Bombushkar, Igor, Gozhenko, Anatoliy, Korda, Inna, Badiuk, Nataliya, Zukow, Walery and Popovych, Igor. Features of the exchange of electrolytes and nitrogenous metabolites under different options of uric acid exchange in healthy female rats. Journal of Education, Health and Sport. 2020;10(4):405-415. eISSN 2391-8306. DOI http://dx.doi.org/10.12775/JEHS.2020.10.04.043
https://apcz.umk.pl/JEHS/article/view/39438
https://zenodo.org/record/8380624

The journal has had 5 points in Ministry of Science and Higher Education parametric evaluation. § 8. 2) and § 12. 1. 2) 22.02.2019.

Received: 01.03.2020. Revised: 18.04.2020. Accepted: 30.04.2020.

FEATURES OF THE EXCHANGE OF ELECTROLYTES AND NITROGENOUS METABOLITES UNDER DIFFERENT OPTIONS OF URIC ACID EXCHANGE IN HEALTHY FEMALE RATS

Igor S. Bombushkar[1], Anatoliy I. Gozhenko[1], Inna V. Korda[2], Nataliya S. Badiuk[1], Walery Zukow[3], Igor L. Popovych[1,4]

[1]Ukrainian Scientific Research Institute of Medicine for Transport, Odesa
prof.gozhenko@gmail.com; badiuk_ns@ukr.net
[2]IY Horbachevs'kyi National Medical University, Ternopil' kordai@tdmu.edu.ua
[3]Nicolaus Copernicus University, Torun', zukow@umk.pl
[4]OO Bohomolets' Institute of Physiology, Kyïv i.popovych@biph.kiev.ua

Abstract

Background. We previously identified 4 variants-clusters of uricemia and uricosuria both in rats and in humans. It was shown that the clusters differ from each other in the constellation of immune, autonomic and endocrine parameters, which correlate with uricemia and uricosuria. The aim of this study was to identify the electrolytes and nitrogenous metabolites, the combination of which differentiates previously formed quantitative and qualitative variants of uric acid metabolism in rats. **Materials and Methods**. Experiment was performed on 60 healthy female Wistar rats 220-300 g. The plasma and urine levels of the uric acid, urea, creatinine, calcium, phosphates, chloride, magnesium, sodium and potassium (also in erythrocytes) as well as glucose (in plasma only) were determined. **Results**. 10 metabolic parameters characteristic of four variants of uric acid exchange were identified: the concentration of glucose, urea, phosphates, magnesium and potassium in plasma, and the latter in erythrocytes, as well as the excretion of creatinine, urea, phosphates and calcium with urine. The accuracy of discrimination of clusters based on the totality of this metabolic constellation together with uricemia is 95%. The cumulative determining influence of the parameters of uric acid exchange (due to the significant advantage of uricosuria over uricemia) on the constellation of metabolic parameters is 56%. Diuresis and excretion of phosphates and potassium are subject to the maximum positive determination from the side of uric acid; excretion of calcium, creatinine and urea are determined to a lesser extent; levels of creatinine, urea and potassium in the plasma are even less, and magnesiumuria is subject to the minimum

determination. **Conclusion.** Uric acid is naturally associated with the state of electrolytes and nitrogenous metabolites exchange in healthy female rats.

Keywords: uricemia, uricosuria, electrolytes, nitrogenous metabolites, relationships, female rats.

INTRODUCTION

We previously identified 4 variants-clusters of uricemia and uricosuria both in rats [1-3] and in humans [4-6]. Using the method of discriminant analysis, it was shown that the clusters differ from each other in the constellation of immune [3,5,6], autonomic and endocrine [7] parameters, which to one degree or another correlate with uricemia and uricosuria. Even earlier in our laboratory, the connection of uricemia with parameters of electrolytes and nitrogenous exchange in urological patients was revealed [8]. Therefore, the aim of this study was to identify the electrolytes and nitrogenous metabolites, the combination of which differentiates previously formed quantitative and qualitative variants of uric acid metabolism in rats.

