavonoids of *S. baicalensis* are baicalein and baicalin. Due to its anti-inflammatory and immunomodulatory effects, baicalin has been successfully used in the treatment of cerebrovascular and neurological diseases, which has been confirmed by numerous in vivo and in vitro studies [41]. Baicalin can penetrate the blood–brain barrier and be distributed in the nuclei of the brain [42,43]. In recent years, a number of researchers have shown that baicalin has powerful neuroprotective effects in various models of neuronal injuries [44,45].

The neuroprotective effects of baicalin and baicalein have been confirmed by a number of studies on many models of ischemic neuronal injuries in vitro and in vivo [44,45]. Pharmacological mechanisms have shown that these substances exhibit several biological activities, including antioxidant, anti-apoptotic, anti-inflammatory and anti-excitotoxicity activities, the protection of the mitochondria, and the promotion of the expression of neuronal protective factors as well as the effects of adult neurogenesis, etc. [42]. Zhang et al. [46] described the potential biochemical mechanisms of action of skullcap flavonoids in spinal cord injuries. The therapeutic potential of baicalein has been demonstrated in the cases of Parkinson's and Alzheimer's diseases due to its key pharmacological properties— the reduction of oxidative stress, anti-inflammatory action, inhibition of the aggregation of disease-specific amyloid proteins, the stimulation of neurogenesis and differentiation and its anti-apoptotic activity [47]. Hussain et al. [48] reviewed the active components of different *Scutellaria* species and their mechanisms of action to prevent chronic neurological disorders that involve neuroinflammation and neurodegeneration. Ashbaugh & McGrew [49] examined the most recent evidence regarding *S. baicalensis* and the supplements and vitamins used for the treatment and prevention of concussions. The neuroprotective activity of the plant itself and its isolated flavonoids in various neurodegenerative diseases modelled in vitro and in vivo were also indicated by Gaire et al. [50].

The non-toxicity of different doses of flavones isolated from the skullcap root, when used as neuroprotective substances for the brain, was demonstrated in studies by Gasiorowski et al. [51]. Their neuroprotective properties have been illustrated in the cases of oxidative stress-induced as well as amyloid-beta- and alpha-synuclein-induced neuronal death models. Baicalein inhibits the aggregation of neuronal amyloidogenic proteins and causes the dissolution of the formed amyloid. Baicalein also exhibits strong antioxidant and anti-inflammatory effects and possesses anticonvulsant, anxiolytic and mild sedative actions, while significantly enhancing the cognitive and mnestic functions in animal models of ageing brains and neurodegeneration [52]. The toxicity of *S. baicalensis* mainly manifested in liver fibrosis and allergic reactions and was mainly caused by baicalin [31].

The anti-inflammatory, anti-cancer and anti-viral effects of baicalin are associated with its regulatory effect on the immune system [52]. Baicalin improves chronic inflammation, immune imbalance, lipid metabolism disorders, apoptosis and oxidative stress, thus playing an important role in preventing the onset and progression of cardiovascular system diseases (atherosclerosis, hypertension, myocardial infarction and heart failure) [53]. Chien et al. [54] compiled and discussed the biological analytical methods of using herbal medicines containing *S. baicalensis* and other plant species for the protection of the liver.

Numerous collected data show that *S. baicalensis* exhibits a powerful anticancer activity. A review by Li-Weber [55] summarized the results obtained over the past 20 years and highlighted the main molecular mechanisms of its action.

Park et al. [56] attributed the relief of symptoms of cancer cachexia through *S. baicalensis* to the plant's anti-inflammatory effects, regulation of the neuroendocrine pathway and modulation of the ubiquitin-proteasome system, or protein synthesis. Zhang et al. [57] associated the antitumor effect of *S. baicalensis* with the mechanism of angiogenesis inhibition through the inhibition of cytokines (vascular endothelial growth factor), which initiate this process. The extracts and basic flavonoids of *S. baicalensis* have shown anti-cancer activities in several cancer cell lines in vitro and in vivo [58]. In a review, Bie et al. [59] summarized the various anti-cancer effects of baicalein on hepatocellular carcinoma (HCC) and their underlying molecular mechanisms based on the in vitro and in vivo experimental evidence discovered thus far. In light of this research, baicalein may be developed as a potential, novel anticancer drug for HCC treatment. Liu et al. [60] also associated the antitumor activity of baicalein with its ability to inhibit cyclin complexes in the regulation of the cell cycle and scavenging free radicals, to attenuate enzyme activity (mitogen-activated protein kinase (MAPK), protein kinase B (Akt), or the mammalian target of rapamycin (mTOR)) to induce apoptosis by activating caspase-9/-3, and to inhibit tumor invasion and metastasis by reducing the expression of matrix metalloproteinase-2/-9 (MMP-2/-9) [60]. Baicalein induces apoptosis in cancer cells and induces cell cycle arrest, as indicated by Gao et al. [61]. Chen et al. [62] considered the anticancer activities of baicalin and its aglycone baicalein through their effects on signaling pathways and their potential biological mechanisms in different types of hematologic malignancies, as well as their combined effects as chemotherapeutic adjuvants in the treatment of these diseases.

