The predictive potential of sorbitol in assessing the liver functional state of productive animals

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Abstract. The work examines the sorbitol biochemical transformation issues in animals. Also it analyzes the hepatobiliary system role in these processes. Respectively basic principles for assessing sorbitol in liver pathologies pointed. Article proposes ways for studying correlation between sorbitol and enzymes. Article opened the sorbitol main metabolic features for hepatopathologies diagnosis.

1 Introduction

The liver is one of the most important organs and performs many functions, including metabolism and detoxification. Liver diseases, such as dystrophy and hepatitis, can affect its functionality, which entails deterioration in the productive functions of animals. In this regard, assessing the condition of the liver is important for the diagnosis and treatment of these diseases. One method of assessing the functional state of the liver is liver clearance testing. These tests determine the rate of a particular substance's elimination from the blood by metabolism in the liver and excretion through the bile ducts[1].

Sorbitol is one of the substances used in liver clearance tests. During the study, sorbitol is administered to animals, and the concentration of sorbitol in the blood is measured. Since the liver is the main organ of sorbitol metabolism, changes in its concentration in the blood may indicate liver dysfunction.

However, for a full assessment of the predictive potential of sorbitol as one of the most important chemical agents when conducting dynamic clearance assessment methods, it is necessary to fully consider the issues of its metabolism and pharmacokinetics, so that in the future it will be possible to develop a full-fledged scientifically based model of its use, which is the purpose of this publication.

2 Materials and methods

The search and processing of scientific publications were carried out according to H. Snyder's recommendations for writing review articles [2]. The bibliographic databases (Elibrary, CyberLeninka, Pubmed, Scopus (Elsevier), and Web of Science (Clarivate)), in English and Russian, were searched for thematic publications using the keywords

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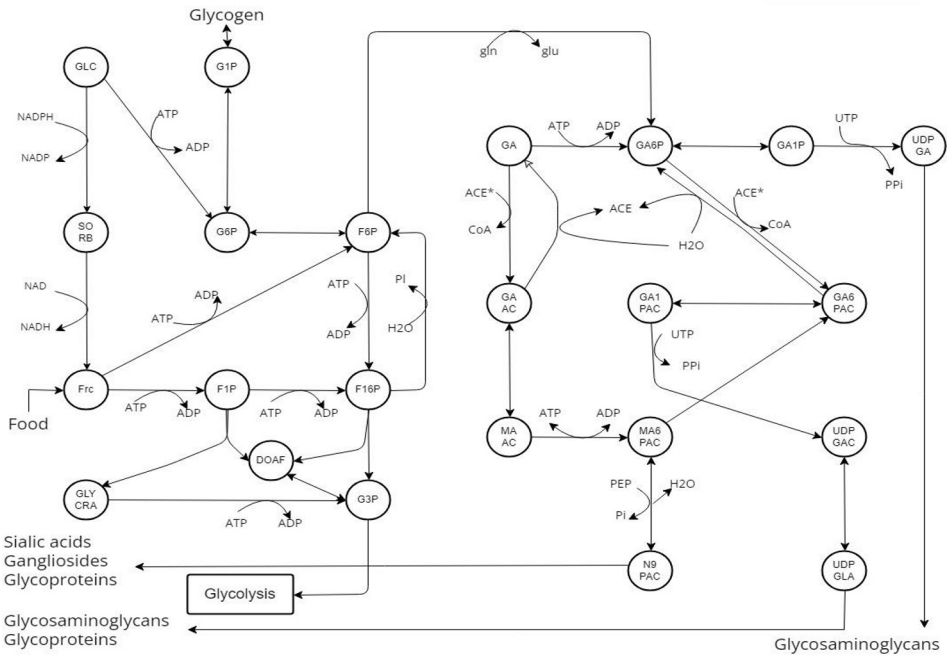
"pharmacokinetics of sorbitol", "sorbitol metabolism", "role of sorbitol in biochemical processes» with further selection of the most cited ones. Articles published before 2013 were used only if they contained information critical to the topic that was not present in more recent publications. The figures in the article were made using Visual Paradigm online.

3 Results

The biochemical composition of sorbitol is glutaraldehyde and cellulose. Glutaraldehyde is a key component of sorbitol synthesis, and cellulose serves as the basis for its production. This is because sorbitol is widely distributed in plants and fungi [3-4].