MATERIAL AND METHODS

Experiment was performed on 60 healthy female Wistar rats 220-300 g. Of these, 10 remained naïve, while others received drinking water of various compositions during the week. The day after the completion of the drinking course animals were placed in individual chambers with perforated bottom for collecting daily urine. The experiment was completed by decapitation of rats in order to collect as much blood as possible. The plasma and urine levels of the uric acid (uricase method), creatinine (by Jaffe's color reaction by Popper's method), urea (urease method by reaction with phenolhypochlorite), glucose (in plasma only; glucose-oxidase method), calcium (by reaction with arsenase III), phosphates (phosphate-molybdate method), magnesium (by reaction with colgamite), chloride (mercury-rhodanidine method), sodium and potassium (both also in erythrocytes; by flamming photometry) were determined. The analyzes were carried out according to the instructions described in the manual [9].

The analyzers “Pointe-180” ("Scientific", USA) and “Reflotron” (Boehringer Mannheim, BRD) were used with appropriate sets and a flamming spectrophotometer “СФ-47”.

Digital material is statistically processed on a computer using the software package "Statistica 5.5".

RESULTS AND DISCUSSION

The discriminant analysis procedure [10] included in the model, in addition to uricemia, 10 variables characteristic of four clusters (Tables 1 and 2). They represent the concentration of glucose, urea, phosphates, magnesium and potassium in plasma, and the latter in erythrocytes, as well as the excretion of creatinine, urea, phosphates and calcium with urine. Other registered parameters of metabolism, primarily uricosuria and urine osmolality, as well as excretion of sodium, chloride, magnesium and phosphates as well as plasma levels of

creatinine, calcium, chloride and sodium, and the latter in erythrocytes, were outside the discriminant model.

Table 1. Summary of the step-by-step analysis of metabolic variables ranked by the Λ criterion

Variable Enter	F to entrer	p-value	Lambda	F-value	p-value
Uricemia	45,6	0,000000	0,290	45,6	0,000000
Magnesium Plasma	9,9	0,000026	0,189	23,9	0,000000
Phosphates Plasma	5,6	0,002132	0,144	17,8	0,000000
Phosphates Excretion	5,1	0,003749	0,112	15,1	0,000000
Potassium Plasma	4,3	0,008442	0,090	13,4	0,000000
Urea Plasma	3,5	0,021897	0,074	12,1	0,000000
Potassium Erythrocytes	2.7	0.055483	0.064	11.0	0.000000
Creatinine Excretion	1,7	0,173862	0,058	9,9	0,000000
Glucose Plasma	1,2	0,330486	0,054	9,0	0,000000
Urea Excretion	1,1	0,349804	0,050	8,2	0,000000
Calcium Excretion	1,2	0,308472	0,047	7,6	0,000000

The identifying information contained in the 11 discriminant variables is condensed into three roots. The first root contains 71,9% of the discriminant power (r^*=0,915; Wilks' Λ=0,047; $\chi^2_{(33)}$=158; $p<10^{-6}$), second - 24,0% (r^*=0,795; Wilks' Λ=0,286; $\chi^2_{(20)}$=65; $p=10^{-6}$), and the third only 4,1% and, moreover, is insignificant (r^*=0,474; Wilks' Λ=0,775; $\chi^2_{(9)}$=13; p=0,158).

Further, on the basis of the coefficients given in the Table 3 (see the appendix), the individual root values were calculated with subsequent visualization of cluster members in their information field.

In the Table 4 metabolic parameters are grouped and ranked according to their structural coefficients, and together with discriminant variables, variables that did not enter the model, but still carry recognizable information, are also considered.