Although the chemopreventive properties of baicalin and baicalein are significant and associated with the induction of apoptosis, triggering autophagy, cell cycle arrest, the suppression of metastasis and the inhibition of 12-lipoxygenase, they are characterized by poor solubility and low oral bioavailability; thus, their clinical use is limited [63]. Restrictions on the use and continued research on the mechanisms of action of *S. baicalensis* flavonoids are required due to the fact that they cause an increase in the activity of the immune system [64–66]. At the same time, it is known that many diseases, including tumors and neurodegenerative diseases (Alzheimer's disease), are accompanied by inflammatory reactions, and the inflammation of the neurons is often the result of excessive immune activity [67–69]. *Scutellaria baicalensis* root flavonoids can only aggravate the course of these diseases [70].

Despite numerous reports on the pharmacological effects of baicalin and baicalein, some reports have indicated that baicalin, due to its form, is unlikely to be absorbed in the

intestine, and that it must be pre-hydrolyzed to baicalein for absorption to take place [71,72]. Most likely, the pharmacokinetic characteristics of baicalin and baicalein are influenced by the intestinal microflora [73,74].

Wogonin is a widely studied product obtained from the roots of the plant *S. baicalensis*. Its popularity stems from its antioxidant, antiviral, anti-inflammatory, anti-allergic and anti-thrombotic properties, leading to its applications in the treatment of cardiovascular disease [75–77]. Experimental and clinical data prove that wogonin exhibits a variety of biological activities, such as anti-cancer and anti-inflammatory activities, and it is used to treat bacterial and viral diseases [78]. Wogonin is safe, exhibits negligible organ toxicity at high doses and is non-toxic with long-term intravenous use, facilitating apoptosis and endoplasmic reticulum (ER) stress in the cells, suggesting its potential for use as a therapeutic agent in the treatment of diabetic cardiomyopathy [75–78].

The objective of this study was to determine the general effects of *S. baicalensis* and *O. vulgare* on the growth, changes in the organ mass index, biochemical and morphological blood parameters, and functional state of the nervous system of white outbred laboratory rats fed on a high-fat content diet.

2. Materials and Methods

The choice of animals for the experiment, the research protocols, and the withdrawal of animals from the experiment were approved by the local ethical committee of Dnipro State Agrarian and Economic University (Dnipro, Ukraine). The maintenance, nutrition care of the animals and their withdrawal from the experiment were carried out in accordance with the principles set forth in the "European Convention for the Protection of Vertebrate Animals used for Experimental or other Scientific Purposes" (Strasbourg, France, 18 March 1986, ETS No. 123) and in Law of Ukraine "On protection of animals from cruel treatment" (Kyiv, Ukraine, 21 February 2006, No. 3447-IV).

A total of 24 outbred male laboratory rats of 1.5 months of age were randomly divided into three groups (8 rats/group), so that the average body weight was the same for each group. The body weight range did not exceed ±20% of the average body weight at the beginning of the experiment. The rats were kept in polycarbonate cages with steel lattice lids and a feeding recess, with 4 individuals per cage. The rats were kept in a room at a temperature of 20–22 °C and relative humidity of 50–65%. The light regimen was 12 h of light and 12 h of darkness. According to this regime, ventilation was provided. The animals received water *ad libitum* [79].

From the first day of the experiment, the diet of all animals had an excess fat content. The high-fat diet was based on a standard diet (75% grain mixture (corn, sunflower grain, wheat, barley), 8% root crops (potatoes, carrots), 2% meat and bone meal and 2% mineral-vitamin complex)) with the introduction of 15% sunflower oils [80,81]. The control group animals received a high-fat diet, and the experimental group received a high-fat diet with the addition of medicinal plants. The high-fat diet of the first experimental group was supplemented with 5% dry *O. vulgare* leaves, and the second experimental group was supplemented with 5% crushed *S. baicalensis* roots.

Origanum vulgare plants were collected from the Botanical Garden of the Oles Honchar Dnipro National University (48.435509 °N, 35.043132 °E) on 15 June 2021. The plants were dried under a tent with no exposure to direct sunlight. The above-ground part was fragmented and all rough parts were removed, leaving only the leaves and soft parts of the inflorescences.

The roots of *S. baicalensis* were dug out on 20 November 2021 in the Botanical Garden of the Oles Honchar National University. The roots were cleaned of soil, rinsed, dried and fragmented with a knife into small pieces no larger than 2–3 mm. The obtained plant material was dried to an air-dried condition for two days in a dark, dry room at the temperature of 25 °C. After drying, fragments of the roots of *S. baicalensis* were 1.2–2.0 mm and were not fragmented further.

The main ingredients of the rats' diet were ground in a mill (grain, meat and bone meal, mineral and vitamin complex, dry shoots of medicinal plants) and mixed, then sunflower oil was added and the granules were produced at the rate of 4200 g for each group for the entire period of the experiment (30 days). Root crops, in the appropriate amount and in fresh form, were additionally given every day. The animals had free access to food. The rats were observed daily and their body weight, food intake and water intake were recorded. Morphometric parameters (live body weight, abdominal volume) were determined on the first day of the experiment and on the 30th day [82]. The total body weight gain of the animals and the daily gain in live weight were calculated. The average body weight per group was calculated weekly based on the individual animals.

The orientation-physical activity and emotional status of the experimental animals were studied in an "open field" test. We used an installation consisting of a square area of 1 m^2, divided into 16 squares and limited by an opaque wall that was 20 cm high. The experiment was conducted in complete silence, with intense lighting of the field itself. The experimental animal, taken from a cage in a previously darkened room, was placed in the center of the field. The exposure time was 2 min. The animals were tested for four days (days 1–4) at the beginning of the experiment and four days at the end (days 26–30). The number of crossed squares was counted. The parameters included: the peripheral and central floorspace—for assessing the rats' physical activity; the peripheral (leaning against the wall) and central (without leaning against the wall) racks—for the orientation activity; and the number of acts of grooming, defecation and urination—for assessing the animals' emotional status [83].

