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CERTAIN PROBLEMS OF SPACE BIOTECHNOLOGY

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16. Abstract

This work presents the basic problems in the development of space biotechnology -- a new direction in space technology.

A definition of the concept of space biotechnology is given.

Certain results of experiments in the field of biotechnology conducted by the USA "Apollo" and "Skylab" space probes are given, as well as in the joint Soviet-American Apollo-Soyuz Test Project (ASTP).

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CERTAIN PROBLEMS OF SPACE BIOTECHNOLOGY

V. N. Gilyarov

The utilization of space apparatus for conducting a series of technological processes opens additional new possibilities in the field of biology and medicine. This is conditioned by: the lack of weightlessness in heat convection (i.e., the lack of any internal processes of movement in material except for insignificant convective-like currents due to variation in surface tension and non-uniformity of thermal expansion); the lack of sedimentation and division by weight not only of solid, liquid, and gaseous products of reactions, but also directly in the processes of growth and development of microorganism and tissue cultures. As a result, the effectiveness and degree of purity in the division of mixtures during electrophoresis is increased, which may be used for obtaining pure specimens of albumen, subcellular particles, and other biological materials and for obtaining vaccines with a very high degree of purity. /3*

The totality of processes conducted under conditions of space flight during which qualitative changes take place in a utilized biological material and as a result of which new medical or biological materials are obtained, as well as the scientific description of these processes is the new field of space technology -- biotechnology.

Scientists abroad had begun developing this new direction as early as the end of the 60's. Included among prospective technological operations in NASA's plans in the 70's in developing a project for a long-term orbital station was the process of obtaining vaccines by means of electrophoresis under conditions of space flight [1]. /4

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*Numbers in margin indicate pagination in original foreign text.

Electrophoresis is the movement of disperse particles found in a suspended state under the action of an external electrical field. Their movement is associated with the existence of a double electrical layer on the boundary with the medium.

Most molecules or organic substances found in aqueous solution of acid or alkali take on small electrical charges, and move through this solution under the influence of applied electrical field. Since different molecules move at different speeds, the faster molecules in a mixture of organic substances, which begin to move from one end of a tube filled with solution to the other, will go ahead of the slower molecules.

The effect of dividing a homogeneous mixture of biological materials during flow in a uniform electrical field opens new possibilities for cytology, immunobiology, and general chemistry. Under earth conditions, the effectiveness of separation is reduced due to sedimentation and convective currents.

Electrophoretic division of biological compounds in a liquid medium was first conducted on the "Apollo-14" spacecraft (1971). These operations were recorded on film and transmitted by television.

The apparatus for such division consisted of three tubes: 1 - containing a mixture with red and blue organic dyes; 2 - containing human hemoglobin; 3 - containing DNA from salmon roe, suspended in a dissolved electrolyte solution (a mixture of water, boric acid, and sodium hydroxide). All these organic compounds have different molecular weights. /5

The device also included: a pump with motor, gas separator, fluorescent lamps, energy source, and thermometer. The weight of the entire device was

4.082 kg in a packaging size of 177 x 127 x 101.6 mm.

The power consumed was 30 W from a source of alternating current with frequency of 400 Hz. While the experiment was being conducted, all equipment was secured with the aid of straps. The experiment lasted 1 hour. All processes were filmed on color film with the aid of a 70-mm on-board camera.

Each of the three tubes had electrodes built into its ends. The electrodes were separated from the medium by porous membranes. Power was fed to the electrodes, and the electrolyte circulated due to the operation of the pump which was powered by a motor. A constant current was passed through the liquid (230 W). Hydrogen and oxygen formed in the solution were absorbed by gas separators. The fluorescent lamps illuminated the tubes for photography. Visible light was used for illuminating the dyes and the hemoglobin, and ultraviolet light was used to illuminate the salmon roe DNA.

The equipment for electrophoresis on the "Apollo-14" spacecraft was developed by General Electric under contract with the Center for Manned Space Flight in Houston [2, 3].

In 1972 on the "Apollo-16" spacecraft, along with biological experiments on the study of the influence of individual factors of space flight on bacteria, fungi, and viruses, cellular elements in the blood of humans and rabbits were also divided.

The demonstration of electrophoretic separation was intended for testing technical solutions for the preparation of the process of obtaining pure specimens of organic substances in space. In particular, this experiment had in perspective an important practical significance for the preparation of vaccines.

