5. Shaker B, Ahmad S, Lee J, Jung C, Na D. In silico methods and tools for drug discovery. Computers in Biology and Medicine. 2021 Oct 1; 137: 104851.
6. Mishra KP, Ganju L, Sairam M, Banerjee PK, Sawhney RC. A review of high throughput technology for the screening of natural products. Biomedicine & Pharmacotherapy. 2008 Feb 1; 62(2): 94-8.
7. Chang Y, Hawkins BA, Du JJ, Groundwater PW, Hibbs DE, Lai F. A Guide to In Silico Drug Design. Pharmaceutics. 2023 Jan;15(1): 49.
8. Katsila T, Spyroulias GA, Patrinos GP, Matsoukas MT. Computational approaches in target identification and drug discovery. Computational and Structural Biotechnology Journal. 2016 Jan 1; 14: 177-84.
9. M.B. King, H. Al-Najjar, Chem. Eng. Sci. 29 (1974) 1003-1011.
10. M.B. King, Transactions of the Institution of Chemical Engineers 54 (1976) 54-60.
11. Sahoo MR, Marakanam SU, Varier RR. Development and Evaluation of Essential Oil-based Lozenges using Menthol and Eucalyptus and in vitro Evaluation of their Antimicrobial activity in S. aureus and E. coli. Research Journal of Pharmacy and Technology. 2022; 15(11): 5283-8.
12. Oz M, El Nebrisi EG, Yang KH, Howarth FC, Al Kury LT. Cellular and molecular targets of menthol actions. Frontiers in Pharmacology. 2017; 8: 472.

BIOCATALYTIC REDUCTION OF CARBON MONOXIDE IN AQUEOUS-ORGANIC ENVIRONMENT

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The influence of organic solvents of various nature on the enzymatic activity of cell extracts was studied D. desulfuricans B-1388. Enzymatic reduction of hexene-1 in the presence of various surfactants in the atmosphere was carried out CO/H2 – buffer – octane. It is shown that the direction of the process and the yield of products are affected by the nature of the surfactant. The dynamic structure of the reaction medium was characterized using NMR1 H and EPR spectroscopy.

It is known that enzymes are active and highly selective catalysts for many chemical reactions, and their use for fine organic synthesis is very promising [1, 2]. However, the unique properties of enzymes are usually preserved in an aqueous solution, in a narrow range of pH and temperatures, while the thermodynamic conditions for the highest yield of products in the catalyzed reaction may not coincide with the conditions for maintaining enzymatic activity. A general solution to the problem can be an equilibrium approach, i.e. an approach that allows

increasing the yield of the target product in a thermodynamically unfavorable reaction by shifting the chemical equilibrium. For this purpose, aqueous-organic media are used to transfer water-insoluble products into the organic phase and surfactants to create conditions for the functioning of enzymes without loss of operational activity [3]. The objective of this study was to investigate the enzymatic reduction of carbon monoxide catalyzed by sulfate-reducing bacterial cell extracts within a stable reaction system. Research methods The study used bacteria Desulfo-vibrio desulfu-ricans B-1388 from the VKM collection. Cell extracts were obtained in accordance with the method [4], CO-dehydrogenase activity of cell extracts was determined as described in [4], hydrogenase activity was recorded spectrophotometrically according to [5]. To determine the effect of organic solvents, cell extracts were incubated for 30 min at room temperature with an organic solvent, and then CO-dehydrogenase and hydrogenase activities were determined. Enzymatic synthesis was carried out in hermetically sealed penicillin vials, previously pumped with the required gas mixture, into which 5 ml of the reaction mixture was introduced, consisting of 3.5 ml of buffer (pH 8.0), 0.5 ml of an organic solvent, 0.5 ml of the appropriate surfactant, 0.5 ml of cell extract (10–15 mg of protein). Before the reaction, the reaction mixture was “sonified” using an ultrasonic disintegrator UZDN-2T (22 kHz, 30 s). The reaction products were analyzed by the GLC method according to [6]. The yield of reaction products – hydrocarbons (HC) and oxygen-containing compounds (OCC) – was determined as the sum of the concentrations of individual products, multiplied by the number of carbon atoms in the molecule of each product (this is the so-called carbon yield). The total yield was determined as the sum of the hydrocarbon and the KS. The work used organic reagents (Serva, Switzerland and Fluka, Germany), inorganic salts for the preparation of buffer solutions of "reagent grade" of domestic production. Results and discussion We have previously shown that cell extracts Desulfovibrio desulfuricans B-1388 catalyze the reduction of carbon monoxide by molecular hydrogen [7]. The reaction occurs at room temperature in neutral buffer solutions. The reaction products are paraffin hydrocarbons from C8 to C24, insoluble in water. The yields of products in this process are low, and it is not possible to increase them significantly by changing the physicochemical parameters (temperature, pressure, reagent concentrations, etc.). The reaction medium is a complex heterogeneous two-phase system, where one phase is gas (carbon monoxide and hydrogen), the other is liquid (extract of sulfate-reducing bacteria cells in a buffer solution). In such a system, the kinetics of a heterogeneous reaction is determined both by the rate of the enzymatic conversion itself and by the transfer processes (diffusion) necessary to replenish the consumption of reactants and remove reaction products from the reaction zone. By introducing an organic solvent that is not miscible with water but dissolves paraffins, it is possible to remove the products from the reaction sphere. The necessary condition for this is the preservation of the catalytic activity of the enzyme complex. The determining condition for the implementation of the process is the presence in the catalytic complex of enzymes specific to carbon monoxide and hydrogen – CO-dehydrogenase and hydrogenase, respectively – and