Sorbitol synthesis is an important process in the organism that is carried out using the enzyme aldose reductase. Sorbitol is an important source of energy and is an essential component of carbohydrate metabolism [5-7].

The process of sorbitol synthesis begins with glucose, the main sugar found in the blood. Glucose enters cells and undergoes conversion to sorbitol by aldose reductase [8-11]. This enzyme catalyzes the oxidation-reduction reaction that converts glucose to sorbitol (Figure 1).



Frc - Fructose; NAD - nicotinamide-adenine dinucleotide; NADP - nicotinamide-adenine dinucleotide phosphate; SORB - Sorbitol; GLC - Glucose; ATP - Adenosine triphosphate; ADP - Adenosine diphosphate; G6P - glucose 6-phosphate; G1P – glucose 1-phosphate; F6P - fructose 6-phosphate; F16P - fructose 1,6-phosphate; F1P - fructose 1-phosphate; DOAF - dihydroxyacetone phosphate; G3P - glucose 3-phosphate; GLYCRA - Glyceraldehyde; gln - Glutamine; glu - Glutamic acid; GA6P - glucosamine 6-phosphate; GA - glucosamine; GA1P - glucosamine 1-phosphate; UTP – Uridine triphosphate; PPi - Pyrophosphate; UDPGA - Uridine Diphosphate Glucuronic Acid; ACE - Angiotensin-converting enzyme; CoA - Coenzyme A; GAAC - N-acetyl-D-glucosamine; GA1PAC - N-acetyl-D-glucosamine 1-phosphate; GA6PAC - N-acetyl-D-glucosamine 6-phosphate; MAAC - N-acetyl-D-mannosamine; MA6PAC - N-acetyl-D-mannosamine 6-phosphate; UDPGAC - Uridine Diphosphate N-acetyl-D-glucosamine; PEP - Phosphoenolpyruvate; Pi - orthophosphate; N9PAC - N-acetylneuraminate 9-phosphate; UDPGLA - uridine diphosphate galactose.

Fig. 1. Metabolism of sorbitol.

The activity of sorbitol dehydrogenase (SDH) is recorded only in the liver. SDH oxidizes the polyhydric alcohol sorbitol into the monosaccharide fructose. The latter is phosphorylated by fructokinase or hexokinase, which allows the resulting compound to enter into glycolysis (the breakdown of glucose). Detection of sorbitol dehydrogenase activity and sorbitol itself in blood plasma serves as a unique marker of liver pathology [12-13].

Sorbitol dehydrogenase is an organ-specific liver enzyme that catalyzes the reversible conversion of sorbitol to fructose with the participation of NAD as a coenzyme. The enzyme is localized in the hepatocyte cytoplasm. Serum enzyme activity increases in viral hepatitis [14]. An increased activity of SDH is observed in the pre-icteric period of viral hepatitis. This precedes an increase in the activity of other enzymes, reflecting liver damage.However, high levels of SDH activity are detected at the height of the disease, in other words, the test is inferior in sensitivity to other organ-specific enzymes and determination of aminotransferase activity [15]. In addition, SDH activity normalizes faster than aminotransferase activity, which is also a disadvantage of the test. Other liver diseases (toxic hepatitis, cirrhosis, and hypoxic liver lesions) are accompanied by a slight increase in enzyme activity (Figures 2–7) [16-19].

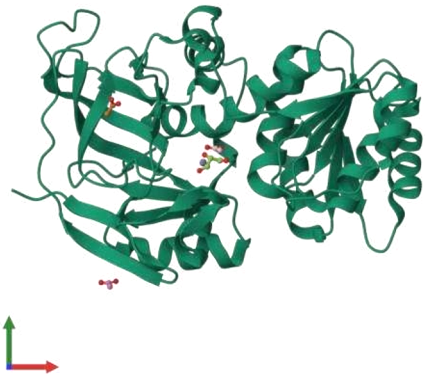


Fig. 2. Sheep liver sorbitol dehydrogenase [16].

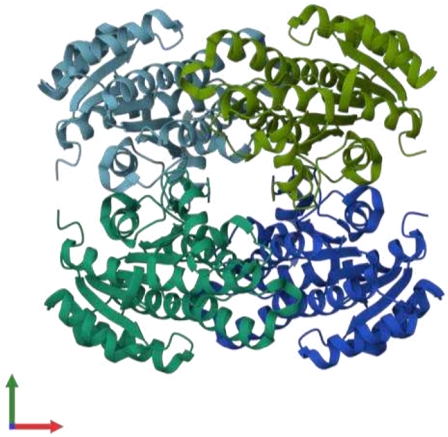


Fig. 3. Structure of sorbitol dehydrogenase Sinorhizobium meliloti 1021 associated with sorbitol[16].