The euthanasia of the animals was performed on the 30th day of the experiment under anesthesia (80 mg/kg ketamine and 12 mg/kg xylazine, intraperitoneally) by total bloodletting from the heart. After autopsy, the condition of the internal organs was visually assessed for the presence of pathological changes [84]. Selection of organs and tissues (heart, liver, lungs, thymus, spleen, stomach, small and large intestines, kidneys) was performed with surgical instruments. The mass of the internal organs was determined with an accuracy of ±10 mg.

Blood samples taken during euthanasia were used for biochemical and hematological analyses. Biochemical parameters were determined using an automatic analyzer, Miura 200 (I.S.E. Srl, Rome, Italy), and High Technology reagent kits (High Technology Inc, North Attleborough, MA, USA), PZ Cormay S.A. (Cormay Diagnostics, Lublin, Poland) and Spinreact S.A. (Spinreact, Girona, Spain). The numbers of erythrocytes and leukocytes in the stabilized blood of the mice were determined using an automatic hematology analyzer, BC-2800Vet (Mindray, Shenzhen, China). Pappenheim blood smears were prepared for the leukogram, followed by Romanovsky–Gimza staining. The numbers of erythrocytes and leukocytes in the stabilized blood of the mice were determined using an automatic hematology analyzer, BC-2800Vet, and Mindray [81].

The data were analyzed using the Statistica 8.0 program (StatSoft Inc., Tulsa, OK, USA). The tables demonstrate the results as x $\pm$ SD (mean $\pm$ standard deviation). Differences between the values of the control and experimental groups were determined using Tukey's test (with consideration of Bonferroni's correction), where the differences were considered significant at $p < 0.05$.

3. Results

In the control group, the body weight increased to 111.5% from baseline, and in the group of rats fed on the dry shoots of *O. vulgare*, it increased to only 105.5% (Figure 1). Contradictory changes in body weight, compared to the control group, were observed in the animals fed with crushed roots of *S. baicalensis*. Their body weight increased to 124.0% relative to their initial weight, i.e., more than in the control group (Figure 1).
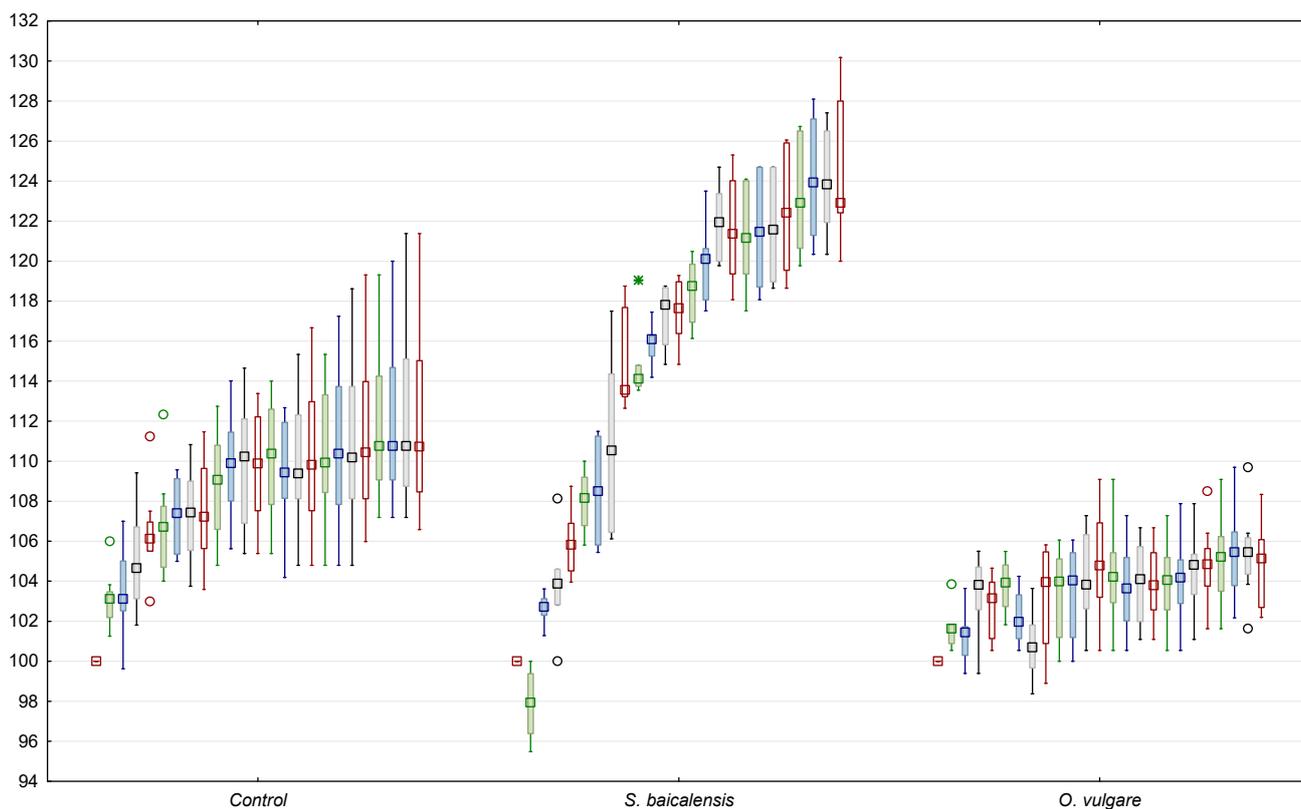
Figure 1. Changes in the body weight of rats when shredded shoots of *Origanum vulgare* L. and roots of *Scutellaria baicalensis* Georgi were added to their diet. The details are as follows: on the abscissa axis—the day of the experiment for the control, *O. vulgare* and *S. baicalensis* groups; on the ordinate axis—body weight of the animals (% relative to the baseline body weight before the start of the experiment, taken as 100% for each of the experimental animals); small square—median, the upper and lower boundary of the rectangle, being 75% and 25% of the quartile; vertical line—minimum and maximum values; circles—outliers; *n* = 8.