Table 2. Summary of the analysis of discriminant functions for metabolic variables ranked by structural coefficient

Step 11, N of vars in model: 11; Grouping: 4 grps; Wilks' Λ: 0,0466; approx. $F_{(33)}$=7,6; $p<10^{-6}$

	Clusters of Uric acid Exchange (n)				Parameters of Wilks' Statistics					
Variables currently in the model	S+Un+ (9)	Sn+U± (19)	SnUn+ (17)	S-Un- (15)	Wil-ks' Λ	Parti-al Λ	F-re-move	p-level	Tole-rancy	Norm (10)
Uricemia, µM/L	1379	865	554	259	0,154	0,302	35,4	10^{-6}	0,840	662
Creatinine Excretion µM/100 g•24h	11,9	12,6	12,6	8,6	0,052	0,903	1,65	0,190	0,460	8,7
Potassium Erythrocy-tes, mM/L	89,6	87,3	86,2	85,0	0,055	0,847	2,77	0,052	0,771	87,0
Glucose Plasma, mM/L	5,63	5,27	5,29	5,28	0,050	0,926	1,22	0,314	0,889	4,95
Urea Plasma, mM/L	5,29	8,76	9,29	9,39	0,056	0,824	3,27	0,029	0,656	7,42
Magnesium Plasma, mM/L	0,84	0,78	1,27	0,45	0,067	0,690	6,88	0,001	0,809	0,88
Phosphates Plasma, mM/L	0,84	1,11	1,19	0,46	0,078	0,596	10,4	10^{-4}	0,630	0,72
Calcium Excretion, µM/100 g•24h	2,60	4,17	4,27	2,89	0,050	0,926	1,23	0,308	0,275	2,90
Potassium Plasma, mM/L	3,63	3,37	3,87	3,25	0,061	0,767	4,66	0,006	0,642	4,23
Phosphates Excretion, µM/100 g•24h	9,0	12,7	10,4	9,3	0,052	0,895	1,80	0,160	0,229	9,4
Urea Excretion µM/100 g•24h	231	264	224	144	0,054	0,865	2,39	0,081	0,151	169
Variables currently not in the model	S+Un+ (9)	Sn+U± (19)	SnUn+ (17)	S-Un- (15)	Wil-ks' Λ	Parti-al Λ	F to enter	p-level	Tole-rancy	Norm (10)
Uricosuria, µM/100 g•24h	7,00	6,63	5,46	3,31	0,047	0,999	0,01	0,999	0,478	5,72
Osmolality Urine, mOsm/L	611	550	523	530	0,046	0,986	0,21	0,889	0,729	559
Sodium Excretion, µM/100 g•24h	201	184	149	118	0,046	0,996	0,07	0,977	0,517	135
Chloride Excretion, µM/100 g•24h	213	190	136	154	0,046	0,984	0,24	0,867	0,692	144
Creatinine Plasma, µM/L	50	81	97	81	0,044	0,942	0,92	0,439	0,219	73
Potassium Excretion, µM/100 g•24h	193	214	182	185	0,044	0,950	0,79	0,503	0,283	189
Magnesium Excretion, µM/100 g•24h	2,81	3,62	4,56	5,02	0,046	0,989	0,17	0,915	0,557	3,30
Sodium Erythrocytes, mM/L	23,1	23,6	23,1	20,4	0,045	0,969	0,47	0,703	0,588	22,0
Sodium Plasma, mM/L	129,4	128,7	130,8	127,4	0,046	0,978	0,33	0,802	0,746	128,6
Calcium Plasma, mM/L	2,92	2,69	2,41	2,78	0,044	0,943	0,91	0,445	0,783	3,35
Chloride Plasma, mM/L	93,8	92,0	94,8	90,7	0,045	0,958	0,65	0,587	0,639	94,3

Table 3. Standardized and unstandardized coefficients and constants for discriminant metabolic variables

	Standardized Coefficients		
Variable	Root 1	Root 2	Root 3
Uricemia	-0,975	-0,230	0,094
Magnesium Plasma	-0,267	0,589	-0,682
Phosphates Plasma	-0,539	0,711	0,593
Phosphates Excretion	0,078	0,117	1,408
Potassium Plasma	-0,447	0,548	0,167
Urea Plasma	0,162	0,624	0,042
Potassium Erythrocytes	-0,386	-0,333	0,127
Creatinine Excretion	-0,099	0,359	-0,736
Glucose Plasma	-0,147	-0,320	0,002
Urea Excretion	-0,963	-0,206	-0,629
Calcium Excretion	0,527	0,159	0,310