By 1974 it became clear that electrophoresis was not only possible under conditions of space flight, but also opened up great possibilities for the purification and separation of biological materials. /6

Conditions in space create an exceptionally favorable environment for obtaining vaccines in large quantity and of high quality. In the absence of gravitational forces, the speed of growth of microorganisms may be doubled. The processes of fermentation and bacteria culture turn out better in space than they do on Earth. The lack of gravity "unhinders" their metabolism and facilitates their oxygen supply.

Further, viruses which serve in the preparation of vaccines must be separated from the nutrient medium on which they are grown. Weak admixtures in vaccines prepared on Earth may cause undesirable side effects. The concentration of useful agents in these vaccines is also insufficient for their necessary effectiveness. Also, on Earth, due to convective currents, it is possible to purify solutions which are subjected to an electrical field either in the form of a thin film or in porous material, which makes it impossible to obtain vaccine in large volume [4 - 7].

On the basis of experiments conducted on the Apollo program and Skylab, American scientists believe that in space it will be possible to purify the 10 most necessary types of vaccines. Moreover, they feel that in one year it is possible to obtain 1 ton of vaccine (10 types), which would supply the needs of the entire world, with an expenditure of several million dollars for obtaining this vaccine. In particular, it is planned that the shuttle program (multi-use transport space vehicle) and rocket satellites found in a state close to weightlessness for a period of 5 - 12 min [8] are to be used for this purpose.

Aside from an economic advantage, the production of vaccines in space will make it possible to obtain vaccines of the highest effectiveness in combatting flu, infections, and catarrhal diseases. Components may be separated and concentrated with a high degree of accuracy. /7

Already now NASA and ESA (European Space Administration) are working on developing equipment for static electrophoresis, for measuring the mobility of material, for flowing materials and isotachophoresis, where the sample mixture is layered between substances with different ion properties.

Among the scientific experiments in the joint Soviet-American ASTP program (1975) was the electrophoretic separation for medical-biological research: obtaining pure and isolated specimens. The experiment studied the effectiveness of using electrophoretic processes for separating lymphocytes, enzymes, as well as other components of blood and tissue liquid of man under conditions of weightlessness. In preparation for the experiment, an improved method of freezing and subsequent long-term storage (up to 5 years) of white blood corpuscles (granulocytes) without altering their immunological properties was developed [9, 10].

The separation of human cells in closed tubes filled with immobile medium was envisioned. The purpose was to attempt to separate certain types of cells, which is difficult or completely impossible on Earth.

In planning the conditions for conducting the experiment, it was necessary to solve the problems of creating equipment capable of withstanding acceleration during launch and descent, the problem of removing gas bubbles from the electrodes and keeping the results of the experiment.

A device weighing 26 kg was designed by the MVV company (German Federal Republic), and the Planck Institute of Biochemistry was in charge of the experiment [9 - 12].

Four samples were tested in the course of the experiment: a mixture of human and rabbit erythrocytes, cells from rat spleen, cells from rat bone marrow, and a mixture of lymphoid cells of rats and human erythrocytes. Three electrophoresis regimes were tested. In the first, the field intensity comprised 60 V/cm, the speed of pumping buffer solution -- 0.275 ml/sec, and speed of sample flow -- 5 ml/hr. In the second regime, the speed of sample flow was reduced to 1 ml/hr; in the third it remained equal to the value of the second regime, but the field intensity and speed of buffer solution flow were reduced by 1/3. /8

The quality of separation was improved by ~10 times [11 - 15].

The second experiment consisted of separating from the nutrient medium active kidney cells possessing the property of producing the enzyme urokinase, which hinders the formation of blood clots in human blood vessels. Urokinase dissolves the blood cell membranes and is used as an initial raw material for the creation of effective preparations for treating phlebitis. Urokinase is produced by ~5% of kidney cells. Their separation in flight with the aid of electrophoresis was implemented as follows: Kidney cells were introduced into one end of a tube filled with water, and then an electrical field was created. Due to the different polarization of active and inactive kidney cells, their speed of movement in the electrical field in the absence of gravity is also different, and this leads to their separation [16].

If this experiment were to be conducted under earth conditions, gravitation would cause convective currents, and then all the cells would

settle. It was noted that under conditions of space flight, the cells excreted 6 - 7 times more urokinase than on earth. Moreover, for the production of considerable quantities of urokinase, a large amount of initial material is necessary. Thus, obtaining this substance under conditions of weightlessness is economically expedient.