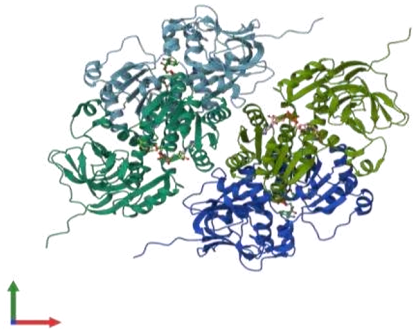


Fig. 4. Human SDH/NAD+ complex[16].

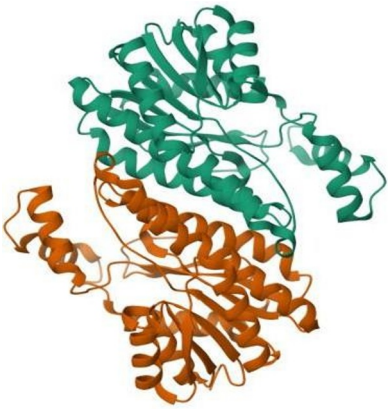


Fig. 5. Crystal structure of sorbitol dehydrogenase from *R. sphaeroides* [16].

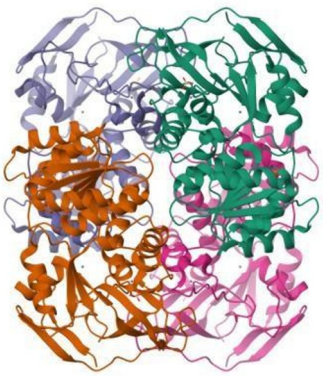


Fig. 6. Ketose reductase (sorbitol dehydrogenase) from silverleaf whitefly [16].

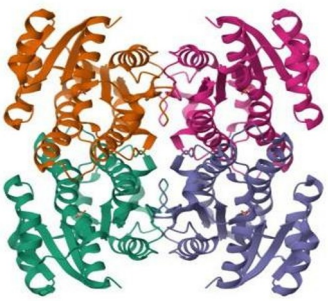


Fig. 7. Structural characterization of the thermostable Bradyrhizobium japonicum d-sorbitol dehydrogenase [16].

In cases where the metabolism of sorbitol is impaired, there is a risk of developing various liver diseases and functional disorders. For example, with a deficiency of the enzymes responsible for the sorbitol metabolism, accumulation of sorbitol in the liver may occur, leading to the development of fatty liver (and other complications of this nosological entity) and disruption of its normal function [20-22].

4 Conclusion

In conclusion, sorbitol is an important marker for the diagnosis and evaluation of liver state. Detecting elevated or decreased levels of sorbitol in the organism can help identify pathological changes in the liver and take appropriate steps to treat and control them. The determination of sorbitol levels in the body is an important diagnostic tool for identifying liver pathologies. By identifying the presence of pathology and determining its severity, this study helps veterinarians choose the most effective treatment methods and monitor the effectiveness of the therapy. In addition, measuring sorbitol levels may be useful in assessing disease prognosis and determining the effectiveness of rehabilitation measures.

