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Section 1. Biology

Venger Andrii,
Assistant, of department of microbiology,
virology and immunology, Ph D.,
Odessa national medical university,
E-mail: venger87@ukr.net;

Kolesnyk Olga,
junior scientific researcher, Ph D.,
The Plant breeding and genetics Institute
National center of seed and cultivar investigation,
E-mail: emerald-olga@ukr.net

Malynovsky Volodymyr,
professor assistant, of department of medical
chemistry and biology, Ph D.,
International Humanitarian University,
E-mail: vmalinovskii@gmail.com

Zaitsev Andrii,
Student, of department of microbiology,
virology and immunology
Odessa national medical university,
E-mail: zayceva1957@ukr.net

Masloboeva Taisia,
Student, of department of microbiology,
virology and immunology
Odessa national medical university,
E-mail: sovushka21tasa@gmail.com

Hruzevskyi Oleksandr,
professor assistant, of department of microbiology,
virology and immunology, Ph D.,
Odessa national medical university,
E-mail: hruzevskiy@ua.fz

MOLECULAR SIZE DETERMINATION OF HYALURONIC ACID

Abstract: Hyaluronic acid (HA) is polysaccharide widely used in the medicine. In the usage of HA the size of molecules has a very important significance. Identification of HA size is usually carried out by paper chromatography method or by filtration through micropores with markers of molecular

size. However, the mentioned methods are very expensive and need extra time to be completed. The aim of scientific research was to detect the possibility of separation and identification of molecular size of HA by electrophoresis in the polyacrylamide gel. Possibility to separate and identificate the specific size of HA molecules was shown in polyacrylamide gel by electrophoretic method. This method requires less time and resources than ones which are usually used and can be applied both in industry and medicine.

Keywords: hyaluronic acid, molecular size, electrophoresis, molecular markers.

Introduction

Hyaluronic acid (HA) is polysaccharide, which is consisting of remainders of glucuronic acid and n-acetylglucoseamine, connected by β 1.3' – bonds. HA is used for treatment of bones, conjunctivitis, infertility, and also it is widely applied in cosmetology etc [1, P. 612–618]. HA is a glicosamineglycane present in the extracellular matrix of cumulus oophorus around the oocyte that proves to play the important role in natural human fertilization has anti-adhesive, anti-inflammatory, and lubricating properties, so could potentially be useful for spinal pain [2, P. 573–581]. HA administered epidurally had a therapeutic effect on the allodynia and hyperalgesia induced by chronic compression of the dorsal root ganglion. Degradation of HA is a step-wise process that can occur via enzymatic or non-enzymatic reactions [3, 12]. A reduction in HA mass or molecular weight via degradation or slowing of synthesis affects physical and chemical properties such as tissue volume [1, P. 612–618]. It was shown, that extracellular matrix contains high molecular weight hyaluronic acid (HMWHA; ~ 2×106 Da). During injury, HMWHA breaks down to low molecular weight hyaluronic acid (LMWHA; ~ $0.8 – 8 \times 105$ Da) [4, 10].

In the usage of HA the size of molecules has a very important significance. Thus, in the producing of ophthalmology drugs it is preferred to use fractions of HA with larger size. Identification of HA size is usually provided by paper chromatography method or by filtration from micropores with markers of molecular size. However, the mentioned methods are very expensive and need extra time to be completed [5, 2359–2367].

The aim of scientific research was the finding of possibility to separate and identificate the molecular size of HA by electrophoresis in the polyacrylamide gel.

Materials and methods. The electrophoresis of 0.1%, 0.2%, 10% solutions of HA, "Oxyal" and "Biotrue"medicaments, which contain HA conducted in polyacrylamide gel. The size of HA molecule was calculated by markers of molecular weight Ladder 50 and pUC19 Msp I with the help of TotalLab program. Visualization of HA and markers in polyacrylamide gel was provided by $AgNO_3$.

Results. The identified molecular sizes of HA are present in table.

Table – 1. Molecular sizes of HA

Substance	Concentration of HA,%	Size of HA according to base pairs of DNA
HA solution	0.10	1752; 1850
	0.20	1752; 1850
	10.00	1752; 1850
Oxyal	0.20	1745; 1841
Biotrue	0.24	1747

By results, HA in 0.1%, 0.2%, 10% solutions has the size which is equivalent to 1752–1850 base pairs of DNA. HA in "Oxyal" medicament was consisted of two fractions equivalent to 1745 and 1841 base pairs of DNA. HA in "Biotrue" medicament was consisted of two fractions equivalent to 1747 base pairs of DNA.

Discussion. As follows, possibility to separate and identificate the specific size of HA molecules in polyacrylamide gel by electrophoretic method was shown. This method requires less time and resources and can be used in the industry and medicine.

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Section 2. Medicine

Gusakova Iruna,
Ph D., in Medicine, docent,
E-mail: irina@mail.ru

Omelrenko Oksana,
Ph D., in Medicine, docent,
E-mail: oksana12.11.61@gmail.com

Nikolaenko Oksana,
Ph D., in Biology, docent,
E-mail: oksnikolaienko@gmail.com

Konovalov Sergey Viktorovich,
Ph D., in Medicine, docent,
E-mail: ksv55_5513@rambler.ru

Bogomaz Olga,
Ph D., in Biology, docent,
Department of Normal physiology,
Vinnitsia national Pirogov' memorial
medical university, Ukraine
E-mail: bogol@gmail.com

SLEEP QUANTITY AND QUALITY IN THE SECOND-YEAR MEDICAL STUDENTS OF VINNITSIA NATIONAL PIROGOV' MEMORIAL MEDICAL UNIVERSITY WITH ENGLISH FORM OF STUDYING

Abstract: Medicine is one of the most stressful fields of education because of its highly demanding professional and academic requirements. Sleep quality of medical students is reduced during exam periods and that poor sleep is associated with low academic performance.

Keywords: foreign students, sleep, medicine study.

As said the greatest English poet William Shakespeare "we are such stuff as dreams are made on, and our little life is rounded with a sleep" (The Tempest (4.1.168–170)). We spend a third of our life for sleep and it is difficult to over-estimate its significance. Many factors can affect sleep quality and influences of profession as well as intensity of job are among them. Medicine is one of the most stressful fields of education due to its high professional and academic requirements [1, P. 13–15].

Anxiety, depression, stress and sleep disturbances are highly prevalent in medical students. It finds its reflection in poor sleep, negative consequences for academic performance and well-being [2, P. 1618–1622]. Moreover, poor sleep is associated with impaired daily functioning, elevated risk of psychiatric symptoms, and somatic complaints [8, P. 1189–1199]. Sleep deprivation (less than six to seven hours per day) can evoke considerable violations in cognitive performance and psychomotor functions (reduction of concentration, memory and thinking strategies), daytime dysfunction, increased incidence of accidents and diminished academic performance [9, P. 231–237]. Our study aimed at examining the sleep quality and quantity in medical students having arrived for studying in Vinnitsia national medical university from different countries in the middle of the fall semester (relatively calm period of the studies).

112 second-year medical students of Vinnitsia national medical university with English form of studying (56 males and 56 females) were interrogated using Pittsburgh Sleep Quality Index (PSQI). The mean age of the students was 21.10 ± 0.28 years (in males – 20.64 ± 0.36 and in females – 21.55 ± 0.42 years respectively). Students who demonstrated an interest in participating in the investigation were invited to meet in their classroom where they were informed about the aim of the study. All participants answered the standardized questionnaire PSQI for subjective evaluation of sleep quality [3, P. 193–213; 4, P. 5–13]. The PSQI is an established questionnaire consisting of 9 selfreport items and one additional item asking for observations made by room/bedmates. The additional item was not assessed in our investigation. Responses to all 9 questions were summarized into 7 components: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication and daytime dysfunction. Poor sleep has been defined as a PSQI global score of ≥ 5.

Statistical package Microsoft Excel was used for coding and analyzing the data. Data was summed up using means (± standard error) for continuous variables and counts and percentages (± standard error) for categorical variables. Student's t-test was used to compare means between two quantitative variables (statistical significance was set at $p < 0,05$).