	Raw Coefficients		
Variable	Root 1	Root 2	Root 3
Uricemia	-0,0040	-0,0010	0,0004
Magnesium Plasma	-0,6112	1,3477	-1,5617
Phosphates Plasma	-1,2330	1,6275	1,3584
Phosphates Excretion	0,0149	0,0223	0,2690
Potassium Plasma	-0,5778	0,7096	0,2156
Urea Plasma	0,0577	0,2219	0,0150
Potassium Erythrocytes	-0,0617	-0,0532	0,0202
Creatinine Excretion	-0,0214	0,0774	-0,1585
Glucose Plasma	-0,1864	-0,4069	0,0028
Urea Excretion	-0,0056	-0,0012	-0,0036
Calcium Excretion	0,2278	0,0689	0,1339
Constant	12,9270	-0,7885	-3,6300

Table 4. Correlations between metabolic variables and roots, centroids of clusters and Z-values of clusters

	Correlations Variables-Roots			S+Un+	Sn+U-+	SnUn+	S-Un-
Root 1(71,9%)	Root 1	Root 2	Root 3	**-3,39**	**-1,05**	**+0,06**	**+3,30**
Uricemia	**-,663**	-,325	,101	**+2,10**	+0,59	-0,32	**-1,18**
Uricosuria	currently not in the model			**+0,24**	+0,17	-0,05	**-0,45**
Creatinine Excretion	**-,133**	,168	,077	**+0,74**	+0,90	+0,88	**-0,03**
Potassium Erythrocytes	**-,102**	-,057	-,006	**+0,38**	+0,04	-0,12	**-0,29**
Glucose Plasma	**-,047**	-,077	-,150	**+0,62**	+0,29	+0,31	**+0,30**
Sodium Erythrocytes	currently not in the model			**+0,23**	+0,35	+0,24	**-0,37**
Sodium Excretion	currently not in the model			**+0,79**	+0,59	+0,17	**-0,19**
Chloride Excretion	currently not in the model			**+0,70**	+0,47	-0,09	**+0,10**
Osmolality Urine	currently not in the model			**+0,37**	-0,06	-0,26	**-0,21**
Urea Plasma	**,170**	,235	,262	**-1,24**	+0,78	+1,09	**+1,15**
Magnesium Excretion	currently not in the model			**-0,24**	+0,15	+0,61	**+0,83**
Root 2(24,0%)	Root 1	Root 2	Root 3	-1,88	+0,28	**+1,63**	-1,08
Magnesium Plasma	-,142	**,426**	-,585	-0,07	-0,17	**+0,64**	-0,72
Phosphates Plasma	-,193	**,411**	,132	+0,28	+0,85	**+1,02**	-0,57
Calcium Excretion	-,023	**,225**	,195	-0,20	+0,83	**+0,90**	-0,01
Potassium Plasma	-,094	**,183**	-,017	-0,85	-0,69	**-0,51**	-1,39
Creatinine Plasma	currently not in the model			-0,93	+0,35	**+1,02**	+0,34
Sodium Plasma	currently not in the model			+0,16	+0,02	**+0,43**	-0,23
Chloride Plasma	currently not in the model			-0,08	-0,33	**+0,07**	-0,50
Calcium Plasma	currently not in the model			-0,42	-0,65	**-0,92**	-0,56
Root 3(4,1%)	Root 1	Root 2	Root 3	-0,53	**+0,71**	-0,48	-0,03
Phosphates Excretion	-,038	,108	**,446**	-0,06	**+0,52**	+0,16	-0,02
Urea Excretion	-,101	,085	**,199**	+0,46	**+0,71**	+0,41	-0,19
Potassium Excretion	currently not in the model			+0,03	**+0,21**	-0,05	-0,03