which are key in the processes of transformation of carbon oxides. As shown earlier [8], the culture used in the experiments Desulfovibrio desulfuricans has a powerful biochemical potential and cell extracts contain active CO-dehydrogenase and hydrogenases. The effect of organic solvents of different nature that are immiscible with water (chloroform, carbon tetrachloride, benzene, diethyl ether, octane) on the enzymatic activity of cell extracts was studied. Enzymatic (hydrogenase and CO-dehydrogenase) activity is completely suppressed in the presence of chloroform and carbon tetrachloride and is practically preserved in the presence of octane. When carrying out enzymatic synthesis in the system (CO + H2) – buffer solution – octane, it becomes necessary to introduce surfactants that reduce the surface tension at the gas – liquid and liquid – liquid phase boundaries. In addition, surfactants must stabilize the enzyme globule, ensuring the preservation of enzymatic activity. When surfactants are added in concentrations greater than 10%, stable emulsions of octane in water (1:10) are formed, the shelf life of which is several weeks. By reducing the concentration of surfactants in the medium to 0.1%, after the reaction is complete, the emulsion can be destroyed by adding salt (NaCl) and the reaction products in each phase can be analyzed by GLC. It was found that cationogenic surfactants containing halide ions as counterions, for example, cetylpyridinium bromide, irreversibly inactivate the enzyme complex of the extracts and cannot be used to stabilize the system. The effect of various surfactants on the direction and yield of enzymatic reduction in a water-octane medium of the unsaturated hydrocarbon hexene-1 with a mixture of CO – H2 (1:1) and pure carbon monoxide was studied. In the presence of sodium dioctyl sulfosuccinate (AOT) both in an atmosphere of 100% CO and in an atmosphere of CO and hydrogen (1:1), only dimerization of hexene into dodecane occurs. The degree of hexene conversion is 20%. In the presence of a surfactant of a different nature (nonionic surfactant) polyoxyethylene sorbitan monooleate (Tween-80), the direction of the reaction becomes completely different. Reductive carbonylation of hexene occurs, and saturated hydrocarbons are also synthesized; the degree of hexene conversion in this case is significantly higher (more than 40%); the content of saturated hydrocarbons, apparently built due to the homologation of hexene, in the reaction products is 53.2%. A slightly smaller proportion (42.2%) is made up of carbonyl compounds – products of the addition of carbon monoxide to the double bond of hexene. In addition, hydrogenation of hexene into hexane occurs, the proportion of hexane is 4.6%. The direction of the enzymatic process obviously depends not only on the nature, but also on the structure of the surfactant. We have shown that in a series of similar surfactants (Tween-20, Tween-65, Tween-80, Tween-85) not only the degree of substrate conversion differs, but also the yield of products. It can be assumed that the structure and size of the hydrocarbon radical in the surfactant molecule determine the shape and mobility of surfactant associates with the organic component of the reaction medium, and this, in turn, affects the activity of the enzyme complex and ultimately determines the direction and efficiency of the process. The dynamic structure of the reaction medium using the Tween-80 – octane – water system as an example was characterized using

physical methods (1 H NMR with Fourier transform by a pulsed magnetic field gradient and EPR). The self-diffusion coefficients obtained for all components of the reaction medium allowed us to suggest the following most probable structural model for it. The organic components of the mixture (hexene and octane) exist in the form of microdroplets with a radius of several hundred angstroms, surrounded by a monolayer of surfactant (Tween-80). These microdroplets are suspended in an aqueous medium. The EPR data obtained using 7-doxyl stearic acids as a paramagnetic probe are consistent with the proposed structure of the reaction medium. The EPR spectra have a five-component form, which indicates the limited mobility of the 7-doxyl-stearic acid molecule. This fact indicates the density of the surfactant molecule packing in the monolayer surrounding the microdroplets where the paramagnetic probes are embedded. Further modeling of the reaction medium for enzymatic conversion of CO will be continued in the direction of searching for optimal surfactants, organic phase, synthesis conditions, as well as studying the dynamic structure of the system.

REFERENCES:

1. Гладилин А.К., Левашов А.В. // Успехи биол. химии. 1996. 36. С. 141.
2. Klibanov A.M. // Accounts Chem. Res. 1990. 23. P. 114.
3. Хмельницкий Ю.Л., Левашов. А.В., Клячко Н.Л., Мартинек К. // Биотехнология. 1988.
4. С. 292. 4. Тарасова Н.Б., Мухитова Ф.К., Рязанцева И.Н., Беляева М.И. // Биохимия. 1985. 50. С. 454.
5. Кияшко С.В., Мухитова Ф.К., Рябцева О.А. // Биохимия. 1994. 59. С. 220.
6. Беляева М.И., Мухитова Ф.К., Золотухина Л.М., Багаева Т.В., Карпилова И.Ю. // Микробиология. 1992. 61. С. 194.
7. Lapidus A.L., Grobovenko S.Y., Mukhitova F.K., Kiyashko S.V. // J. Mol. Cat. 1989. 56. P. 260.
8. Мухитова Ф.К., Кияшко С.В., Лапидус А.Л. // Прикл. биохим. микробиол. 1999. 35. С. 308

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