When the dry grass of *O. vulgare* was added to the diet of the animals, their feed intake decreased to 80.0% compared to the control group (Table 3). The addition of the dry roots of *S. baicalensis* to the feed did not affect the rate of feed consumption but increased the amount of daily water intake to 116.0% compared to the rats in the control group. The daily weight gain in the rats fed with the *O. vulgare* supplementation decreased to 205 mg/day, while rats fed with the supplementation of *S. baicalensis*, on the contrary, exhibited a daily weight gain increased to 1417 mg/day compared to the 700 mg/day in the control group (Table 1). Significant changes in the abdominal volumes of the experimental groups of animals were not observed.

The addition of the *O. vulgare* dry grass to the diet of animals did not cause significant changes in the relative mass of their organs (Table 2). The addition of *S. baicalensis* roots to the diet over the period of the increase in the total body weight significantly reduced the relative weight of the thymus (to 50.0%) and the brain (to 74.6% of the control group level, Table 2).

Table 1. Changes in the body weight and fodder consumption of young male rats under the impacts of the addition of *Origanum vulgare* L. and *Scutellaria baicalensis* Georgi to their rations (x ± SD, *n* = 8, duration of experiment—30 days).

Parameter	Control	O. vulgare	O. vulgare Compared to the Control, %	S. baicalensis	S. baicalensis Compared to the Control, %
Consumption of food, g/day	20.09	16.07	80.0	19.79	98.5
Consumption of water, g/day	18.42	18.13	98.4	21.35	116.0
Change in body weight, %/day	13.6 ± 5.9	3.7 ± 3.2 ***	27.1	26.3 ± 7.4 **	193.2
Change in body weight, g/day	0.700 ± 0.271	0.205 ± 0.181 ***	29.3	1.417 ± 0.326 ***	202.4
Abdominal volume, cm	14.00 ± 0.46	13.36 ± 0.64	95.4	14.42 ± 0.34	103.0

** $p < 0.01$, *** $p < 0.001$, significant differences within one line of the table according to the results of the ANOVA with Bonferroni correction.

Table 2. Changes in the relative mass of the organs (%) of male rats under the influence of the additions to their rations of *Origanum vulgare* L. and *Scutellaria baicalensis* Georgi (x ± SD, *n* = 8, duration of experiment—30 days).

Organ	Control	O. vulgare	O. vulgare Compared to the Control, %	S. baicalensis	S. baicalensis Compared to the Control, %
Heart	0.352 ± 0.023	0.363 ± 0.038	103.3	0.373 ± 0.035	106.2
Liver	4.08 ± 0.17	4.10 ± 0.48	100.6	3.74 ± 0.68	91.6
Lungs	0.98 ± 0.17	1.06 ± 0.10	107.9	1.05 ± 0.27	106.9
Thymus	0.285 ± 0.046	0.243 ± 0.036	85.1	0.143 ± 0.065 ***	50.0
Spleen	0.370 ± 0.036	0.401 ± 0.046	108.3	0.422 ± 0.111	114.0
Stomach	0.699 ± 0.060	0.825 ± 0.129	118.0	0.845 ± 0.221	120.9
Small intestine	2.58 ± 0.52	2.74 ± 0.67	106.3	2.52 ± 0.18	97.6
Cecum	0.509 ± 0.176	0.547 ± 0.172	107.5	0.382 ± 0.216	75.1
Large intestine	0.374 ± 0.085	0.405 ± 0.135	108.3	0.465 ± 0.140	124.5
Rectum	0.398 ± 0.073	0.457 ± 0.076	114.8	0.361 ± 0.126	90.6
Right kidney	0.358 ± 0.031	0.357 ± 0.047	99.8	0.352 ± 0.035	98.4
Left kidney	0.372 ± 0.040	0.369 ± 0.040	99.2	0.348 ± 0.035	93.6
Brain	0.867 ± 0.052	0.926 ± 0.055	106.8	0.647 ± 0.170 *	74.6

* $p < 0.05$, *** $p < 0.001$, significant differences within one line of the table according to the results of the ANOVA with Bonferroni correction.