The obtained data are summarized in the tables 1, 2 and 3. More than half (73.21 ± 4.18%) of the students scored equal and higher than 5 on the PSQI, which allowed to suspect sleep disorders (67.86 ± 6.24% of males and 78.57 ± 5.48% of females. $p > 0.05$). The mean global PSQI score was 6.74 ± 0.28 (in males – 6.13 ± 0.32, in females – 7.36 ± 0.45, $p < 0.05$). But self-estimation of sleep quality (subjective sleep quality) showed high percentage of persons estimating themselves as good sleepers (74.11 ± 4.14% among all persons, 76.79 ± 5.64% among males and 71.43 ± 6.04% among females, $p < 0.05$).

Mean total sleep time was 6.37 ± 0.15 hours for all students (6.45 ± 0.22 hours in males and 6.29 ± ± 0.20 in females, $p > 0.05$). Sleep duration ≤ 6 hours was detected in each second student (50.00 ± 4.72%. in equal percentage of males and females). Time taken to fall asleep less 15 minutes was revealed only in 41.07 ± 4.65% persons (51.79 ± 6.68% of males and 30.36 ± 6.11% of females, $p < 0.05$). Mean score for time taken to fall asleep was 27.22 ± 2.32 min. (in males – 24.68 ± 3.62 min., in females – 29.77 ± ± 2.90 min., $p > 0.05$). Percentage of students with sleep efficiency less than 65% was 3,57 ± 1,75%. Difficulties to maintain enthusiasm were typical for 66.07 ± 4.47% of medical students (60.71 ± 6.53% of males and 71.43 ± 6.04% of females, $p > 0.05$), but difficulties to stay awake were met in lesser amount (38.39 ± 4.60% of all persons. 35.71 ± 6.40% of males and 41.07 ± 6.57% of females, $p < 0.05$). Amount of students using sleeping medication in the last one month was 12.50 ± 3.13% (14.29 ± 4.68% of males and 10.71 ± 4.13% of females, $p < 0.05$).

Table 1.– Sleep quality and its components scores among medical university students

Variables (n=112)	Options	Frequency	Percentage
Sleep Duration	Greater than 7 hrs 6–7 hrs 5–6 hrs Less than 5 hrs	37 38 23 14	33.04% 33.93% 20.54% 12.50%
Sleep latency	0 1 2 3	25 33 40 14	22.32% 29.46% 35.71% 12.50%
Day time dysfunction	0 1 2 3	29 57 21 5	25.89% 50.89% 18.75% 4.46%
Sleep efficiency	> 85% 75–84% 65–74% < 65%	73 28 7 4	65.18% 25.00% 6.25% 3.57%
Subjective Sleep quality	Very good Fairly good Fairly bad Very bad	13 70 21 8	11.61% 62.50% 18.75% 7.14%
Sleep disturbance	0 1 2 3	4 76 30 2	3.57% 67.86% 26.79% 1.74%
Use of sleep medication	Not during the past month Less than once a week Once or twice a week Three or more times a week	98 5 4 5	87.50% 4.46% 3.57% 4.46%
Sleep quality score	Good sleep Poor sleep	30 82	26.79% 73.21%

Table 2.– Mean scores of PSQI and its components (± standard error)

PSQI components	All students (n = 112)	Males (n = 56)	Females (n = 56)	P value
1	*2*	*3*	*4*	*5*
Subjective sleep quality	1.21 ± 0.07	1.18 ± 0.10	1.25 ± 0.10	p > 0.05
Sleep latency	1.38 ± 0.09	1.18 ± 0.13	1.59 ± 0.12	**p < 0.05**
Sleep duration	1.13 ± 0.10	1.02 ± 0.12	1.23 ± 0.15	p > 0.05
Habitual sleep efficiency	0.48 ± 0.07	0.38 ± 0.09	0.59 ± 0.11	p > 0.05
Sleep disturbances	1.27 ± 0.05	1.20 ± 0.07	1.34 ± 0.08	p > 0.05
Use of sleeping medications	0.25 ± 0.07	0.29 ± 0.10	0.21 ± 0.09	p > 0.05

1	*2*	*3*	*4*	*5*
Daytime dysfunction	1.02 ± 0.08	0.89 ± 0.10	1.14 ± 0.11	p > 0.05
Global PSQI	6.74 ± 0.28	6.13 ± 0.32	7.36 ± 0.45	**p < 0.05**

Female students had higher scores than male in global PSQI and sleep latency, which were statistically significant (p < 0.05 in both events). However, there was no difference between males and females on other component scores. Among the signs of sleep disturbance (look the table 3) the dominant were: waking up in the middle of the night or early morning (70.54 ± 4.31% of students), sensation of cold (68.75 ± 4.38%), necessity to get up to use the bathroom (61.61 ± 4.60%). Female students significantly more frequently complained of inability to fall asleep rapidly (within 30 minutes, p < 0.005) and problems with comfortable breathing (p < 0.05).

Table 3.– The signs of sleep disturbance **(**percentage ± standard error)

The signs of sleep disturbance	**All students (n = 112)**	**Males (n = 56)**	**Females (n = 56)**	**P value**
A. Cannot get to sleep within 30 minutes	56.25 ± 4.69%	37.50 ± 6.47%	75.00 ± 5.79%	**<0.005**
B. Wake up in the middle of the night or early morning	70.54 ± 4.31%	71.43 ± 6.04%	69.64 ± 6.14%	>0.05
C. Have to get up to use the bathroom	61.61 ± 4.60%	64.29 ± 6.40%	58.93 ± 6.57%	>0.05
D. Cannot breathe comfortably	25.00 ± 4.09%	16.07 ± 4.91%	33.93 ± 6.33%	**<0.05**
E. Cough or snore loudly	25.89 ± 4.14%	28.57 ± 6.04%	23.21 ± 5.64%	>0.05
F. Feel too cold	68.75 ± 4.38%	71.43 ± 6.04%	66.07 ± 6.33%	>0.05
G. Feel too hot	44.64 ± 4.70%	44.64 ± 4.70%	44.64 ± 6.64%	>0.05
H. Have bad dreams	55.36 ± 4.70%	50.00 ± 6.68%	60.71 ± 6.53%	>0.05
I. Have pain	38.39 ± 4.60%	32.14 ± 6.24%	44.64 ± 6.64%	>0.05
J. Other reason(s)	21.43 ± 3.88%	28.57 ± 6.04%	14.29 ± 4.68%	>0.05

A significant persentage (73.21%) of medical students from Vinnitsia national Pirogov' memorial medical university with english form of studying was classified as having poor sleep quality. The proportion of students with poor sleep quality in our study generally consistent with reports from other scientists. Thus, the incidence of sleep problems (59.4%) is enough high among medical students in Lithuania [6, 482–493] 55.8% of students in two universities of Ethiopia also were classified as having poor sleep quality. German students from two public Universities of Regensburg demonstrated high proportion of poor sleepers (53.3%) during an exam period and smaller their amount before and after an academic exam period (34.5% and 21.4% respectively). Much higher percentage of poor sleepers (77.02%) was fixed by Waqas et al. in medical students studying in the Combined Military Hospital Lahore Medical College and the Institute of Dentistry in Lahore (CMH LMC), Pakistan. The mean global PSQI score was the same in our, Ethiopian and Lithuanian students (6.74. 6.23 and 6.56 respectively), significantly higher in Pakistani students (8.1) and fluctuating in German students (6.25 during an exam period, 4.95 before exams and 4.10 after an academic exam period). The comparison of PSQI components in the indicated students is given in the (table 4).

