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CORRELATION RELATIONS OF THE COMPOSITION OF SALIVA AND BLOOD PLASMA IN THE NORM

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Abstract Saliva is the only biological fluid with a unique set of research capabilities that provide for complete non-invasiveness, multiple and almost unlimited sampling of material. Unfortunately, the mechanism that regulates the maintenance of a certain composition of saliva is still unclear. The main attention of clinical specialists is attracted by new laboratory methods for analyzing saliva in order to obtain a variety of diagnostic information. Advances are predicted in the field of diagnosing various diseases, taking into account the properties of saliva. We studied the relationship between the biochemical composition of saliva and blood plasma in normal conditions in our experimental condition, and they are given in this paper**.**

Keywords: saliva, blood plasma, biological fluid, protein, diagnostics**.**

Introduction

Recently, the attention of researchers to the study of the properties of human saliva as a material with unique properties and diagnostic capabilities has increased. The study of saliva refers to non-invasive methods and is carried out to assess the age and physiological status, identify somatic diseases, pathology of the salivary glands and oral tissues, genetic markers, drug monitoring, etc. [1, 2, 3, 4]. Saliva contains many biological molecules, including DNA, messenger RNA (mRNA), microRNA, protein, metabolites, and microbiota. Changes in their concentration in saliva can be used to detect systemic diseases and diseases of the oral cavity in the early stages, as well as to assess the prognosis of the course of diseases and control the response to treatment [5]. In 2008, the term “salivaomics” was proposed, which combines knowledge about various components in saliva, including the genome, epigenome, transcriptome, proteome, metabolome and microbiome [6, 7]. Saliva is an ultrafiltrate of blood plasma and contains proteins that are synthesized in the salivary glands or enter it from the blood.

To date, researchers have identified 2340 proteins in the saliva proteome, of which 20–30% are also found in the blood [8], which is an encouraging indication of the clinical usefulness of saliva. Unlike blood plasma, the proteome of which is

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formed by 99% of the total protein content due to 22 main proteins, in saliva, 20 main proteins make up only 40% of the total protein content [9]. As a result, it is practically easier to detect biomolecules with high sensitivity and specificity in saliva than in blood. Saliva can also be used to detect substances from the blood, such as steroid hormones [10]. Nevertheless, the question of the relationship between the biochemical composition of saliva and blood remains not fully understood [11, 12, 13, 14], and the presence of a correlation between the content of individual components is unproven [15, 16, 17]. In this regard, in our opinion, it is relevant to compare the biochemical composition of saliva and blood plasma in order to establish the absence of a relationship between the compositions of these biological fluids in the norm.

Purpose of the research

The purpose of the study is to study the relationship between the biochemical composition of saliva and blood plasma in normal conditions.

Materials and Methods

The study involved 107 volunteers, including 46 women (age 37.2 ± 3.9 years) and 61 men (age 36.1 ± 2.8 years). Blood and saliva sampling was carried out at the blood transfusion station of the Clinical Oncological Dispensary. In all samples of saliva and blood plasma, 23 biochemical parameters were determined, including mineral and protein composition, enzyme activity, as well as indicators of endogenous intoxication and lipid peroxidation.

The content of total calcium (in μmol/l) was determined photometrically on a StatFax 3300 semi-automatic biochemical analyzer by reaction with Arsenazo III, magnesium - by reaction with xylidyl blue, phosphorus - by reaction with ammonium molybdate, chlorides - by reaction with mercury thiocyanate using ZAO kits "Vector-Best" (Novosibirsk) [18]. The concentration of urea (in μmol/l) was determined photometrically by the urease-salicylate method according to Bertlot, total protein (in g/l) - by reaction with pyrogallol red [19], albumin (in μmol/l) - by reaction with bromcresol green, diazo compounds (μmol/l) - by diazotization reaction in the presence of sulfanilic acid [20], sialic acids (in μmol/l) - according to the Hess method [21]. The concentration of uric acid (in μmol/l) was determined by the uricase method, the intensity of nitric oxide synthesis was estimated by the content of stable products of its oxidation - nitrate ions (in μmol/l) by capillary electrophoresis (KAPEL-105M, Lumeks) [22]. The activity of ALT and AST was determined by the colorimetric dinitrophenylhydrazine method according to Reitman-Frenkel, ALP - by the end point method according to Bessey-Lowry-Brock, LDH - by the kinetic UV method according to the rate of NADH oxidation, GGT - by the kinetic method using L-gamma-glutamyl-3- carboxy-4-nitroanilide as a substrate according to Seitz-Persin, catalase (in μmt/l) according to Korolyuk et al. [23]. Additionally, the value of the de Ritis coefficient calculated as the ratio of AST/ALT activity (in conventional units) was evaluated. The content of substrates for lipid peroxidation processes (diene conjugates, triene conjugates, and Schiff bases) was determined spectrophotometrically by the method of I.A. Volchegorsky [24]. The MSM level