Under the influence of *O. vulgare*, added to the diet of the rats, their blood biochemical parameters changed (Tables 3–5). In the rats' blood plasma, the activity of alkaline phosphatase significantly increased (223.8% compared to the control group) and gamma-glutamyl transferase decreased (to a level of 72.3% compared to the control group). In rats consuming *O. vulgare* dry grass, the normalization of the lipid metabolism was observed: the atherogenic index decreased to 33.7% of the control group value, due to an increase in the concentration of high-density lipoprotein cholesterol (increased to 165.8% compared to the value of the control group). The concentration of triglycerides in the blood plasma also sharply decreased (to 38.3% compared to the control). The normalization of the metabolism was also evidenced by a significant decrease in the concentration of glucose in the blood of the animals (ranging from 7.4 to 5.0 mmol/L on average) under the influence the herb *O. vulgare*.

Table 3. Changes in the parameters of lipid and carbohydrate metabolism in the blood of male rats under effects of the addition of *Origanum vulgare* L. and *Scutellaria baicalensis* Georgi to their diet (x ± SD, *n* = 8, duration of experiment—30 days).

Parameters	Control	O. vulgare	O. vulgare Compared to the Control, %	S. baicalensis	S. baicalensis Compared to the Control, %
Glucose, mmol/L	7.4 ± 1.0	5.0 ± 1.2 **	68.3	4.3 ± 0.8 ***	58.2
Cholesterol, mmol/L	1.27 ± 0.14	1.46 ± 0.20	114.6	1.48 ± 0.19	116.7
Blood triglycerides, mmol/L	2.13 ± 0.55	0.81 ± 0.18 ***	38.3	0.98 ± 0.28 ***	46.2
High-density lipoprotein (HDL) cholesterol, mmol/L	0.65 ± 0.13	1.08 ± 0.11 ***	165.8	1.07 ± 0.16 ***	164.2
Low-density lipoprotein (LDL) cholesterol, mmol/L	0.52 ± 0.29	0.72 ± 0.10	138.7	0.51 ± 0.14	98.6
Atherogenic index of plasma	1.04 ± 0.45	0.35 ± 0.28 *	33.7	0.37 ± 0.21 *	35.5

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, significant differences within one line of the table according to the results of the ANOVA with Bonferroni correction.

Table 4. Changes in the parameters of the protein and mineral metabolism in the blood of male rats under the effects of the addition of *Origanum vulgare* L. and *Scutellaria baicalensis* Georgi to their diet (x ± SD, *n* = 8, duration of experiment—30 days).

Parameters	Control	O. vulgare	O. vulgare Compared to the Control, %	S. baicalensis	S. baicalensis Compared to the Control, %
Total protein, g/L	77.0 ± 4.9	80.9 ± 4.5	105.0	73.5 ± 4.3	95.5
Albumins, g/L	39.6 ± 2.6	40.4 ± 2.0	102.2	38.3 ± 2.2	96.9
Globulins, g/L	37.4 ± 3.9	40.4 ± 3.3	108.0	35.2 ± 2.3	94.0
Albumin/globulin ratio, U	1.100 ± 0.151	1.014 ± 0.083	92.2	1.117 ± 0.037	101.5
Urea, mmol/L	6.84 ± 1.02	6.06 ± 0.61	88.5	4.88 ± 0.50 **	71.4
Blood urea nitrogen, mg/100 g	13.1 ± 2.0	11.6 ± 1.2	88.6	9.3 ± 1.0 **	71.5
Creatinine, μmol/L	63.0 ± 4.4	70.1 ± 10.9	111.3	65.8 ± 4.2	104.5
Total bilirubin, μmol/L	6.1 ± 1.7	8.4 ± 1.6	137.6	5.5 ± 1.1	91.1
Total calcium, mmol/L	2.529 ± 0.088	2.671 ± 0.148	105.6	2.583 ± 0.069	102.2
Non-organic phosphorus, mmol/L	3.07 ± 0.58	2.80 ± 0.58	91.2	3.08 ± 0.33	100.4
Ratio of Ca/P	0.843 ± 0.129	0.971 ± 0.191	115.3	0.850 ± 0.138	100.8
C-reactive protein, mmol/L	12.5 ± 5.4	9.9 ± 5.2	79.0	10.0 ± 1.8	79.5

** $p < 0.01$, significant differences within one line of the table according to the results of the ANOVA with Bonferroni correction.

Table 5. Changes in the enzymatic activity in the blood plasma of male rats under the effects of the addition of *Origanum vulgare* L. and *Scutellaria baicalensis* Georgi to their diet (x ± SD, *n* = 8, duration of experiment—30 days).

Parameters	Control	O. vulgare	O. vulgare Compared to the Control, %	S. baicalensis	S. baicalensis Compared to the Control, %
AST, U/L	186 ± 61	179 ± 70	95.9	175 ± 32	94.1
ALT, U/L	131 ± 41	110 ± 52	84.4	116 ± 27	88.7
De Ritis ratio (AST/ALT), U	1.63 ± 0.78	1.99 ± 0.85	121.9	1.58 ± 0.45	97.2
Alkaline phosphatase, U/L	129 ± 64	289 ± 62 ***	223.8	573 ± 303 ***	444.1
Gamma-glutamyltransferase (GGT), U/L	9.3 ± 2.6	6.7 ± 0.5 *	72.3	6.5 ± 2.1	70.0

* $p < 0.05$, *** $p < 0.001$, significant differences within one line of the table according to the results of the ANOVA with Bonferroni correction.