Table 4. – The comparison of PSQI components in students from different countries

PSQI components	Our students (n=112), 2017	Lithuania (n=138), 2010	Ethiopia (n=2551), 2012	Pakistan (n=263), 2014	Germany (n=139), 2014
Global PSQI	6.74	6.56	6.23	8.1	4.95
Subjective sleep quality (bad and fairly bad) (%)	25.9%	19.6%	12.4%	35.7%	11.5%
Sleep latency (time to fall asleep)	27.22 min.	19.16 min.	The median amount –30 min.	36.9% -poor sleep latency	19.6 min.
Sleep duration	6.37 hrs	6.52 hrs	6.79 hrs	< 5 hrs of sleep per day –27.8%	7.35 hrs
Habitual sleep efficiency	<85% – 34.82%, <65% – 3,57%	< 65% – 2.9%	<85% – 29.8%, <65% – 9.6%	11.8% -poor sleep efficiency	0.42 ± 0.68
Sleep disturbance	96.43%	8.0% have a lot of sleep disturbances	95.1%	88.6%	0.99 ± 0.32
Use of sleeping medications	12.5%	8.7%	8.7%	4.9%	0.02 ± 0.15
Daytime dysfunction	74.11%	9.4% with score 3	79.7%	48.7%	1.03 ± 0.75

The significant sex difference in sleep quality was also consistent with other studies conducted among students. Thus, in our study the significantly higher proportion of female students is reported as having longer sleep latency and higher global PSQI scores. Other studies have also informed that female students were more likely to report longer sleep latency [9, P. 231–237], shorter sleep duration [5, 237], sleep disturbance and lower rating of their sleep quality [7, P. 29–33]. But the results having been obtained by many authors didn't indicate that gender has significant influence on global sleep quality. Poor sleep quality is highly prevalent among foreign medical university students studying in Vinnitsia national medical university (even in relatively calm period of the studies). Sleep duration in majority of students is not enough for restoration of forces and high intellectual activity. Gender differences of PSQI components are significant, but not considerable. Students with poor sleep quality should be made aware of the observed sleep problems.

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Zagayko Andriy L.,
Doctor, of Biological Sciences, Professor,
Head of Biochemistry Department
National University of Pharmacy,
E-mail: andrey.zagayko@gmail.com
Briukhanova Tetiana O.,
Teaching assistant, of Biochemistry Department
National University of Pharmacy,
E-mail: tatiana.briukhanova@gmail.com

SOME MECHANISMS OF HYPERURICEMIA DEVELOPMENT UNDER EXPERIMENTAL METABOLIC SYNDROME IN SYRIAN HAMSTERS

Abstract: The article presents results of investigation mechanisms of uric acid increasing level in hamsters' blood under experimental metabolic syndrome. It was found that hyperuricemia formation is caused by an increase activity of purine degradation enzymes 5' – nucleotidase, adenosine deaminase and xanthine oxidase, while inhibition of uricase activity, which was accompanied by a decrease of allantoin content.

Keywords: hyperuricemia, metabolic syndrome, uric acid, insulin resistance.

Introduction. According to WHO data, the last decades there has been an incremental increase number of diseases associated with metabolic disorders [1]. Among such disorders, the insulin resistance syndrome (IR), which is a key link in the number of diseases pathogenesis, occupies one of the leading positions: metabolic syndrome, type 2 diabetes, obesity, etc. It is known that these pathologies are inextricably linked with cardiovascular complications development – one of the leading causes of premature mortality [2].

Among the metabolic pathologies, which significantly affect the UA level, the metabolic syndrome (MS) is a leading one [1–2]. The UA level in patients with MS significantly exceeds the average values in population, and the pronouncement and progression of HU depend on the amount of MS components and the increase with number of latter [1, 4]. At the same time, to date, HU is not included in any version recommendations for diagnosis and treatment of MS. First of all, this is due to lack research biochemical mechanisms leading to an increase of UA level under MS [9]. Thus, the identification of cause-effect relationship mechanisms between HU and pathogenesis of MS is an urgent problem, which solution in the future can reduce the risk of cardiovascular complications in patients with MS by correcting the level of UA in the blood serum.

Materials and methods. 20 male Syrian hamsters (Mesocricetus auratus L.) at the age of 20 weeks at the beginning of experiment were used. Animals were kept in the standard conditions of the vivarium of the Central Scientific Research Laboratory of the National University of Pharmacy at a temperature of 22 ± 1 ° C, humidity 50–60%, in a room with a change day/night mode.

The metabolic syndrome was modeled by the keeping of animals in diet contained 29% of animal's fat with addition of fructose (2.5 g/100 g of body weight per day) (in the form of an aqueous solution) for 5

weeks [10]. Intact animals were kept on the standard diet of the National University of Pharmacy vivarium.

After 5 weeks the animals were decapitated under chloralose-urethane anesthesia. The studies were carried in accordance with national General ethical principles of animal experiments (Ukraine, 2001), which are consistent with provisions of the European Convention for the Protection of Vertebrate Animals used for Experimental and other Scientific Purposes (Strasbourg, 1986).

The studied objects were the blood serum and liver of laboratory animals. A 25% homogenate and cytosol were prepared from perfused liver by differential centrifugation.

The glucose content in the blood was determined by glucose oxidase method using the enzymatic glucose analyzer "Exan-G" (Lithuania). The level of immunoreactive insulin (IRI) was determined by an enzyme immunoassay using the standard set of Rat Insulin ELISA reagents from ALPCO (USA). The index of insulin resistance (HOMA-IR index) was calculated using the Homeostasis Model Assessment of Insulin Resistance algorithm [7].

The content of uric acid (UA) was determined in the fasting blood serum by reaction with phosphatomolibdenic Folin reagent using a set of reagents produced by Filisit-Diagnostika Ltd. (Ukraine). The content of allantoin in the liver homogenate was determined by the acid hydrolysis with 2.4 – dinitrophenylhydrazine formed glyoxylic acid hydrazone in homogenate.

In the liver homogenate, the determination of the activity of xanthine oxidase (XO) was measured by differential spectroscopy for the formation of uric acid. To determine the activity of uricase, a set of reagents "Molecular Probes" (manufactured in the USA) was used. The measurements were carried out on a Specord M40 spectrophotometer at 295 nm [5]. The activity of enzyme adenosine deaminase (ADA, EC3.5.4.4) was determined in the liver homogenate by the amount of ammonia that was released during the enzymatic reaction (adenosine deamination) after incubation with liver homogenate for 15 minutes at 37 ° C. The ammonia content was determined by phenol-hypochlorite method spectrophotometrically (at 630 nm, spectrophotometer SF-46, manufactured by «LOMO») using a calibration curve. Enzymatic activity was expressed in micromoles NH_3 per 1 minute per 1 mg protein. The protein content in the liver homogenate was determined by the Lowry method in the Hartree modification [5]. In the liver homogenate, the activity of the 5' – nucleotidase enzyme (5'-NT, EC3.1.3.5) was determined by the amount of inorganic phosphate that was released during the enzymatic reaction (substrate hydrolysis-AMP) after incubation with liver homogenate for 60 minutes at 37 ° C. The phosphorus content was determined photometrically (at 720 nm, photometer KFK-3) according to the Lowry and Lopez methods. Enzymatic activity was expressed in micrograms of phosphorus for 1 hour per 1 mg of protein [5].

Statistical analysis of the data was performed using Statistica software package (StatSoft Inc., USA, version 6.0). The significance of differences between groups was assessed by non-parametric Mann-Whitney test.

Results and discussion. The animals that were kept on a hypercaloric high-fructose diet developed a simultaneous steady increase in the level of glucose (by 93.1%) and IRI (by 49.5%) (Table 1). At the same time, the insulin resistance index significantly increased 1.69 times, confirmed the development of insulin resistance in hamsters under the conditions of our experiment (Table 1). As is known, insulin resistance is one of the key links in the pathogenesis of MS, which has verified the development of model pathology in animals.

According to clinical and epidemiological studies, MS is often accompanied by HU. The expressiveness of hyperuricemia depends on the number of MS components and is directly related to the increase in their number [1]. Moreover, despite the apparent presence of a correlation of elevated serum uric acid and MS components, the biochemical mechanisms underlying the formation of

hyperuricemia have not been enough identified to date. The results of experimental studies presented in the scientific literature on this issue are single and often quite contrarious. In this regard, hyperuricemia is not included in any version of the recommendations for diagnosis and treatment of MS. Increased uric acid in the blood serum with MS is a prognostic criterion for high cardiovascular risk in this category of patients, which determines need to study biochemical mechanisms of hyperuricemia development as an urgent issue, which was the next stage of our study.

