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PLASTICS AND SYNTHETIC POLYMERS IN MEDICAL MICROBIOLOGY

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Abstract:

A survey of the published literature on the utilization of plastics and other polymeric materials in microbiology and virology is presented. Emphasis is placed on the use of polystyrene, polymethylmethacrylate, polyamides, polyethylene and other plastics and synthetic polymers as materials for growing cell, tissue and virus cultures, performing serological investigations, freezing tissues and cells, and producing antibacterial and antiviral preparations.

PLASTICS AND SYNTHETIC POLYMERS IN MEDICAL MICROBIOLOGY*

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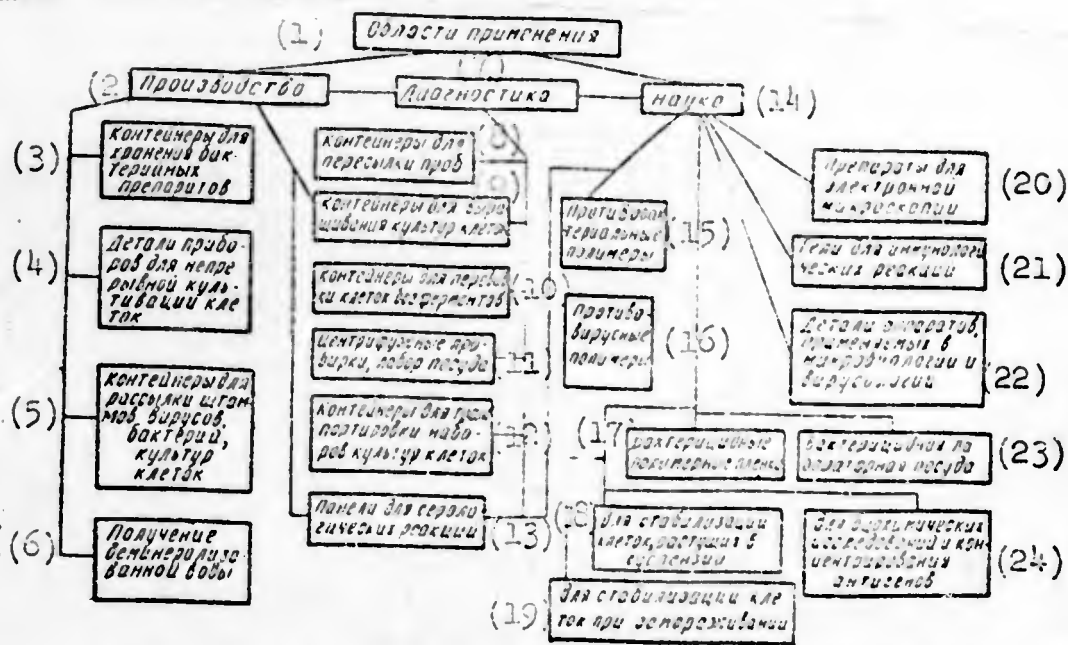
By V. N. Tarasov

The expansion of our knowledge of the nature and etiology of many infectious diseases of humans, as well as the recent advances made in their diagnosis and treatment, are associated with the broad introduction into microbiology of the latest achievements of chemistry, physics, engineering and other sciences. Further advances of our knowledge of the nature of viruses and bacteria, the development of new methods of research and antibacterial and antiviral preparations are connected with the broad introduction into medical microbiology of the latest achievements of the chemistry of synthetics, plastics and other polymeric materials.

Regardless of the field of application of synthetic polymers (production of bacterial preparations, diagnosis, scientific research), three main trends of their application in microbiology have arisen: production of synthetic containers, performance of microbiological and virological research, and synthesis of antibacterial and antiviral preparations (see diagram).

* Paper read at the All-Union Conference on the Uses of Polymers in Medicine and the Medical Industry, 29 October 1964 (Leningrad)

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Synthetic polymers in virology and microbiology

Key: 1. Fields of application; 2. Production; 3. Containers for storage of bacterial preparations; 4. Components of devices for continuous cell cultivation; 5. Containers for sending virus strains, bacteria strains, cell cultures; 6. Production of demineralized water; 7. Diagnosis; 8. Containers for sending samples; 9. Containers for growing cell cultures; 10. Containers for transplanting enzyme-free cells; 11. Centrifuge test tubes, laboratory ware; 12. Containers for transportation of sets of cell cultures; 13. Panels for serological test; 14. Science; 15. Antibacterial polymers; 16. Antiviral polymers; 17. Bactericidal polymeric films; 18. For stabilization of cells growing in suspensions; 19. For stabilization of cells during freezing; 20. Preparations for electron microscopy; 21. Gels for immunological test; 22. Components of apparatus used in microbiology and virology; 23. Bactericidal laboratory ware; 24. For biochemical investigations and concentration of antigens.