The roots of *S. baicalensis* caused similar changes in the blood biochemical parameters of the male rats. Compared to the changes induced by oregano (Table 5), the activity of alkaline phosphatase increased even more strongly (to 444.1% of the control group); however, changes in the activity of gamma-glutamyl transferase were insignificant (enzyme activity tended to decrease). In addition, the concentration of urea and blood urea nitrogen significantly decreased (to 71.4% and 71.5% compared with the control group, respectively). The atherogenic index significantly decreased (to 35.5% of the control) and the concentration of high-density lipoprotein cholesterol increased (to 164.2% of the control group value).

Moreover, as with the use of oregano, under the influence of the dry crushed roots of *S. baicalensis*, the concentration of triglycerides in the blood plasma decreased by more than twice (46.2% of the control group), and the concentration of glucose decreased (to 58.2% compared to the control group, or to 4.3 mmol/L, Table 3).

When added to the diet, *O. vulgare* was not observed in the general analysis of the blood and leukogram of the male rats (Table 6). The roots of *S. baicalensis* contributed to a significant decrease in the number of platelets in the blood of the animals (to 64.7% of the control group) and a sharp increase in the number of leukocytes (to 170.4% of the control group, Table 4).

Table 6. Changes observed in the general analysis of the blood and leukogram of the male rats under effects of the addition of *Origanum vulgare* L. and *Scutellaria baicalensis* Georgi to their diet (x ± SD, *n* = 8, duration of experiment—30 days).

Parameter	Control	O. vulgare	O. vulgare Compared to the Control, %	S. baicalensis	S. baicalensis Compared to the Control, %
Hemoglobin, g/L	126.8 ± 7.0	116.0 ± 9.0	91.5	117.2 ± 10.7	92.4
Hematocrit, %	40.5 ± 2.7	36.3 ± 3.2	89.6	36.9 ± 3.6	91.2
Erythrocytes, 10^{12}/L	6.93 ± 0.29	6.35 ± 0.43	91.6	6.58 ± 0.58	94.9
Erythrocyte sedimentation rate (ESR), mm/h	1.17 ± 0.37	1.14 ± 0.35	98.0	1.00 ± 0.00	85.7
Thrombocytes, 10^9/L	339 ± 66	277 ± 66	81.7	219 ± 58 *	64.7
Leukocytes, 10^9/L	8.6 ± 1.6	8.7 ± 2.3	102.1	14.6 ± 4.5 *	170.4
Leukocytic formula					
Basophils, %	0.0 ± 0.0	0.0 ± 0.0	0.0	0.0 ± 0.0	0.0
Eosinophils, %	1.50 ± 0.76	1.00 ± 1.07	66.7	0.67 ± 0.47	44.4
Myelocytes, %	0.0 ± 0.0	0.0 ± 0.0	0.0	0.0 ± 0.0	0.0
Young neutrophils, %	0.0 ± 0.0	0.0 ± 0.0	0.0	0.0 ± 0.0	0.0
Band neutrophils, %	1.17 ± 0.69	1.00 ± 0.76	85.7	1.17 ± 0.69	100.0
Neutrophils with segmented nuclei, %	23.0 ± 8.2	17.7 ± 3.5	77.0	24.2 ± 9.0	105.1
Lymphocytes, %	68.8 ± 8.6	75.6 ± 2.8	109.8	69.2 ± 9.5	100.5
Monocytes, %	5.5 ± 1.3	4.7 ± 2.2	85.7	4.8 ± 1.2	87.9

* $p < 0.05$, significant differences within one line of the table according to the results of the ANOVA with Bonferroni correction.

The physical activity (Figure 2a) of the rats showed a slight tendency to decrease when *O. vulgare* grass and *S. baicalensis* roots were added to their diet. No significant changes in the orientation activity were observed (Figure 2b). Both plants studied contributed to a decrease in the emotional status of the animals, which was most pronounced when oregano grass was added to the feed (Figure 2c).

There were no statistically reliable differences between animal groups (Table 7). Nevertheless, it should be mentioned that there was a prominent decrease in the average fecal boluses (almost 10 times less) and the frequency of urination (more than 3 times lower compared to the control group) when supplementing the rats' diet with the *O. vulgare* herb (Table 7).