Table 1. – Changes in glucose levels, immunoreactive insulin and insulin resistance in hamsters blood under experimental metabolic syndrome, (M ± m, n = 10)

Indices	Intact animals	MS group
Glucose, mmol/l	5.80 ± 0.44	11.20 ± 0.39*
IRI, pmol/l	92.50 ± 2.31	138.28 ± 2.41*
Index of IR (HOMA-IR)	1.78	3.02

** the differences are substantial as related to intact animals ($p \leq 0.05$)*

In animals with experimental MS, we observed a significant, more than twofold (2.09 times) increase of uric acid level (Table 2). The mechanism of the hyperuricemia formation could be complex and includes several components. On the one hand, there is increased destruction of nucleic acids due to metabolic disorders high doses of fructose, which is known to cause hypoxia, lactic acidosis and subsequent necrosis of cells, which is accompanied by the release of nucleic acids that are degraded to uric acid [3, 6]. In addition, insulin is known as a potent stimulator of urate reabsorption in the kidneys, which, given the pronounced hyperinsulinemia in animals with MS, apparently took place [6]. Hyperglycemia, which developed against the background of our experiments, stimulated alternative ways of using glucose, in particular – the pentose phosphate pathway, in which ribozo-5 – phosphate is formed – a necessary component for *de novo* nucleotide synthesis, although taking into account the predominance of catabolic processes in this pathology, This mechanism is of secondary importance. Thus, under the conditions of model pathology, hyperuricemia was primarily caused by increased destruction of nucleic acids with the formation of uric acid with a delay in its removal from the body due to stimulation of urate reabsorption in kidneys.

Table 2. – Changes in the content of uric acid and allantoin in hamsters blood under experimental metabolic syndrome, (M ± m, n =10)

Indices	Intact animals	MS group
Allantoin, mmol/l	45.16 ± 0.75	37.87 ± 0.88
Uric acid, mmol/l	3.01 ± 0.23	6.29 ± 0.45*

** the differences are substantial as related to intact animals ($p \leq 0.05$)*

Our hypothesis that hyperuricemia state is due to an increase in the disintegration of nitrogenous bases was confirmed by a change in the activity of enzyme systems that are involved in the purine degradation processes, namely, 5'-NT and ADA. The activity of these enzymes in the liver of animals with model pathology significantly increased – by 28.69% and 33.45%, respectively, in comparison with the indices of intact hamsters (Table 3). As is known, 5'-NT and ADA are the key enzymes of the first stages of the purine base disintegration, catalyzing the reaction of hydrolytic cleavage of phosphate from AMP (5'-NT enzyme) and further deamination of adenosine with the formation of inosine and xanthine (ADA enzyme), which are substrates for XO [3].

Table 3. – Changes in the activity of enzymes involved in the degradation of purine bases in the liver of hamsters with an experimental metabolic syndrome, (M ± m, n = 10)

Indices	Intact animals	MS group
XO activity (nmol UA x mg^{-1} protein x min^{-1})	2.35 ± 0.09	4.58 ± 0.12*
Uricase activity (nmol allantoine x mg^{-1} protein x min^{-1})	1.42 ± 0.26	1.16 ± 0.11*
5'-NT activity (μg Pi x h^{-1} x g tissue)	8.12 ± 0.18	10.45 ± 0.15*
ADA activity (mmol/l NH_3 x min^{-1} x g tissue)	7.95 ± 0.66	10.61 ± 0.93*

** the differences are substantial as related to intact animals ($p \leq 0.05$)*

The activity of XO enzyme catalyzing the formation of uric acid also increased significantly in animals with MS – by 94.9% compared to healthy animals (Table 3). Probably, such a pronounced increase in the activity of XO was the result of a complex influence number of factors, in particular, an increase in the level of the counterinsulant hormone cortisol (as is well known, hypercortisolemia is part of the pathogenesis of MS), which is capable of increasing the activity of XO [3]. The increase in the uric acid formation in the early stages of the metabolic syndrome could be compensatory, since glucose toxicity is accompanied by the development of oxidative (auto-oxidation of glucose and products of glycosylation with active oxygen forms) and deoxidizing stress (due to the development of pseudohypoxia and accumulation of NADH(H^+) and NADPH (H^+) in the intima of the vessels), which drain reserves of antioxidant enzymes – superoxide dismutase, glutathione peroxidase, etc., and uric acid has antioxidant properties. It should be noted that for uric acid is characterized by the so-called antioxidant-paradox: when the concentration increases, it begins to exhibit prooxidant properties, which intensifies oxidative damage [8]. It is also known that uric acid is a factor contributing to the formation of nephropathy in patients with MS, which is accompanied by the development of kidneys ischemic damage, which in turn activates the XO, which further increases the formation of uric acid, closing the vicious circle [11].

It is known that most animals in the body synthesize an enzyme uricase, which splits uric acid with the formation of allantoin. According to the results obtained, in experimental animals, the activity of uricase in the liver was significantly decreased in animals (by 18.4% relative to healthy hamsters), which was naturally manifested also by a decrease in the level of allantoin in the blood – by 16.2% compared to the same index of intact animals. The described changes are consistent with the data obtained by us regarding a significant increase in the level of uric acid in the blood, which indicates the interruption of the purine degradation process at the level of uric acid formation without subsequent conversion of the latter into allantoin by the action of uricase.

Conclusions. Experimental metabolic syndrome in Syrian golden hamsters is accompanied by pronounced hyperuricemia, which could be caused by increased destruction of purine nucleotides, as evidenced by an increase in the activity of enzymes involved in degradation of purines – 5' – nucleotidase, adenosine deaminase and xanthin oxidase, among which the most significantly increased activity of xanthin oxidase. Decrease in the background of this activity of uricase led to the accumulation of uric acid in the blood, which mediated the development of hyperuricemia.

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Section 3. Physics

Barykinsky Gennady Mikhailovich,
Institute of conceptual studies,
Moscow, Russia
E-mail: k@genn.ru

WORLD LAW OF SCALING

Abstract: in this paper, on the basis of deductive logic and analysis of known mathematical expressions that determine some physical parameters of existing things in Nature, conclusions are obtained, the generalization of which corresponds to the status of the law, which determines the scaling of the fundamental properties of things in Nature in the widest range – from elementary particles to composite matter, including the ratio of the parameters of different Universes.

Keywords: elementary particles, monopole, universe, physical parameters, space, energy, scaling.

By getting into the swing of things,
We gain understanding.
And by realizing the meaning of things,
We create consciousness [1].

Current concepts of elementary particle physics and the universe are based on the absence of adequately acceptable models. For this reason, the theoretical description and further experimental development of physics in these directions has slowed down. Further attempts to develop particle physics at accelerators the continuously increasing capacity are becoming more futile. The logic of this futile is a simple aphorism: "You can't make an omelette without breaking eggs" (Literal translation: If you hew trees the chips must fly), and if the power output of the hewing process increases to "madness", then the whole forest turns into chips. The situation has reached a point where many hundreds of supposedly short-lived useless particles had been already registered as "chips". It should not be forgotten, however, that the cost of such experiments is commensurate with the budgets of many States participating in these projects. Therefore, the methods of non-accelerator and theoretical physics are becoming more and more important [2].

Desired models are those that could combine, for example, the properties of the internal structure of elementary particles with the properties of experimentally observed interactions of these particles with their environment. There is a need for more realistic models of the Universe, since the current standard models of the Universe is built on the "Big Bang" theory and is burdened with problems leading the theory of the Universe to a dead end. The futility of this theory has stand out a mile for a long time, because this theory does not correspond to one of the fundamental principle of the existence of everything – objectives definition; moreover, the idea of a singularity itself is absurd.

As one of the many approaches addressed to the solving of issues discussed above, it would be advisable to consider: "Is there a law according to which

the symmetry that determines the world of fundamental properties of elementary particles is scaled and respectively destructed?" It is still unclear under what law the fundamental properties of elementary particles are changed as they move in space from their centre to the periphery and further up to distances much larger than their own sizes. It is also still unclear in what ratio is the existence genesis of a huge variety of objects in the universe, and in particular of the objects that owe their existence to the action of various manifestations of forces of electromagnetic and gravitational origin.