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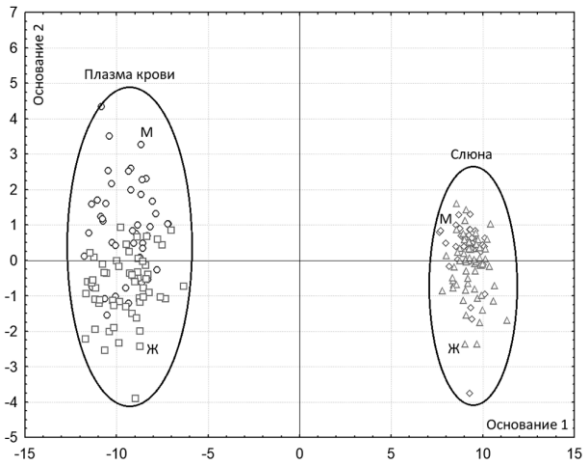
was determined by UV spectrophotometry at wavelengths of 254 and 280 nm [25]. The results were expressed in units quantitatively equal to the extinction indices. Additionally, the value of the distribution coefficient (MSM 280/254 nm) was evaluated as the ratio of extinctions at wavelengths of 280 and 254 nm, respectively. The studies were approved at a meeting of the ethics committee of the Clinical Oncology Center of the Omsk region dated July 21, 2016, protocol No. 15. Statistical analysis was performed using the Statistica 10.0 software (StatSoft, USA) and the R package (version 3.2.3) by a non-parametric method using the Mann-Whitney U test. The description of the sample was made by calculating the median (Me) and the interquartile range in the form of the 25^{th} and 75^{th} percentiles [LQ; UQ]. Differences were considered statistically significant at $p < 0.05$. Multivariate statistical analysis was carried out using the discriminant method, which is based on the construction of discriminating (canonical) functions that allow for the best discrimination (separation) between all groups. The nature of discrimination is assessed by scatterplots of canonical values, on which the values of the corresponding discriminant functions (base 1 and 2) are plotted along the axes, while the greater the distance between the centers of the groups in the diagram, the greater the differences between the groups.

Results and Discussion

At the first stage, the nature of the distribution and the homogeneity of the dispersions in the groups were checked. Content according to the Shapiro-Wilk test. Fig.1. Results of the discriminant analysis of the composition of blood plasma and saliva.



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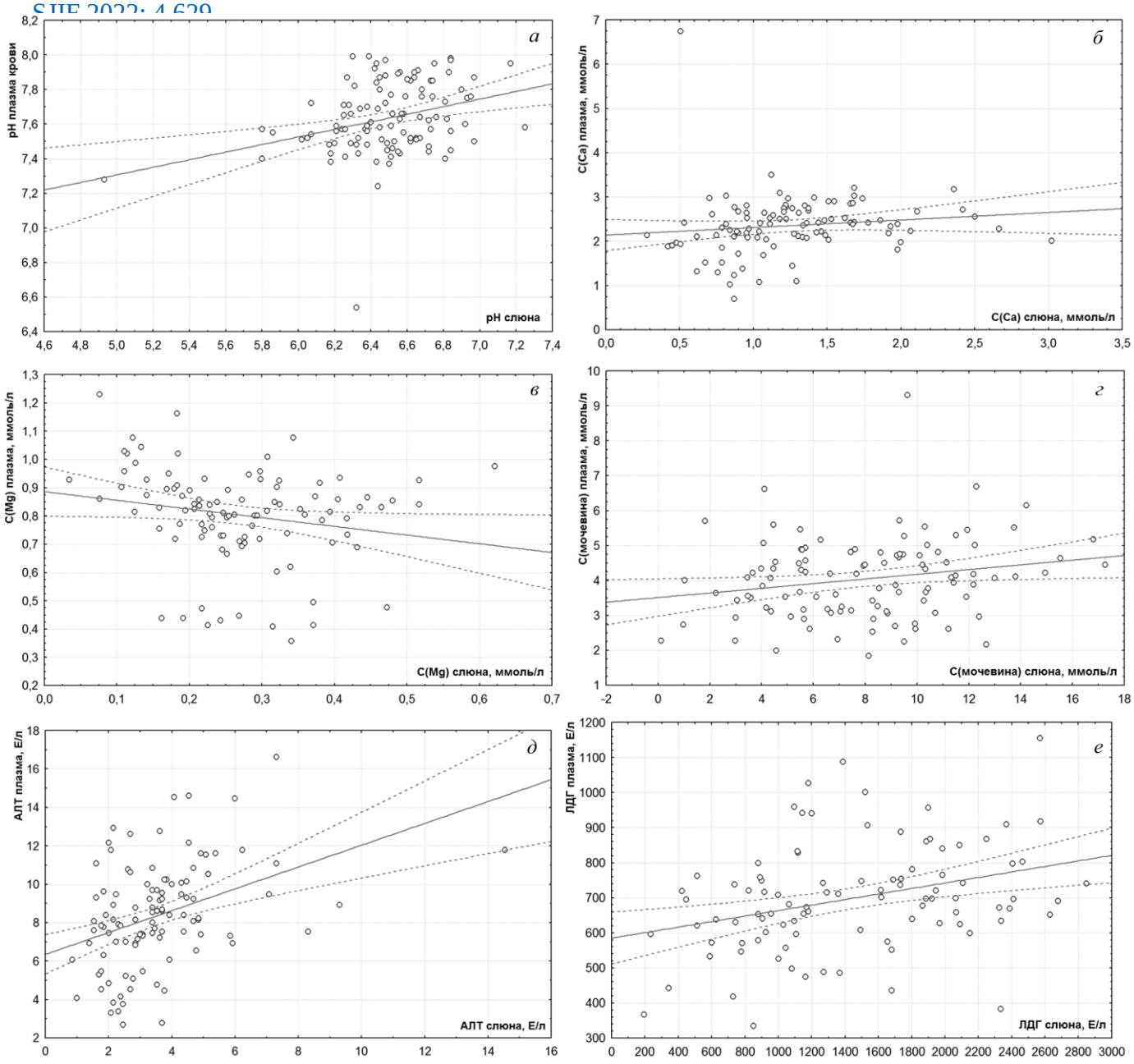