Fig. 1 shows that the extreme left zone of the first root axis is occupied by members of the **S+Un+** cluster. Such localization reflects the combination of hyperuricemia with increased (and maximal for the sample) levels of creatinine excretion, erythrocyte potassium and glycemia, and a reduced level of urea in the plasma. Worthy of attention are the maximum normal levels of uricosuria, erythrocyte natriuresis, and urine osmolality for the sample, and elevated levels of natriuria and chlorideuria, instead of minimal normal magniuria. The opposite polar position is occupied by the members of the **S-Un-** cluster, which are characterized by a combination of hypouricemia with a reduced content of potassium in erythrocytes, normal, but minimal for the sample, uricosuria, creatinineuria, and glycemia, instead, maximally elevated levels of urea in plasma and magnesia. Members of the other two clusters occupy an intermediate position along the axis of the first radical and are partially mixed.

Mixing also takes place along the axis of the second radical, but to a lesser extent. At the same time, members of the **SnUn+** cluster are characterized by maximally increased levels of magnesium, phosphatemia, and calciuria (as well as abnormal creatinineemia and natriemia) in combination with minimally reduced potassium (as well as maximally reduced calcium).

An additional unclear demarcation of these clusters occurs along the axis of the third radical, due to the maximally increased excretion of phosphates and urea (as well as potassium) in the members of the **Sn+U-+** cluster.

Despite the visual mixing, in the information space of the three discriminant roots, the last two clusters are statistically significantly separated from each other, which is confirmed by the calculation of the squares of the Mahalanobis distances between them, not to mention even the visually clear separation of the first two clusters (Table 5).