The general analysis of the difficult problems of the theory of the Universe shows that many physical parameters characterizing the objects of a single or composite matter in the Universe are functionally linked. This linkage is a result of the world law of scaling, which is based on classical geometric progression: $a_n = a_1 g^{n-1}$, where: a_1 and a_n – are the first and following terms of the sequence; g – is a ratio of the progression, n – is a quantum number of scaling.

The destruction of simple symmetries, due to which objects of a matter of increased complexity or new forms of interactions are created, occurs in points of a geometric mean, see Figure below:

The next part of this work is a continuation of the work cycle under the title (Figure 1).

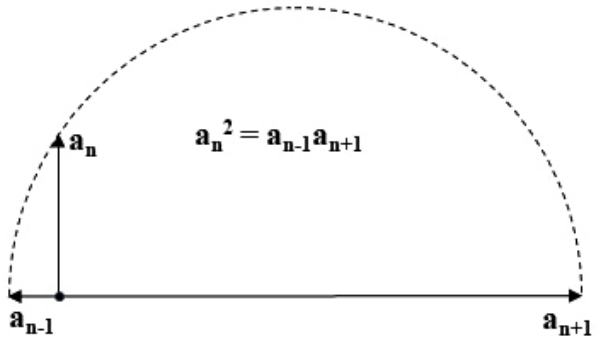

Figure 1.

The relativity of the fundamental properties of the electron [3]. The comment of the authors of the works [4] highlighting relevance of the problem under discussion is of interest in this regard: "There is no doubt that the understanding of the structure of elementary particles will be as important as the discovery of the atomic and nucleus structure".

The vector defining the seek search directions and development of ideas related to the solution of such complex problems is represented by the outstanding physicist and philosopher Niels Bohr, who has repeatedly noted that it is important to create theories as insane as possible, but at the same time he believed that these theories ought to lend themselves to simple the description [5].

At this point, expressions for a number of spatial characteristics of elementary particles are well known, for example, for electrons such as: classical electron radius r_e, the Compton wavelength λ_k, Radius of Bohr's Orbit r_b, de Broglie wavelength λ_b, mean square displacement of electron r_v, determined by the impact on the electron of virtual vacuum particles, and some others. Separate links between these characteristics are also known. Despite the fact that the essence of these and some other parameters needs its clarification, it would be desirable that there was a mathematical expression, shedding light on the essence and meaning of the hierarchy of stepwise complexity of the existing forms of elementary matter.

The analysis of above mentioned and some other mathematical expressions describing the different spatial characteristics of the r_n electron leads to a generalization that corresponds to the status of the law of scaling [6]:

$$r_n = r_k \beta^{2n}, \qquad (1)$$

where: r_k and λ_κ – are Compton radius and wavelength: $\lambda_\kappa = 2\pi r_k$, β – is a common ratio of geometric progression, which is determined by the equations: $\beta^2\alpha = 1$ or $e\beta = q$, α – is a fine-structure constant, q – is an internal charge of the electrons, e – is an outer electric charge of electron, n – is a quantum number of scaling, which takes an integer or a half-integer value.

Association of Electron Properties with the world law of scaling.

The following table No.1, based on the law defined by the formula (1), presents the expressions

and corresponding values of the electron's spatial characteristics. Full compliance of the obtained data with the already known table proves that the proposed expression (1) can be used to describe the spatial scaling law of the fundamental properties of the electron.

Table 1.

n	Parameter	(cm)	Name of the parameter
–3	$r_m = r_k\beta^{-6} = e^6/m_e c^4\hbar^2 = e^2/m_\mu c^2$	$1.5\cdot10^{-17}$	Classical monopole radius
–2	$r_\mu = r_k\beta^{-4} = e^4/m_e c^3\hbar = \hbar/m_\mu c$	$2.06\cdot10^{-15}$	Compton radius of the monopole
–1	$r_e = r_k\beta^{-2} = e^2/m_e c^2$	$2.82\cdot10^{-13}$	Classical electron radius
0	$r_k = r_k\beta^0 = \hbar/m_e c$	$3.86\cdot10^{-11}$	Compton radius of the electron
1	$r_b = r_k\beta^2 = \hbar^2/m_e e^2$	$5.29\cdot10^{-9}$	Min atomic size, Bohr radius
2	$r_a = r_k\beta^4 = \hbar^3 c/m_e e^4$	$7.25\cdot10^{-7}$	Max atomic size
3	$r_м = r_k\beta^6 = \hbar^4 c^2/m_e e^6$	$9.94\cdot10^{-5}$	Size of biomolecules

The (table No. 1) shows that each point corresponding to the current discrete spatial parameter of the electron is the geometric mean of the two neighbouring:

$r_\mu^2 = r_e r_m$
$r_e^2 = r_\mu r_k = r_m r_b$
$r_k^2 = r_e r_b = r_\mu r_a = r_м r_m$
$r_b^2 = r_k r_a = r_м r_e$
$r_a^2 = r_b r_м$

Moreover, these are the points where a certain part of the previous symmetries is destroyed.

The spatial scaling of the electromagnetic forces, which is based on the Coulomb's law $F_{кул} \sim 1/r^2$, is responsible for the decay of the seemingly simple Coulomb force into residual and more complex forces that determine the interatomic and intermolecular interaction. For example, such residual forces as: dipole, quadrupole, ionic, metal, hydrogen, valence, covalent, Van der Waal's, polarization, induction, dispersion, orientation and some others.

It should be noted that the electric force itself, as determined by the Coulomb's law, is also residual, since the outer electric charge of the electron e is β times less than the internal q, i.e. $q = e\beta$. For this reason, it is the internal charge, which is the primary source of all the others, determines the interaction of the electron with the external vacuum environment.

Table 2.

$r_{-1} - r_{-2} = 2.82\cdot10^{-13}–2.06\cdot10^{-15}$	Effect of monopole. K-capture. Muon.
$r_0 - r_{-1} = 3.86\cdot10^{-11}–2.82\cdot10^{-13}$	Inner energy effect – $m_e c^2$.
$r_1 - r_0 = 5.29\cdot10^{-9}–3.86\cdot10^{-11}$	Effect of the charge q, force field generation
$r_2 - r_1 = 7.25\cdot10^{-7}–5.29\cdot10^{-9}$	Range of electron shells of atoms.
$r_3 - r_2 = 9.94\cdot10^{-5}–7.25\cdot10^{-7}$	Water molecule, DNA, viruses.
$r_4 - r_3 = 1.36\cdot10^{-2}–9.94\cdot10^{-5}$	Bacteria, erythrocytes, cell nucleus.
$r_5 - r_4 = 1.86\cdot10^{-1}–1.36\cdot10^{-2}$	Skin cells, a large bacterium, amoeba.
$r_6 - r_5 = 2.55\cdot10^{1}–1.86\cdot10^{-1}$	Ant, chicken egg.
$r_7 - r_6 = 3.49\cdot10^{3}–2.55\cdot10^{1}$	Human

As a result of scaling of the fundamental properties of the electron there are functional spatial ranges with high specificity, between which, starting from the centre, the gradual complication of the created objects of matter occurs when moving, i.e. the formation of forms from simple to more complex, which is shown in (table No. 2). It is obvious that not only the electron, but also more important particles such

as proton and neutron are responsible for the formation of many forms, as they are also structurally made up of electric charges, and therefore have their own specific scaling ranges.