Fig 2. Correlations between the composition of blood plasma and saliva. a – pH; b - calcium; c - magnesium; d - urea; e - alanine aminotransferase; (e) lactate dehydrogenase.

Not all determined parameters correspond to the normal distribution ($p < 0.05$). The test for the homogeneity of variances in groups (Bartlett's test) made it possible to reject the hypothesis that variances are homogeneous across groups ($p = 0.00017$). Therefore, nonparametric statistical methods were used to process the obtained data. It has been shown that for most parameters the ranges of determined concentrations overlap, with the exception of total protein, albumin and sialic acids, for which the content in blood plasma is an order of magnitude higher than in saliva. The results of the discriminant analysis showed that blood plasma and saliva are completely different in terms of the set of determined parameters (Fig. 1). Additional calculations showed that statistically significant differences were observed for each parameter (p

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< 0.0001), with the exception of diene conjugates, for which no statistically significant differences were found between blood plasma and saliva (p = 0.9639). All the revealed correlation relationships are positive, except for the magnesium concentration (Fig.). According to the results of the study, it is difficult to establish an unambiguous relationship between biochemical parameters, including mineral and protein composition, enzyme activity, as well as indicators of endogenous intoxication and lipid peroxidation, saliva and blood plasma.

Despite this, numerous studies clearly show that the determination of the listed parameters is informative when saliva is used as a substrate. In particular, the acidity of the environment is an important indicator [26, 27] and mineral composition [28]. It is known that the determination of the concentration of inorganic ions is important from a medical point of view [29, 30]. So, the exchange of inorganic ions plays a significant role in such vital processes as cardiac activity, acid-base balance, regulation of intracellular homeostasis [31]. The important role of calcium and inorganic phosphorus levels in maintaining the balance of mineralization and demineralization processes in the oral cavity has been shown [32, 33]. To study oxidative stress, saliva can be used along with blood, since it contains antioxidant enzymes (catalase, superoxide dismutase, glutathione peroxidase), antioxidant vitamins (A, E, C), lipid peroxidation products (diene and triene conjugates, Schiff bases) [34, 35, 36, 37]. Important information can be provided by determining the level of nitric oxide in saliva [38, 39] as well as the concentration of uric acid, which refers to the antioxidant system of the body [40].

It is known that the concentration of most electrolytes and trace elements in saliva is comparable to their concentration in blood serum and plasma [41]. However, many organic components are found in saliva at much lower concentrations than in blood plasma, in particular, the concentration of albumin in saliva is only 0.1-1% of its concentration in plasma. Discrepancies with literature data were revealed, according to which the activity of alkaline phosphatase and ALT in saliva is almost 2 times lower than in the blood, while the activity of AST is almost the same [41]. According to our data, the activity of alkaline phosphatase in saliva is 4–5 times lower than in plasma, while the activity of ALT and AST in saliva decreases proportionally by approximately 2–2.5 times. Of interest is the almost complete coincidence of the indicators of lipid peroxidation in the blood and saliva, which has not previously been covered in the literature. Thus, saliva is a clinically informative biological fluid, but further study and verification of saliva biomarkers is necessary for implementation in clinical laboratory diagnostics.

Conclusion

Determining the composition of saliva may have an independent diagnostic value; in this case, drawing a parallel with the composition of serum and blood plasma is not always necessary. Nevertheless, the use of saliva in clinical laboratory diagnostics is associated with the need to establish norm and pathology criteria for each biochemical parameter. A promising area of research, in our opinion, is to increase the list of biomarkers determined in saliva, as well as to test the sensitivity

and accuracy of their detection, increase the sensitivity and reproducibility of analyzes, and evaluate the cost-effectiveness of their introduction into routine clinical diagnostics.

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