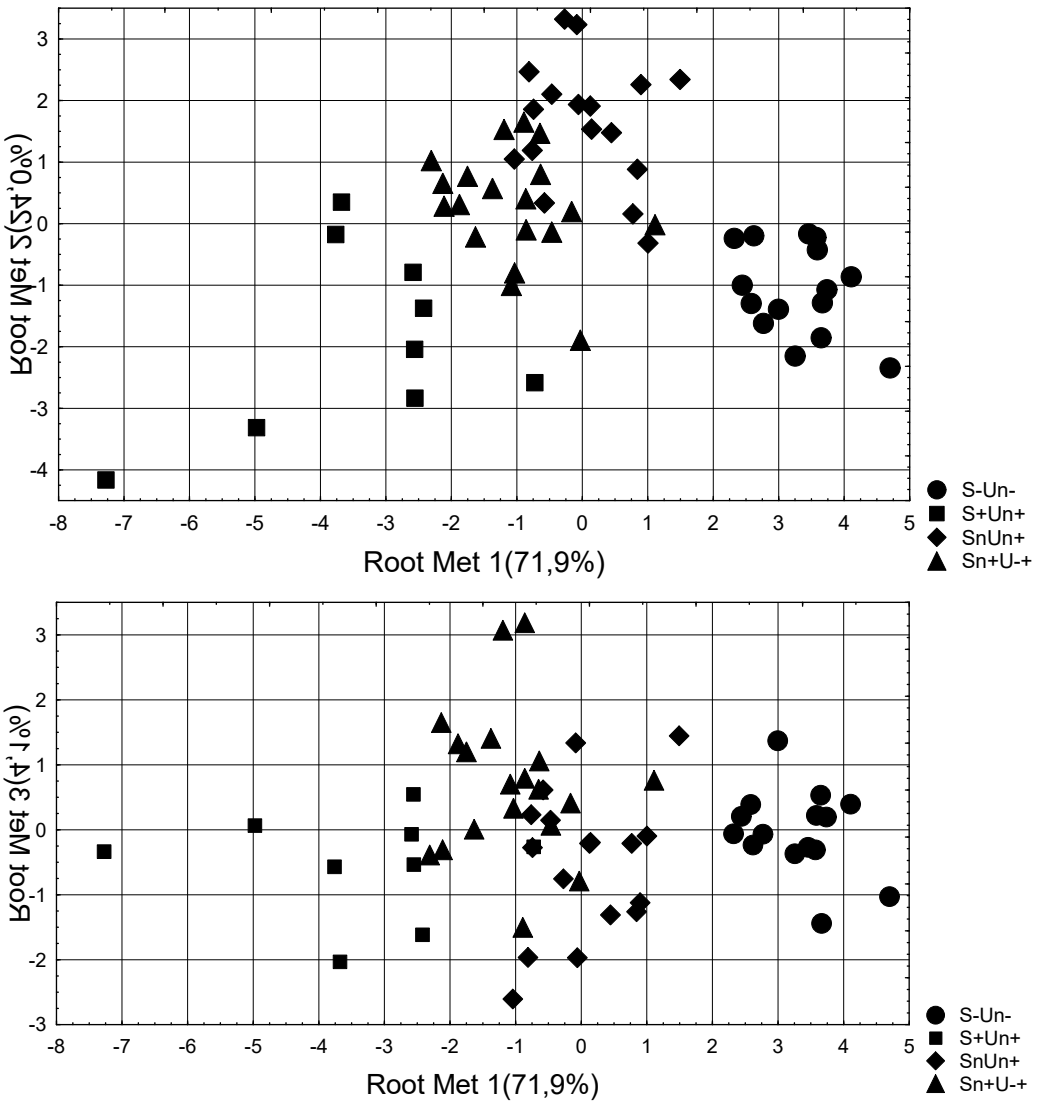


Fig. 1. Scattering of individual values of the first and second (top) and first and third (bottom) discriminant metabolic roots of rats of different clusters

Table 5. Squares of Mahalanobis distances between clusters (above the diagonal) and F-criteria (df=11,5) and p-levels (below the diagonal)

Clusters	S-Un-	S+Un+	SnUn+	Sn+U-+
S-Un-	0	46	18	21
S+Un+	19,2 10^{-6}	0	24	12
SnUn+	10,7 10^{-6}	10,6 10^{-6}	0	5
Sn+U-+	13,3 10^{-6}	3,6 10^{-4}	3,0 0,005	0

The application of classification functions (Table 6) enables the retrospective identification of the first two clusters without error, and the other two with 1 and 2 errors, which gives a total accuracy of 95,0% (Table 7).

Table 6. Coefficients and constants of classification functions for metabolic accompaniment of clusters of uric acid metabolism

Variable	S-Un- p=,250	S+Un+ p=,150	SnUn+ p=,283	Sn+U-+ p=,317
Uricemia	0,032	0,060	0,043	0,049
Magnesium Plasma	0,443	4,229	6,779	3,770
Phosphates Plasma	15,39	21,65	23,18	23,98
Phosphates Excretion	1,478	1,226	1,369	1,644
Potassium Plasma	11,63	14,81	15,32	15,27
Urea Plasma	0,059	-0,512	0,466	0,122
Potassium Erythrocytes	2,858	3,304	2,905	3,069
Creatinine Excretion	-1,476	-1,316	-1,126	-1,396
Glucose Plasma	11,99	13,56	11,49	12,25
Urea Excretion	0,044	0,084	0,060	0,064
Calcium Excretion	-1,650	-3,296	-2,263	-2,446
Constant	-182,7	-268,9	-220,4	-237,3

Table 7. Classification matrix for uric acid exchange clusters
Rows: observed classifications; columns: predicted classifications

Clusters	Percent Correct	S+Un+ p=,150	Sn+U-+ p=,317	SnUn+ p=,283	S-Un- p=,250
S+Un+	100	9	0	0	0
Sn+U-+	94,7	0	18	1	0
SnUn+	88,2	0	2	15	0
S-Un-	100	0	0	0	15
Total	95,0	9	20	16	15

At the last stage, we will analyze the connections between the parameters of uric acid and electrolyte-nitrogen exchanges. The correlation matrix shows that uricemia is significantly associated with plasma levels of urea and creatinine and magnesia (Table 8).