Let's write down the expression for the force acting between the internal electron charges for $n = 0$ as follows: $F_q = q^2/r_0^2$. This expression is completely symmetrical in relation to the electric e and magnetic μ of the electron charges. Write down the expression $F_{кул}$ for $n = 1$ and -1:

$F_{кул} = q^2/r_1^2\beta^2$, for $q^2/\beta^2 = e^2$, $\rightarrow F_{кул} = e^2/r_1^2$. (2)

$F_{кул} = q^2\beta^2/r_{-1}^2$, for $q^2\beta^2 = \mu^2$, $\rightarrow F_{кул} = \mu^2/r_{-1}^2$ (3)

It follows from (2) and (3) that the symmetry of the electron internal charge q has fallen into classical charges: electric **e** and magnetic μ. Excluding from (2) and (3) β and considering that $q^2 = \hbar c$, we get:

$$e\mu = \hbar c, \quad (4)$$

In 1931, P.A.M. Dirac, who proposed the idea of the existence of magnetic monopoles, derived an equation for quantization of the electric charge as follows [7]:

$$e\mu = (n/2)\,\hbar c, \quad (5)$$

In the calculations (5) was used the condition that the electron orbital magnetic moment is quantized. However, in our case, $n = 1$, as for (4) in (2) and (3) was considered only the basic state, and the deuce should be absent, because in calculations of the electron magnetic moment (as part of a more modern electron model) the full area of current sheet is covered completely when turning not on 2π, two times less. Therefore, the formulas (4) and (5) are the same.

If the right side of equation (4) is multiplied and divided by β^2, and considering that:

$$e^2 = \hbar c/\beta^2, \quad (6)$$

$$\mu^2 = \hbar c\beta^2, \quad (7)$$

the following system of equations is obtained:

$$\mu = (n/2)e\beta^2, \quad (8)$$

$$e = (n/2)\mu/\beta^2. \quad (9)$$

Solving the system of equations (8, 9) referred to μ or e, we get: $n = \pm 2$, which proves the coincidence of formulas (4) and (5).

Solving the system of equations (6, 7) referred to β, and considering that $q^2 = \hbar c$, we get:

$$q^2 = e\mu. \quad (10)$$

The expression (10) shows that the internal charge of the electron q, is the geometric mean between the external electric charge of the electron e and its internal magnetic charge μ.

With expressions and their corresponding values (see the table No. 1), characterizing the classical radius of electron and monopole, it becomes possible to calculate the mass of monopole. In order to do this we shall write down the ratio of the two radii in the following form and we get:

$$m_\mu = (r_e/r_\mu)m_e = 1.88\cdot10^4\, m_e. \quad (11)$$

m_μ value in (11) is 4 times higher than the value of the monopole mass obtained in [2]. This non-coincidence is due to the fact that the calculations in [2, P. 354] are based on the equation (5), while the present calculations are based on a more correct equation (4). Proof of this conclusion is the fact that m_μ is also subject to the scaling law, i.e.:

$m_\mu = \beta^4 m_e = 1.88\cdot10^4 m_e$, as according to the law (1) $r_e = r_\mu\,\beta^4$.

Let's write down (1) for $n = -1/2$:

$$r_{-1/2} = r_\nu = r_k/\beta, \quad (12)$$

The analysis shows that the expression (12) up to the weakly varying logarithm coincides with the known expression for the mean square displacement of r_ν electron in its interaction with the field of vacuum virtual photons [8], the author of this work has considered this phenomenon by the methods of the classical theory. It should be noted that this phenomenon in the scientific literature is more known as "Lamb shift". It should be added that $\mathbf{r}_\nu$ obeying law (1) is connected with other important spatial characteristics of electron by the geometric mean ratio:

$$r_\nu^2 = r_k r_e. \quad (13)$$

Association of properties of the universe with world law of scaling.

Examples of the application of the law of world scaling in different spheres of existence of matter in the Universe are represented in the following

§ § 5, 6, 7, 8. Obviously that this list is not exhaustive, and in fact there are countless examples of this.

Up-to-date information about the distribution of matter in the Universe, that become standard, shows that the major global types of matter are approximately within the following percent range, the values of which are specified in (table No. 3), but for quite a long time, the results of the study of these ranges are increasingly converging to their geometric mean ratio, and therefore increasingly satisfy the law of world scaling:

Table 3.

	Type of matter in the universe	%	Average
M_o	ordinary matter	4–6	$M_{dm}^2 = M_o M_{de}$
M_{dm}	dark matter	18–24	
M_{de}	dark matter	68–75	

The following (table No. 4) shows the geometric mean ratio of the fundamental forces in the universe at the Planck's extreme values:

Table 4.

	Fundamental forces at the Planck point	Average
F_g	Gravity: $F_g = m^2/r^2$	$F_c^2 = F_e F_g$
F_c	Electromagnetic: $F_e = q^2/r^2$	
F_e	Elastic: $F_e = kr$, where: $k = m\omega^2$	

DNA and blood are the most important components of living matter in the universe. (Tables No. 5) and 6 indicate that the main constituents of these components are also connected by the geometric mean ratio. The value ranges of the constituents shown in (table No. 5), as well as in (table No. 3), are increasingly converging to their geometric mean ratio as the relevant studies develop.

Table 5.

	Genetic variation in DNA	%	Average
G_{cp}	genes encoding proteins	2–5	$G_{rs}^2 = G_{cp} G_{ep}$
G_{rs}	repetitive gene sequences	20–30	
G_{ep}	genes that do not encode proteins	70–80	

Table 6.

	Blood corpuscles	pcs/mm^3	Среднее
$k_л$	leukocytes	$8 \cdot 10^3$	$k_m^2 = k_л k_э$
k_m	platelets	$3 \cdot 10^5$	
$k_э$	erythrocytes	$5 \cdot 10^6$	

(Tables No. 7) and 8 indicate the values and their compliance to the law (1) the most important parameters of living and inanimate matter in the Universe. The tables show that the most important members of the matter in the Universe: living-human, and inanimate – electron, hold their geometric mean positions in the Universe respectively, which is fully consistent with the law of world scaling.

Table 7.

	Masses of objects and the universe	g	Average
m_{mu}	min mass of object in the Universe	10^{-48}	$m_p^2 = m_{mu} m_u$
m_p	human mass	10^4	
m_u	mass of the Universe	10^{56}	

Since the human mass accurately holds his average geometric position in the Universe, it is fair to conclude that the estimation of the mass of the Universe as a whole as $m_u = \mathbf{10^{56}}$g is realistic. If this is so, it is reasonable and logical to assume that the human size must also correspond to his geometric mean position in the Universe. However, recent developments in astrophysics show that the size of the Universe is equal to $r_u = \mathbf{10^{27}cm}$, which is 10^{10} times less than the number specified in the table No. 8. This contradiction does not conform to the law of world scaling, which requires that the size of the universe correspond to the value specified in table No. 8, which means that the real size of the corresponds to $r_u = \mathbf{10^{37}cm}$.

Table 8.

	Sizes of the objects and the universe	cm	Average
r_{mo}	min size of object in the Universe	10^{-33}	$r_p^2 = r_{mo} r_u$
r_p	human size	10^2	
r_u	size of the Universe	10^{37}	

Let us imagine that, according to the existing embedded universe theory, there are Universes that differ in size as they are embedding: the upper – U_{-1}, "our" current – U_0 and the lower – U_{+1}. Assuming that the ratio of Universes sizes corresponds to the law of world scaling, it is logical to assume that the ratio of these sizes also satisfies the geometric mean, as shown in (table No. 9), where common ratio of the progression is chosen equal to 10^{21}.

Table 9.

	Sizes of the embedded universes	cm	Average
U_{-1}	Size of the upper Universe	10^{58}	$U_0^2 = U_{-1} U_{+1}$
U_0	Size of the current Universe	10^{37}	
U_{+1}	Size of the lower Universe	10^{16}	

Thus, it should be considered to be proven that the fundamental fact – the law of world scaling exists. 18 fundamental examples in a wide range and the correspondence of the law to reality, which are represented in this paper, prove conclusively its universality. This universality is based on the principle of objectives definition, without which the Universe cannot exist.

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Section 4. Economic

Eshov Mansour Pulatovich,
Candidate, of economic sciences, associate professor,
Dean of the Faculty of Accounting and Auditing
of the Tashkent State University of Economics,
E-mail: uralqodirov@gmail.com
Shaymardanov Shakhzod Robertovich,
Student, in faculty of Accounting and audit
in The Tashkent state university of economy, Tashkent, Uzbekistan.
Mamadaliev Doniyorbek Shuhratbekovich,
Student, in faculty of Information technology in economics,
in The Tashkent state university of economy, Tashkent, Uzbekistan.
Alimov Gayratjon Abduraxmonovich,
Student, in faculty of Economy,
in The Tashkent state university of economy,
Tashkent, Uzbekistan.