Synthetic Laboratory Ware for Microbiological and Virological Purposes

In recent years laboratory ware made of synthetics has begun to be widely employed in microbiology. This is due to the convenience of using unbreakable containers of this kind, whose surfaces contribute to an improved growth of tissue-culture cells, as well as to the economic expediency of using plastic ware.

Of special value to the conduct of many virological investigations is the synthetic ware developed for handling cell and tissue cultures. Abroad this ware is often fabricated from polystyrene (Hood and Norris, 1961; Fedor, 1962; Stanfield and Lyman, 1963). The findings on the growth of tissue cultures on polymer surfaces show that cellulidene, polyglycol methacrylate, polydiglycolmethacrylate and polythene may also be used for this purpose (Tarasov, 1960; Fulton, 1960; Dreifus et al., 1962; Freed, 1963).

During 1962-1964 16 polymers were investigated at the Military-Medical Academy with the object of determining the possibility of using them for the manufacture of various containers (Petri dishes, vials, matrices). The suitability of the polymers was determined according to the growth rate of cell cultures on their surfaces. The highest growth rate of cell cultures was observed on the surfaces of polymethylmethacrylate, nitrocellulose, translucent polystyrene, fluoroplast-30, and pentaplast. Polyethylene and polypropylene, on the other hand, proved to be less suitable for these purposes (Tarasov and Bashmakov, 1964).

The information obtained on the biological characteristics of the high-molecular polymers investigated, as well as the available literature, shows that the synthetic ware most suitable for virological and microbiological purposes is that fabricated from "pure" polymers, i.e. from plastics to which no plasticizers, dyes or other substances that may sometimes contain toxic components are added (Autian, 1963; Tarasov and Bashmakov, 1964).

Studies of the applicability of Soviet-produced synthetic ware have conclusively demonstrated that it is a promising material for the many virological and microbiological purposes. In particular, the matrices and vials of polyethylene produced by the Leningrad Komsomol'skaya Pravda Factory are suitable for the storage of many bacterial preparations (synthetic medium No 199, growth media, saline solutions) and for the growing of certain stable cell cultures (Bashmakov and Tarasov, 1963). Screw-on dishes made of LPT polymethylmethacrylate proved to be extremely convenient for growing cell cultures and performing many virological operations. The value of synthetic ware made of fluoroplast-30 and pentaplast has been admitted. Various cell cultures have been observed to grow intensively within this ware; it is more translucent than polyethylene and can be subjected to autoclave treatment. In specimens of containers made of polymethylmethacrylate, fluoroplast-30, pentaplast, and nitrocellulose no delay has been observed in the proliferation of intestinal and respiratory viruses during the study of their reproduction in susceptible cell cultures (Tarasov and Bashmakov, 1964).

Plastic panes often are used in the conduct of serological investigations. Among these, of special value are the Takachi devices for performing the complement binding test by the micromethod (Salk et al., 1954; Tsemba and Peshek, 1961; Selivanov, 1964; Voroshilova et al., 1964).

Of course, the range of applications of synthetic high-molecular polymers (plastics) is not confined to the production of matrices, Petri dishes, vials and panes alone; present-day polymeric materials may be used in the production of containers for the shipment of samples and strains of bacteria, viruses, cells, as well as of test-tube racks, syringes and many other accessories.

2. Use of Polymers in Microbiological and Virological Investigations

Synthetic polymers are used in microbiology and virology to cultivate cell, bacterial and viral cultures, to perform immunological investigations, to store cells at low temperatures, to obtain ultrafine sections, etc.

In some cases synthetic polymers are irreplaceable when carrying out microbiological investigations.

As regards the uses of polymers in immunology, their utilization for the purification and concentration of viruses is of considerable interest. With the aid of ion exchangers of the DEAE and TEAE-cellulose type it is possible to obtain highly purified preparations of viruses for the conduct of many immunological investigations and for the study of the structure of microorganisms. Ion exchangers of this kind may be utilized for the tentative differentiation of viruses according to the degree of their elution from the polymer surface (Hoyer et al., 1958; Hodes et al., 1960; Zalmanzon and Lobreva, 1964).

Recently new findings have been made concerning the possibility of using synthetic gels to organize the precipitation test and electrophoresis. Synthetic gels for these purposes have been obtained from low-molecular polymers of the acrylic acrylamide type (Raymond et al., 1962). These types of polymers have been used by Weintraub and Raymond (1963) as adjuvants and by Bernfield and Wan (1963) for the fixing of insoluble antigens.

The aqueous fractions of certain polymers may be used to cultivate molds and bacteria. For example, polyethylene-glycol with a molecular weight of 3000-3700 has been used in the reproduction of Bact. megaterium and Bact. subtilis (Albertson, 1958; Sax, 1961).