Table 8. Matrix of correlations between parameters of uric acid and electrolyte-nitrogen exchanges

Variable	Uricemia	Uricosuria
CrE	0,15	0,39
Diur	0,09	0,54
CrP	-0,28	0,13
KE	0,09	0,46
MgE	-0,30	-0,06
CaE	-0,03	0,33
PE	0,02	0,50
UreaE	0,12	0,35
UreaP	-0,31	0,06
KP	0,05	0,20

However, when constructing a regression model by stepwise exclusion, the program left creatinineuria in the model, excluding creatinineemia. As a result, the determination rate was 26% (Table 9).

Table 9. Regression model for metabolic parameters and uricemia

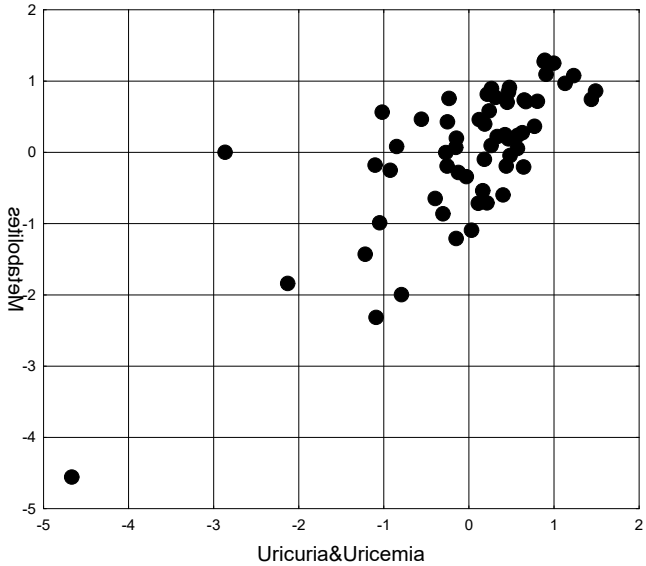
N=60	R=0,509; R^2=0,259; Adjusted R^2=0,219; F(3,6)=6,5; p=0,0007					
	Beta	St. Err. of Beta	B	St. Err. of B	t(56)	p-value
Intercpt			926,31	179,17	5,17	0,000003
Cr E	0,353	0,127	31,84	11,41	2,79	0,007176
Mg E	-0,394	0,128	-60,43	19,55	-3,09	0,003108
Urea P	-0,282	0,117	-39,98	16,62	-2,41	0,019495

Instead, the connections of uricosuria are more numerous and stronger. The descending series consists of: daily diuresis, urinary excretion of phosphates, potassium, creatinine, urea and calcium. Interestingly, with stepwise elimination, the last two parameters were not included in the regression model, while plasma potassium was. The rate of determination of the listed parameters by uricosuria is 39% (Table 10).

Table 10. Regression model for metabolic parameters and uricosuria

N=60	R=0,621; R^2=0,386; Adjusted R^2=0,329 F(5,5)=6,8; p=0,00006					
	Beta	St. Err. of Beta	B	St. Err. of B	t(54)	p-value
Intercpt			-0,071	1,853	-0,04	0,969
Cr Excr	-0,404	0,238	-0,268	0,158	-1,70	0,096
Diurese	1,023	0,452	4,301	1,900	2,26	0,028
K Excr	0,338	0,144	0,011	0,005	2,34	0,023
P Excr	-0,388	0,350	-0,234	0,211	-1,11	0,272
K Plasma	0,123	0,111	0,496	0,450	1,10	0,275

According to the results of the canonical correlation analysis, the total determining influence of the parameters of uric acid exchange (due to the significant advantage of uricosuria over uricemia) on the constellation of parameters of electrolyte and nitrogen exchange reaches 56% (Fig. 3).



R=0,751; R^2=0,563; $\chi^2_{(20)}$=65; $p<10^{-6}$; Λ Prime=0,292

Fig. 3. Scatterplot of canonical correlation between uricosuria and uricemia (X axis) and metabolic parameters (Y axis) of female rats

The factor loadings on the metabolic canonical root indicate that diuresis and excretion of phosphates and potassium are the most positively determined; calcium, creatinine and urea excretion are less determined; creatinine, urea and potassium levels in plasma are even less determined, and magnesiumuria is the least determined (Table 11).