ORGANIZATION OF ADDITIONAL PROFESSIONAL EDUCATION OF ACCOUNTANTS

Abstract: In this article, it is given solutions of the problems of the organization and especially in trade, consists in the necessity to be settled within the complex mechanism of modern dynamical market formed in Russia.

Keywords: dynamical market, financial statement, managerial reporting, bookkeeper, balance-sheet.

The problem of the organization and especially In trade, consists in the necessity to be settled within the complex mechanism of modern dynamical market formed in Russia.

What practical steps should be undertaken for acceleration of the given process? How to overcome «old traditions» and to apprehend new approaches? How to change the mentality of bookkeepers? How to convince the manager and the bookkeeper of the necessity of drawing up of financial statement and managerial reporting serving as a tool of business management, in interaction with the external partners, the tool for getting credits, going on share market? The novelty of theoretical approaches and the practical mechanisms based on the profound analysis of realization of objects in view are peculiar to the work of M. E. Lianskoy.

The development of new patterns of ownership and organizational – legal forms of enterprises generated a new to Russia type of relations, the relations of the head with the proprietor.

The accounting information to the greater extent turns from means of the accounting and the control over the base of substantiation of the made decisions, and from timeliness of their getting,

quality and reliability, on which more and more depends the extent of the efficiency of the activity of the organization.

The growth of the number of enterprises determined the steady demand for bookkeeper, having confirmed the mass character of the given trade. Now in Russia there are more than 3,5 million bookkeepers, and within the framework of the CIS they make 5 million.

The manager of the enterprise should understand the necessity to raise the prestige of the accounting trade, realize, that the bookkeeper inevitably turns to one of the key figures In the control system of the managing subject. In fact the bookkeeper bears to the great extent the responsibility for skillful use of advantages of the world economic integration, direct foreign economic relations, for search for necessary means and ways of the liquidation of technological backlog of Russian economy.

The bookkeeper undertakes also the cardinal reform of the whole system of economic information of the enterprise. Alongside with the financial accounting represented to the external users, and managerial accounting should become the basic part of the mechanism of making managerial decisions providing the growth of the efficiency of the activity integrates the registration, analytical, scheduled and control functions of internal information infrastructure of the enterprise. These data are called to promote the trust and strong long-term connections between the enterprise and its market contractors.

The trade of the bookkeepers in Russia experiences the period of radical changes. With the transition to the market economy the role of the bookkeeper in business management raises immeasurably. The data of managerial accounting become the base for making argued managerial decisions. Huge importance is paid to the balance-sheet and the financial documentation accompanying it in connection with that, they become the objects of public stating.

The relation to the tradeoff the bookkeepers changes also radically. The bookkeeper becomes the managerial professional, which the basic sense of the activity consists in diagnostics and development of actions focused on the preservation of economic well-being of the enterprise during the whole period of its existence. Indissoluble connection of the accounting and financial management, corresponding to the professional standards made in the international practice should be provided.

The development of the economy of Russia depends greatly on quick realization of the Program of reforming of the accounting to the Program of reforming of the accounting according to the International Standards on Accounting. Therefore, the confirmation by the accounting community of the professional level of the representatives occupying certain positions and rendering the kinds of services demanding the corresponding qualification is one of the major ways to raise the economy, to attract the necessary investments into its real sector.

Raising professional skills on accounting is needed as a toolkit for confirmation of the conformity of the bookkeeper to the requirements of professional competence, the level of special formation, the got skills and the accumulated experience in the corresponding field of the activity, ability, of the bookkeeper to organize qualitatively the work of the corresponding services in organizations of various patterns of ownership and the branch belonging, and also the ability to held independently the consultations on problems of the accounting and stating. Thus the absolute readiness of the bookkeeper to observe the norms of professional etiquette is taken into account.

CMA (the certified management accountants) should be given the rights and the opportunity for professional maintenance of real efficiency of economic activities of the enterprise, for development of ways of solving its problems, strategy and tactics of survival. Thus, it is necessary to take into account the problems faced by the concrete enterprise. For example, functioning of public joint-stock companies which shares are quoted on the share market,

is connected with the necessity of the attraction of capital (including the foreign one) for development of the production, on infrastructure, and it demands drawing up of the reporting in full conformity with the International standards on Accounting. Other public joint-stock companies and also federal and large municipal unitary enterprises may also get advantages at transition to the accounting according to the international standards on accounting. The companies with limited liability, except for subjects of small business and noncommercial organizations while are focused on drawing up of the reporting according to the Russian rules of accounting. Subject of small business and the noncommercial organization can make the reporting according to the simplified variant.

It is obvious, that different variants of maintenance of managerial and financial accounting demand the different degree of readiness of the accounting staff.

Lately the requirements shown to the circle of knowledge which the bookkeeper should master have been essentially extended conditions;

– The dynamism and variety of the economy became considerably broader;

– The integration processes amplified;

– The legislative bases and the accounting standards within the framework of which the bookkeeper should work have changed considerably;

– The system of taxation varied;

On the other hand, the facilities and technology of the accounting affair has considerably changed use, in particular, has extended:

– Economic – mathematical modeling,

– The newest software products,

– Computer facilities,

– Information databases,

– Search and information system, etc.

The base of the accounting began to focus the bookkeeper on the comparison of different variants and the choice of that of them, which to the greater extent is adequate to the goals and status of the production.

Such a position of the bookkeeper becomes more and more common. It complies fully with the professional standards common in international practice, and it is maintained with the operating experience of many countries of the world.

Now with the development of normative base of the accounting and perfection of the fiscal system more and more urgent there is a task of retraining and improvement of professional skills of bookkeeper and also of preparation of new staff of bookkeeper. It is necessary to notice especially, that the basic changes in operating conditions of enterprises and macro-economics of Russia assume the necessity of retraining and those qualified bookkeepers who were trained in short-term courses on market economy. Among the bookkeepers there are now many highly skilled experts who have the higher, but not profile education (the programmers, engineers, designers, mathematicians). This category of accountants. Should think over the system of the second higher education. The examination shows, that for successful work under conditions of market economy it is necessary to prepare and train over 3 million person, including:

– the accountants – 1 million person;

– bookkeeper – technicians – 1 million (these professional categories were traditionally prepared for technical schools, i.e. middle special educational schools);

– bookkeepers – economists- 500 thousand person (they are the experts with the higher special education, who are prepared for high schools);

– highly skilled bookkeepers (professional bookkeepers) – 300 thousand persons (the chief accountants of large commercial structures bookkeepers – consultants and the certified public accountants (CPA) of experts);

Professional bookkeeper – financial managers – 100 thousand persons; professional bookkeepers – auditors – 100–150 thousand persons.

The developed system of higher education on preparation of bookkeepers cannot cope with the

task of such a scale. Now the bookkeepers are formed in over 200 high schools, including:

– The profile ones;

– Not profile ones in which there is the corresponding specialization;

– Commercial.

They can form up to 30 thousand experts annually. Hence, at demand for 500 thousand persons for full meeting the demand for bookkeepers more than 15 years are needed. It is unreal.

In the work of Lianskoy M. E the profound analysis of theoretical bases of the created control system of supplementary professional training as an integral component of the state system of supplementary professional training in Russia is made.

The management of supplementary professional training is considered by the author as the object of the research as a component of the system of supplementary professional training Russia. The system of supplementary professional training acts as the mechanism providing management by process of rendering of educational services. The choice of the given objects of research is lawful, since he is dictated by necessity of carrying out of the analysis of interaction of elements of control system of supplementary professional training for changing conditions of the environment, the scientific substantiation of opportunities of formation and effective development of the control system by educational establishments.

The scientific novelty of the work of Lianskoy M. E onsists in that for the first time in Russia the control system of supplementary professional training responding national and international requirements is created.

The practical importance of the work of Lianskoy M. E consists in that the developed concepts, theoretical and methodical bases as the mechanism of the coordination activity of control system of supplementary professional training can be used by the Ministry of education of the Russian Federation in the structure of the uniform system of supplementary professional training for all educational institutions of Russia. In the work the role of leading Russian professional organizations of bookkeepers and auditors is proved, concrete recommendations on the use of their scientific potential in solving problems of supplementary professional training are given.