Separated kidney cells were frozen and returned to earth for subsequent /9
cultivation. These cells are presently being used successfully for forming additional cell structures.

Also, a new coating in the device used for conducting electrophoresis was developed -- methyl-cellulose. It removes certain electrical charges in the medium and this gives an even clearer division of the material. The new coating maintains its properties over a long period of time.

Another candidate for production in space is erythropoietin, which stimulates the formation of red blood corpuscles in bone marrow. On earth it cannot be obtained from kidneys in pure form, and the presence of a number of antitoxins in it causes undesirable side effects [17].

Multi-use transport space vehicles may be used in organizing the production of erythropoietin in quantities sufficient not only for practical utilization, but also for research work. However, obtaining even small quantities of this preparation is important and useful.

Thus, certain results of medical-biological experiments of the ASTP program may find widespread application in medicine. In particular, a new method has already been found for storing donor blood without changes in immunological properties for transfusions to leukemia patients. A new composition of storage medium has been developed, which makes operations for transfusion of granulocytes more reliable and accessible. Also as a

result of these experiments, the possibility was shown for separating from the kidney cell culture a cell subpopulation, which effectively produces urokinase enzyme, which inhibits processes of thrombosis of the cardiovascular system.

According to the evaluation of ESA specialists, conducting technological processes on space vehicles for the purpose of obtaining biological materials may in the future become one of the main aspects of utilizing space and may create a "market" of 1 billion dollars per year. Listed among the materials which may possibly be obtained is an improved serum for use in kidney transplants and certain hormones [18]. /10

A colloquium held at Johnson Center (USA) in March of 1976 was devoted to questions of producing biological materials in space. The colloquium was organized by NASA. It examined the possibilities of conducting medical-biological research on board the space shuttle and in the "Space lab" block. A representative of NASA, in particular, announced that on board the space shuttle and in the Space Lab block, 300 - 400 separate experiments may be conducted during each flight. Specialists at the colloquium examined the possibilities of conducting research in the directions of:

1. Studying the behavior of living cells under space conditions, including the cells of invertebrates. For example, sponge cells produce substances of an anticarcinogenic nature and antibiotic type substances. It would be important to develop such qualities of cells.

2. Studying the influence of high energy particles, for example, on tumoral cells. Under conditions of space flight, particles with energy of up to $\sim$40 MeV are accessible for experiments (under earth conditions using accelerators -- no higher than 2 MeV). Mice which have been contaminated with tumoral cells will be irradiated with the indicated energies for a period of 10 - 30 days.

3. Growing anaerobic organisms by obtaining their metabolic products under conditions of space vacuum and lack of oxygen.

4. Utilizing cosmic ultraviolet radiation for more effective sterilization of viruses with fewer difficulties than under earth conditions using the same radiation. /11

5. Genetic engineering. Under conditions of weightlessness by performing manipulations on genetic systems it will be possible to avoid deviations of the type of branching genetic chains or bonding of these chains.

6. Obtaining biochemical substances under conditions of weightlessness with the lack of convection. For example, a hormone with very promising anti-carcinogenic properties has been discovered. However, under earth conditions they are obtained only in micrograms with excessively high cost. Under conditions of weightlessness, perhaps, it will be possible to obtain this substance in quantities measured in grams.

It was also mentioned at the colloquium that the equipment developed for obtaining materials of this type under conditions of space flight may be used later on earth after appropriate modification, which would give a definite economical advantage [19].

Questions of utilizing conditions of space flight for industrial production in space of certain types of unique preparations are still being discussed to this day. It is not the aerospace organizations of the USA and the European countries who are enlisted for this purpose. The suggested problems are being thoroughly examined and economically analyzed.

It is assumed that a number of problems in space biotechnology will be solved in the space shuttle flights during the time of 1979 - 1982. This concerns, for example, the question of obtaining most important products:

highly pure vaccines, highly effective viral insecticides, highly effective isoenzymes, albumens, hormones, immunoglobulin. The separation of isoenzymes may bring a clear profit of 20 - 29%. There are tentative plans to include on three flights of an orbital laboratory devices for electrophoretic separation of preparations of the urokinase and erythropoietin type [20-22].

From an examination of even this far-from-complete list of problems /12 in space biotechnology, the huge significance of their solution is clearly evident for the purpose of practically obtaining a number of materials as well as for the further development of scientific research work in this field.

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