Table 11. Factor structure of canonical roots of uric acid and neuro-endocrine adaptation factors

Variable	left set R
Uricosuria	-0,910
Uricemia	-0,070

Variable	right set R
Creatinine Excretion	-0,490
Diurese	-0.765
Creatinine Plasma	-0,373
Potassium Excretion	-0,639
Magnesium Excretion	-0,098
Calcium Excretion	-0,519
Phosphates Excretion	-0,745
Urea Excretion	-0,460
Urea Plasma	-0,289
Potassium Plasma	-0,278

CONCLUSION

Uric acid is naturally associated with the state of electrolytes and nitrogenous metabolites exchange in healthy female rats.

A detailed discussion will be conducted after the publication of the results of a similar study in humans.

CONFORMITY TO ETHICAL STANDARDS

Experiments on animals have been carried out in accordance with the provisions of the Helsinki Declaration of 1975, revised and supplemented in 2002 by the Directives of the National Committees for Ethics in Scientific Research.

The conduct of experiments was approved by the Ethics Committee of the SR Institute of Medicine of Transport. The modern rules for the maintenance and use of laboratory animals complying with the principles of the European Convention for the Protection of Vertebrate Animals used for scientific experiments and needs are observed (Strasbourg, 1985).

REFERENCES

1. Gozhenko AI, Smagliy VS, Korda IV, Zukow W, Popovych IL. Cluster analysis of uric acid exchange parameters in female rats. Journal of Education, Health and Sport. 2019; 9(11): 277-286.

2. Gozhenko AI, Smagliy VS, Korda IV, Badiuk NS, Zukow W, Popovych IL. Features of immune status in different states of uric acid metabolism in female rats. Journal of Education, Health and Sport. 2019; 9(12): 167-180.

3. Gozhenko AI, Smagliy VS, Korda IV, Badiuk NS, Zukow W, Popovych IL. Functional relationships between parameters of uric acid exchange and immunity in female rats. Actual problems of transport medicine. 2019; 4(58): 123–131.

4. Smagliy VS, Gozhenko AI, Korda IV, Badiuk NS, Zukow W, Kovbasnyuk MM, Popovych IL. Variants of uric acid metabolism and their immune and microbiota accompaniments in patients with neuroendocrine-immune complex dysfunction. Actual problems of transport medicine. 2020; 1(59): 114–125.
5. Gozhenko AI, Smagliy VS, Korda IV, Badiuk NS, Zukow W, Kovbasnyuk MM, Popovych IL. Relationships between parameters of uric acid exchange and immunity as well as microbiota in patients with neuroendocrine-immune complex dysfunction. Journal of Education, Health and Sport. 2020; 10(1): 165-175.
6. Gozhenko AI, Smagliy VS, Korda IV, Badiuk NS, Zukow W, Kovbasnyuk MM, Popovych IL. Relationships between changes in uric acid parameters metabolism and parameters of immunity and microbiota in patients with neuroendocrine-immune complex dysfunction. Journal of Education, Health and Sport. 2020; 10(2): 212-222.
7. Popovych IL, Bombushkar IS, Badiuk NS, Korda IV, Zukow W, Gozhenko AI. Features of the state of neuro-endocrine factors of adaptation under different options of uric acid metabolism in healthy female rats. Journal of Education, Health and Sport. 2020; 10(3): 352-362.
8. Ivassivka SV, Popovych IL, Aksentiychuk BI, Flyunt IS. Physiological Activity of Uric Acid and its Role in the Mechanism of Action of Naftussya Water [in Ukrainian]. Kyïv: Computerpress; 2004: 163.
9. Goryachkovskiy AM. Clinical Biochemistry [in Russian]. Odesa: Astroprint; 1998: 608.
10. Klecka WR. Discriminant Analysis [trans. from English in Russian] (Seventh Printing, 1986). In: Factor, Discriminant and Cluster Analysis. Moskva: Finansy i Statistika; 1989: 78-138.