The realization of specific targets for achievement of objects in view alongside with the practical use by managers of various enterprises, it is focused on the heads of services of personnel management and their divisions which are engaged in the organization of training is formed by modular principle and allows to adapt the corresponding programs of training under conditions of concrete enterprises.

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Section 5. Jurisprudence

Ogneviuk Ganna Ziniviivna,
Ph D., assistant,' Law Faculty
Kyiv National Taras Shevchenko University,
E-mail: a.ogneviuk@gmail.com

'RES JUDICATA' AS AN ELEMENT OF LEGAL CERTAINTY PRINCIPLE

Abstract: Interpretation of 'res judicata' in connection with legal certainty principle is examined in the article. It is argued that 'res judicata' is an element of legal certainty principle in opposition to the point of view that both these principles have the same meaning.

Keywords: res judicata, legal certainty, rule of law, predictability of law, case-law.

Legal certainty is a general principle of law and as so consists of a number of elements. It is settled to maitain the balance between the interests of a person and the state, to protect a person from excess of sate power, from unpredictability and uncertainty of legal norms and from ambiguity of application.

One of such elements of legal certainty is 'res judicata'. This juridishial termin has a huge historical background. It was formulated in the Ancient Rome, and retained its name in Latin till now. Literal translation of the term means 'judicial case were the final decision is made', 'a settled case'. Actually, now we use the shortened version of the Latin 'res judicata pro veritate habetur' which means that the decision made in judicial case is regarded as verity. In ancient times it was due to this principle, that conditions and facts, which were considered as well as the final judicial decision, became prejudicial facts and had to be executed undoubtedly. Final decision brought an end to the dispute and, despite the fact that each part could have a different meaning, was mandatory. Since that time the concept has developed over the centuries. Nowadays it is well represented in the practice of European Court of Human Rights. In the case-law of this Court a term 'res judicata' is connected with another wider principle such as legal certainty.

Traditionally, the respect to the finally adjudicated judgment is provided on the national level by the norms of the constitution and procedure laws. However a particular judgment not only affects the parties of the dispute, but also has an influence on the stability, predictability of the legal system itself, on the respect to the judicial branch of power.

Apart from the European Court of Human Rights national coutrs also take into consideration legal certainty principle in judicial practice when the case concerns review of the court decision. The Supreme Court of Ukraine issued on 24.12.2015 an order (case № 15–126 (15)) rejecting the claim of the convict to reopen the case. The claim of the convict was based on the argument that the Court applied legal norms differently in similar cases. The reason for bringing the case to the Supreme Court appeared in procedural act two months later after the final decision in the case was made. So the Supreme Court decided that final judgment could not be revoked for such a reason as it 'puts in doubt predictability and

stability of all court decisions which were issued according to the former procedure. This will result in violation of the legal certainty principle and is unacceptable'.

The requirement of stability and mandatory of judgment sometimes is appeared to be in the conflict with the requirement of protection of the human rights, recognized on the highest level. It is in the situation when the court made a serious mistake and final decision seriously influences human rights of the person.

The above regarded case is pretended to be one of those situations. The separate opinion of the judge Korotkevich M. is given about the decision in this case. It says that 'the state could not protect its decision (final juridical decision in this case) from the revolving procedure and the judgment from the possibility of reversal of the judge`s decision in the Supreme Court due to the procedures provided by law'. It seems to be not so evident weather the rights of this person were broken or not by the refusal of revolving the case. From one hand, if the Supreme Court set aside the final judgment and start a new procedure of revolving the case it would be a precedent for others to act the same way and to initiate the hearings of their cases. And such acts could be numerous. This will evidently lead to unpredictability in the legal relations and to irrespective attitude to the judgment. But on the other hand, the amendments, which came into force after the final decision, could seriously influence the rights of the convict.

In such a cases it is always the aim to find weather the rights of the person were violated so seriously that despite negative impact of the revolving, this procedure should take place. But what are the measures of such a procedure?

J. Matveeva says, that final decision of the court in respect of the 'res judicata' should lead to a number of consequences: the execution of the decision could not be postponed without any legal reasons; discretion granted to certain authorities could not be used in the way to delay the execution of the judgment and if this happens an effective supervision of the court should be provided [3, P. 51].

The number of cases of European Court of Human Rights where principle of 'res judicata' is threatened is so called 'third party proceedings' – procedures that can be submitted exclusively by the third parties in exceptional circumstances. In order to fill the application for third party proceedings the contested judgment should bring serious damages to the rights of the third parties. Thus, it is not enough for these parties to have a legitimate interest to protect, but the prejudice suffered by them should be resulted from the content or the motivation of the judgment, in which the situation of the European Court will analyze from case to case, in a serious manner, if their rights have been prejudiced or not [5, P. 2329].

After analyzing a number of cases using 'res judicata' it is stated that: an application for revision shall be admissible only were the applicant was not able for no fault of his or her own, to raise such objection before the judgment became "res judicata" [9, P. 276].

It appears from this case-law practice that 'res judicata' is confronted, to some extend, to the right of the person to appeal which is provided in majority of countries. But it is important to underline that the reason for appeal should not be only a different position of the party, it shouldn`t be as well the attempt to revoke the case because of the unwillingness to obey the court decision using any possibility given by procedure norms. Such situation appeared to happen in the case "Ryabih vs. Russian Federation" about the possibility to revoke the case after the final judgment. In its decision The European Court of Human Rights clearly underlines that in such a cases the main issue is the aim and the meaning of the procedure. It should take place when mistakes, that affected the applicant's rights seriously, were made by the court in previous decisions or procedures. No rejection of revolving the case could be justified by the circumstances that concern only the review of the case in the new procedure and aims in a new and different court decision.

While analyzing this and the other similar cases Alekseeva T. says that The European Court of Human Rights came to the conclusion 'that the right to revoke the case is a right which has a time limit. Court decisions could not be 'in doubt' all the time it could reverse the importance of the judicial procedure. This possibility should be limited in time for everyone, including governmental authorities [1, P. 76].

The huge number of analyzed cases made in her research, lead her to the conclusion that 'res judicata' is only and mainly the principle of the procedural law [1, P. 78].

Principle res judicata is not embodied in the norms of the Convention but its essence results from the Article 6 and is used in case-law. A particular case and procedure where the 'res judicata' is used. But its meaning and impact spreads further than a particular case. It is an indispensable element of the respect for the judicial power, which is a base of the state governing in democratic countries. So it is hard to agree with Alekseeva T., though she regards 'res judicata' as another name for legal certainty.

"The fundamental character of that principle appears from the terms of the Statute and the Charter of the United Nations… That principle signifies that the decisions are not only binding on the parties, but are final in the sence that they can not be reopened by the parties as regardes issues that have been determined save by procedures of an exeptional nature, specially laid down for that purpose". The author says that " two purposes, one general, the other specific, underlie the principle of res judicata, internationally as nationally. First, the stability of legal relations requires that litigation come to an end. The Court`s function, according to Article 38 of its Statute, is to "decide", that is, to bring to an end, "such disputes as are submitted to it". Secondly, it is to the interest of each party that an issue which has already been adjudicated in favour of that party be not argued again [7, P. 45].

Such arguments were considered in he case "Bochan vs. Ukraine". The Court found that there was no justification for rejection of the use of 'res judicata' and legal certainty principles towards the third parties, whose rights should be protected in the case were they didn't participate.

In Ukrainian law doctrine 'res judicata' is regarded as an element of the theoretical principle of legal certinty, while legal certainty in turn is regarded as an element of the rule of law. "Res judicata' or compulsory character of court decision was mentioned as the element of legal certainty by V. Smorodinsky [8, P. 44], M. Kozubra [4, P. 50], S. Pogrebnyak [6, P. 501] as well as european scientists, such as Groussot X. and Minssen T. [2].

When talking about the exceptions of 'res judicata' it is highly important to mention the other aspects of legal certainty, so that it will become evident that the reasons for such an exceptions are rather important and are made with the focus of protection of rule of law and legal certainty.

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