Of special value are the polymers used for the cultivation of cell cultures in suspension. To prevent the breakdown of cells growing in suspension, a number of investigators have used natural and artificial polymers (0.1 percent methylcellulose, 0.2 percent carbomethylcellulose, etc.). Artificial polymers proved to be more suitable, since they inhibited the reproduction of viruses in the suspended cultures. A number of synthetic albumin-free media has been suggested for the same purpose; of these, the most effective proved to be the media in which the serum albumin was replaced with a synthetic polymer (Bryant et al., 1961; Sinclair et al., 1963).

The first investigations of the replacement of glycerol with synthetic polymers in the freezing of human cells have been made. It was established that polyvinyl-glycol (molecular weight 635) is more suitable

for storing erythrocytes at -80° C than glycerol. Similar findings have been made when freezing erythrocytes in polyoxyethylene (Sloviter and Ravdin, 1962; Shrago and Vorotilin, 1964).

The preparation of ultrafine sections of bacteria and viruses for electron microscopy would have been impossible without using polymeric materials. Sections of this kind usually are obtained with the aid of methacrylates and epoxy resins (Aradit and Epon 812). Polyamides (Vestapol and Estroplex) and polyvinyl alcohol (Pavlovskiy, 1962; Biryuzov et al., 1963) also are used for this purpose, though more rarely.

Of special value to microbiology and virology are the organosilicon polymers -- silicones. They are used to work with single-layer and suspended cell cultures. Silicone-treated containers, rubber tubing and metals lose their toxic properties and so can be used for the performance of various virological and microbiological researches. The highly valuable properties of the silicones include their ability to prevent mutual adhesion between cells and their extraordinary activity in suppressing the foaming of liquids (Bryant et al., 1961; Freed, 1963; Mils and Lewis, 1964).

DeminerIALIZED water obtained with the aid of ion-exchange polymers is widely used in the preparation of saline solutions, nutrient media and other reagents for working with cell cultures. Of the numerous studies performed in this direction noteworthy are the investigations of Shtannikov (1964) regarding the use of Soviet-made ion exchangers to obtain highly purified water for medical purposes and to eliminate from it bacterial viruses and toxins.

3. Antibacterial and Antiviral Polymers

The development of new antiviral and antibacterial preparations based on polymeric materials is undoubtedly a major field of application of synthetic polymers in medical microbiology.

The most often used medical polymers are: polyvinyl alcohol, polyvinyl pyrrolidone, polyoxyethylene and copolymers of vinyl alcohol and vinyl pyrrolidone (Ushakov, 1962). The effect of these synthetic polymers is conditioned by their ability to fix and neutralize bacterial toxins as well as toxins of other origin. This accounts for the effectiveness of the use of synthetic polymers in the treatment of dysentery, infectious diseases of coccal nature in the newborn, sepsis, tetanus, diphtheria and experimental botulin poisoning (Schubert et al., 1959; From et al., 1962; From and Sirotin, 1964; Zhuk, 1964).

Among synthetic polymers a major role is played by polymers containing various bactericidal substances -- iodine, paraaminosalicylic acid, phthivazide, antibiotics. These antibacterial preparations are, owing

to the depositing effect of the polymers, more effective than their conventional counterparts (Mokhnach, 1962; Ushakov, 1962).

Polymer films are effective in the prophylaxis of infected wounds. Some of these films contain bactericidal substances which intensify the bacteriostatic effect of the polymers used for these purposes (Wallgren, 1957; Artz et al., 1960; Miller et al., 1961). Synthetic bactericidal gels also have proved to be promising with respect to the therapy of certain chronic infections (Ushakov, 1964; Bogomolova et al., 1962; Kazidze, 1962).

The research and development work on bactericidal fibers being done by Vol'f and Meos (1964) is extremely promising.

Also promising is the development of synthetic polymers for the treatment of human diseases of viral etiology. The promise for the development of antiviral polymers is provided by the observations of various investigators who have shown that certain synthetic and natural polymers (macromolecules) retard the reproduction of viruses and bacteria and inhibit the development of tumors and the action of enzymes (Rot, 1953; Keishaleki et al.; Regelson et al., 1960; Young and Mowra, 1960).

Natural and synthetic polymers, like virus-neutralizing antisera, inhibit the reproduction of the viruses of the tobacco-mosaic, Newcastle and influenza strains (Buerger and Stahmann, 1951; Niver and Kradolfer, 1953; Stahmann and Gothosker, 1958).

Recently published findings by Feltz and Regelson (1962) revealed that the ethylene-maleic-anhydride copolymer (molecular weight 120,000) displays considerable activity with respect to the viruses ECHO 9 and Semliki Forest (arbovirus). According to these investigators, polymers of this kind may also be effective with respect to other viruses. The antiviral effect of polymers is, according to Stahmann and Gothosker (1958), associated with the fact that they block the surface receptors of the sensitive cells.

The data available in the literature on the antiviral effect of polymers point to the presence of a definite possibility of using polymeric materials as the basis for developing highly effective preparations with a broad antiviral spectrum imitating the protective properties of interferon and thermolabile inhibitors.

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