(**a**)　　　　　　　　　　　　(**b**)　　　　　　　　　　　　(**c**)
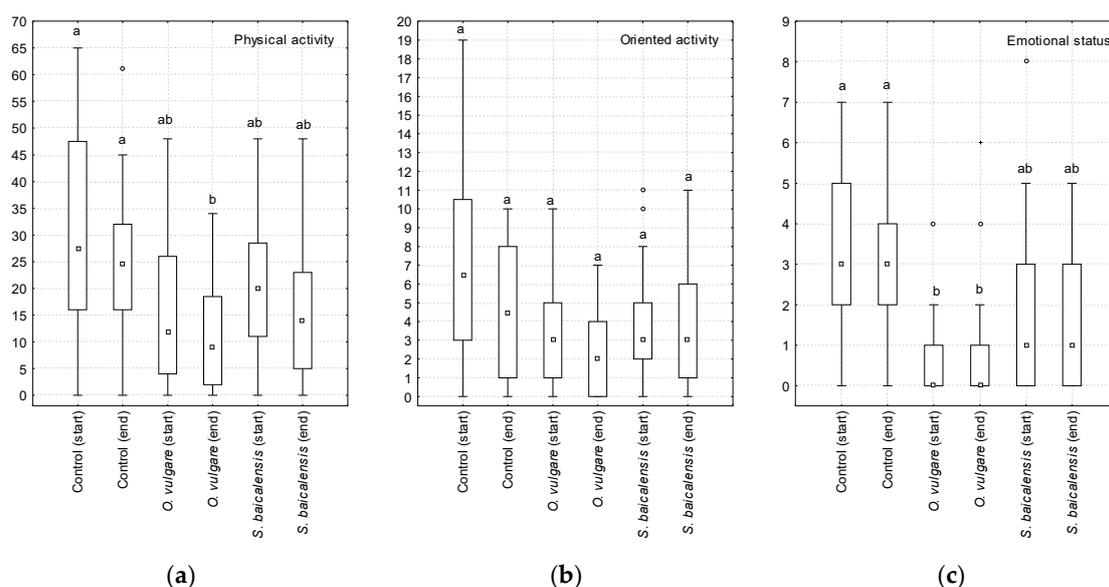
Figure 2. Changes in the levels of physical (**a**) and orientation activity (**b**) and the emotional status (**c**) of male rats when the crushed shoots of *Origanum vulgare* L. and roots of *Scutellaria baicalensis* Georgi were added to their diet. On the abscissa axis ($n = n_1 \times n_2 = 32$: $n_1 = 8$ animals, $n_2 = 4$ experiments with each animal) are the groups of animal which were on a high-fat diet with the addition of the ground shoots of plants (the days after the start of the experiment are in parentheses: 1–4th or 26–30th days). Along the ordinate axis is the absolute number of markers of the following types of behavior over 120 s of the experiment: for the physical activity—the number of visited squares in the "open field"; for the orientation activity—the number of racks; and for the emotional status—the number of grooming, defecation and urination actions. A small square is the median, and the upper and lower borders of the rectangle are 75% and 25% of the quartile, respectively. The vertical line denotes the minimum and maximum values, and the circles are outliers. Different letters within each figure indicate significant ($p < 0.05$) differences between groups according to the Tukey's test results.

Table 7. Changes of the behavioral characteristics of the three groups of rats during 2 min of the experiment, whose diet was supplemented with *Origanum vulgare* L. and *Scutellaria baicalensis* Georgi (x ± SD, *n* = 32, duration of the experiment was 30 days).

Parameters	Control, 1–4th Days	Control, 26–30th Days	*O. vulgare*, 1–4th Days	*O. vulgare* 26–30th Days	*S. baicalensis*, 1–4th Days	*S. baicalensis*, 26–30th Days
Number of visited peripheral squares	28.1 ± 18.0	24.3 ± 14.5	14.5 ± 12.3	10.9 ± 10.0	20.3 ± 11.9	15.5 ± 11.3
Number of visited central squares	1.000 ± 2.341	0.292 ± 1.042	0.429 ± 1.136	0.071 ± 0.378	0.708 ± 2.612	0.417 ± 2.041
Number of racks in peripheral squares	5.58 ± 4.53	3.79 ± 3.13	2.79 ± 2.08	2.00 ± 1.87	3.33 ± 2.04	3.17 ± 2.66
Number of racks in central squares	1.292 ± 1.429	0.708 ± 0.999	0.429 ± 0.997	0.286 ± 0.659	0.500 ± 1.063	0.625 ± 1.056
Number of grooming acts	0.583 ± 0.830	0.583 ± 0.929	0.286 ± 0.535	0.464 ± 0.838	0.625 ± 1.096	0.417 ± 0.830
Number of fecal boluses	2.250 ± 2.027	2.375 ± 1.555	0.250 ± 0.518	0.250 ± 0.701	1.000 ± 1.383	1.083 ± 1.530
Number of acts of urination	0.333 ± 0.482	0.375 ± 0.495	0.107 ± 0.315	0.071 ± 0.262	0.167 ± 0.381	0.083 ± 0.282

There were no significant differences between the groups in all the studied parameters ($p < 0.05$ according to the Tukey's test with Bonferroni's correction).

4. Discussion

In our study, we determined the effects of *O. vulgare* and *S. baicalensis* on the growth and development of laboratory animals in the context of their consumption of a high-fat diet. The lack of unified methods for extracting biologically active compounds from medicinal herbs or medicinal raw materials, and the use of various methods for their extraction,

makes it very difficult to carry out the procedure for identifying and determining the composition of plant objects [85–89]. Therefore, in our study, we selected the strategy of mixing dry crushed plant parts into granulated animal feed.

The research results indicate that the studied medicinal plants significantly affected the body weight gain of the laboratory animals in different ways. Thus, the addition of *O. vulgare* grass to the diet significantly slowed down the weight gain, probably due to the fact that the amount of food consumed was reduced to 80.0% compared with the control group. The average daily weight gain of the rats was lower than in the control group and significantly lower than in the group of rats that consumed the roots of *S. baicalensis*. The addition of *S. baicalensis* dry roots to the high-fat diet of the rats, on the contrary, led to more active growth, and their average daily weight gain was at the level of 1417 mg/day, which was higher than that in the control group of animals. The decrease in the rats' body weight and the average daily feed intake when dry chopped grass *O. vulgare* was added to the diet may be associated with the high content of essential oils in the plant and, as a result, its unpleasant taste. However, preliminary palatability studies of rats showed that the maximum dose that animals consumed, when added to neutral gelatin, was 200 mg/kg of pure *O. vulgare* essential oil [89]. In the same study, it was found that different doses (50, 100 and 200 mg/kg per day) of this essential oil did not lead to significant differences in the final weight, body weight gain or total food intake between groups.