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References

1. A. Yashin, E. Kasatkina, A. Prusakov, V. Ponamarev, A. Lunegov, The T-RFLP research method in the study of rumen microbiota in dairy cows with subclinical ketosis, in Proceedings of the International Scientific and Practical Conference "AGRARIAN SCIENCE - 2023" (AgriScience2023), 25–26 April 2023, Moscow, Russia (2023). DOI 10.1051/bioconf/20236606001
2. Yu.N. Alekhin, O.S. Popova, V.S. Ponamarev, P.A. Parshin, Development and registration medicines **12(2)**, 174-184 (2023) DOI 10.33380/2305-2066-2023-12-2-174-184
3. A.V. Prusakova, N.V. Zelenevskiy, A.V. Prusakov, A.V. Yashin, V.S. Ponamarev, Veterinarski Glasnik **77(2)**, 176-187 (2023) DOI 10.2298/VETGL230615007P
4. A. Prusakova, N. Zelenevskiy, A. Prusakov, A. Yashin, V. Ponamarev, Online J. Anim. Feed Res **13(4)**, 242-245 (2023) DOI 10.51227/ojafr.2023.36
5. V. Ponamarev, A. Yashin, A. Prusakov, O. Popova, Influence of Modern Probiotics on Morphological Indicators of Pigs' Blood in Toxic Dyspepsia, Agriculture Digitalization and Organic Production: Proceedings of the Second International Conference, 06–08 June, 2022 St. Petersburg, 133-142 (2022) DOI 10.1007/978-981-19-7780-0_12
6. Yu.E. Kuznetsov, A.M. Lunegov, V.S. Ponamarev, E.B. Romashova, Agricultural biology **57(6)**, 1217-1224 (2022) DOI 10.15389/agrobiology.2022.6.1217rus
7. V.A. Baryshev, O.S. Popova, V.S. Online, J. Anim, Feed Res **12(2)**, 81-88 (2022) DOI 10.51227/ojafr.2022.11

8. A.A. Adekola, R.E. Antia, A. Ja. Jubril, O.G. Ohore, B.O. Emikpe, Comparative Clinical Pathology **28(6)**, 1537-1546 (2019) DOI 10.1007/s00580-019-02956-5
9. A. Gupta, V.K. Singh, G.N. Qazi, A. Kumar, Journal of Molecular Microbiology and Biotechnology **3(3)**, 445-456 (2001)
10. M.T. Kaleibar, Ja.A. Helan, Comparative Clinical Pathology **22(6)**, 1155-1163 (2013) DOI 10.1007/s00580-012-1543-1
11. V.I. Cherniy, I.P. Shlapak, M.A. Georgiyants, S.G. Tyumentseva, S.E. Kugler, B.B. Prokopenko, Emergency Medicine **7(78)**, 146-156 (2016) DOI 10.22141/2224-0586.6.77.2016.82183
12. V.I. Gidranovich, M.E. Akhtanina, Bulletin of the Vitsebsk State University **1(23)**, 125-131 (2002)
13. D.V. Aleev, G.R. Yamalova, A.V. Malanyev, K.F. Khalikova, G.G. Galyautdinova, Veterinary doctor **6**, 4-10 (2021) DOI 10.33632/1998-698X.2021-6-4-11
14. S.P. Smolina, M.M. Petrova, Emergency doctor **12**, 4-11 (2019) DOI 10.33920/med-02-1912-01
15. V.B. Grinevich, Yu.A. Kravchuk, M.M. Arapkhanova, V.E. Kon, L.V. Mikhailova, A.K. Ratnikova, Experimental and clinical gastroenterology **11(183)**, 20-24 (2020) DOI 10.31146/1682-8658-ecg-183-11-20-24
16. PDBe: Protein Data Bank in Europe, https://www.ebi.ac.uk/pdbe/entry/search/index/?searchParams=%7B%22q_ec_number%22:%5B%7B%22value%22:%221.1.1.14%22,%22condition1%22:%22AND%22,%22condition2%22:%22%3D%22%7D%5D,%22resultState%22:%7B%22tabIndex%22:0,%22paginationIndex%22:1,%22perPage%22:%2210%22,%22sortBy%22:%22%5C%22Sort%20by%5C%22%22%7D%7D
17. O.N. Voloshchuk, G.P. Kopylchuk, I.M. Buchkovskaya, Experimental and clinical gastroenterology **8(108)**, 96-100 (2014)
18. O.N. Voloshchuk, G.P. Kopylchuk, Laboratory diagnostics. Eastern Europe **2(14)**, 94-99 (2015)
19. D. Voloshin, Animal husbandry of Russia **1**, 29-31 (2018)
20. A.A. Reznichenko, L.V. Reznichenko, A.V. Kosov, E.N. Ryabtseva, International Bulletin of Veterinary Medicine **4**, 175-180 (2020) DOI 10.17238/issn2072-2419.2020.4
21. A.A. Alekseev, N.A. Pudovkin, V.V. Salautin, S.D. Klyukin, International Bulletin of Veterinary Medicine **2**, 58-64 (2022) DOI 10.52419/issn2072-2419.2022.2.58
22. A.A. Kirillov, P.N. Yushmanov, A.Ya. Batrakov, International Veterinary Bulletin **1**, 7-12 (2015)