At the end of the experiment, no pathological changes in the internal organs of the studied animals were found. The absence of pathomorphological changes in the organs of animals under the influence of various doses (up to 200 mg/kg of body weight) of *O. vulgare* essential oils in their food was also observed in the studies of Llana-Ruiz-Cabello et al. [89] and Horky et al. [8].

It was determined that the addition of *O. vulgare* to the rats' high-fat diet across the 30-day experiment did not cause significant changes in the relative mass of the individual internal organs. At the same time, the addition of *S. baicalensis* roots over the period of the general increase in body weight caused a decrease in the relative mass of the thymus, which can be explained by the active delymphotization of this organ, which is central to immunogenesis. The regulatory and stimulating effects on the immune system of the main active flavonoid, baicalin, has been observed in many studies [36,52,53]. The significant neuroprotective effects of the *S. baicalensis* active substances, which are actively used in the treatment of neurological and cerebrovascular diseases, has long been known. Possibly, this is the reason for the decrease in the relative mass of the brains in the rats that received *S. baicalensis* roots in their diet, but more thorough and in-depth studies are required to confirm this. When analyzing the blood biochemical parameters of the animals that were consuming *O. vulgare*, it was found that the lipid metabolism was normalized in comparison with the control group (on the high-fat diet). Thus, the atherogenic index decreased to 33.7% of the value of the control group, due to an increase in the concentration of high-density lipoprotein cholesterol, and the concentration of triglycerides decreased. Similar changes in the lipid metabolism were also observed in the rats which were fed *S. baicalensis*. In the blood, the atherogenic index also decreased, and the level of high-density lipoproteins increased in the context of a decrease in the triglycerides. According to Abd Rashed et al. [90], the attenuating effects of essential oils, including *O. vulgare*, on obesity can be explained by several possible mechanisms, which include anti-lipase activity, an increased plasma glycerol concentration, and the inhibition of fat accumulation. Both plants have also been found to lower blood glucose levels. *Origanum vulgare* is among the medical species that have been used in Russia for the management of diabetes, especially when this is accompanied by obesity [3]. The hypoglycemic effects of the active substances of *O. vulgare* across a 90-day experiment were also demonstrated in the studies of Horky et al. [8].

Attention is drawn to the significant increase in the activity of the enzymes in the blood, while the AST and ALT were increased in the blood of animals of all groups, including the control, which can be explained by the significant load on the liver hepatocytes due to excess fat in the rats' diet and the increased work required for its metabolism [80,81,83].

At the same time, the activity of alkaline phosphatase was significantly increased in the blood of the animals that received the tested plants in addition to the diet. It should be noted that the indicators of AP activity did not transgress the physiological limits for this animal species.

When added to the diet, *O. vulgare* was not observed in the complete blood count and leukogram of the male rats. At the same time, the addition of the dry roots of *S. baicalensis* to the feed of the rats led to a significant decrease in the number of platelets and an increase in the number of leukocytes compared with animals in the control group. The antithrombotic effect of wogonin, the active substance of *S. baicalensis*, has been indicated in some publications, which has enabled the use of this medicinal plant in the treatment of cardiovascular diseases [75].

Baicalein has the most pronounced neuroprotective activity [91,92]. It was shown in a meta-analysis to significantly improve the neurobehavioral functions in animal models of Parkinson's disease, in experiments including the spontaneous locomotor test, the pole test, the spinning pole test, the apomorphine-induced rotation test, the grid test and the tremor test [93]. In our study, based on an open field test of healthy rats who received a high-fat diet, the locomotor activity in the group of animals consuming the additional crushed roots of *S. baicalensis* did not significantly differ from the control group and the animals consuming *O. vulgare* grass.

5. Conclusions

In conclusion, the additions of *S. baicalensis* dry roots and the aerial parts of *O. vulgare* to the diet of rats caused noteworthy changes to their bodies and improved their biochemical parameters. During the 30 days of the experiment, rats fed on *O. vulgare* increased in body weight up to only 105.5% of their initial body weight, while the control group's weight increased up to 111.5% and the weight of animals fed on *S. baicalensis* increased up to 124.0%. The addition *O. vulgare* to the diet reduced the intake of the ingested food to 80.0% of the control group value. Under the influence of *O. vulgare* in the rats' blood plasma, the lipid metabolism was normalized: the atherogenic index decreased to 33.7% compared to the value of the control group due to the increase in the concentration of high-density lipoprotein cholesterol (to 165.8% of the control group). The concentration of triglycerides decreased (to 38.3% of the control) and the concentration of glucose decreased as well (from 7.4 to 5.0 mmol/L). The roots of *S. baicalensis*, as a supplementation to the diet of the rats, reduced the atherogenic index (to 35.5% of the control) and increased the concentration of HDL cholesterol (to 164.2% of the value of the control group), while it decreased the concentration of triglycerides in the blood plasma (to 46.2% of the control group) and reduced the concentration of blood glucose in the animals (to 4.3 mmol/L).

Our study revealed the potential of using *O. vulgare* and *S. baicalensis* to normalize the lipid and carbohydrate metabolism among humans and domestic animals. Taking into account the multi-year studies that have been conducted previously, together with the results of our experiments, we believe that the leaves and inflorescences of *O. vulgare* plants can be recommended for domestic animals and humans who are overweight in complex therapies for obesity, hyperlipidemia and type-2 diabetes mellitus.

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Informed Consent Statement: Not applicable.

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Conflicts of Interest: The authors declare no conflict of interest.

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