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Polymer degradation and its role in nature and modern medical technologies

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Abstract. The published data on the degradation of natural and synthetic polymers in the environment are analysed. The use of polymer degradation in the most advanced biomedical technologies is considered. The bibliography includes 221 references.

I. Introduction

Degradation of polymers is a global process occurring in the biosphere of the Earth, which has an enormous impact on its formation and human activity. In nature, polymer degradation determines the material balance in the biosphere. It was estimated [1] that at least 10^{15} kg of cellulose, the most abundant plant polymer, is produced on Earth annually by photosynthesis. Multiple catabolic – anabolic conversions of cellulose yield a variety of other products. As a result, the major part of the cellulose formed undergoes degradation with the formation of low-molecular-mass (predominantly, gaseous) products, while the other part is stored in the uppermost layers of the Earth's crust where it makes the major contribution to the formation of the topsoil or undergoes partial mineralisation.

Considering the role of polymeric materials in the development of material and spiritual culture of Mankind, it may be conjectured that polymer degradation is a critical factor in this process. Polymeric materials constitute the basis of clothing, building, shipbuilding and, which is even more important, of recording, reproduction and storage of information (paper and book- printing, cine- and magnetic films, *etc*.). However, the degradation of polymeric articles that are vitally important for human life reduces critically their service lives. Therefore, since ancient times the Man considered polymer degradation as an inevitable evil and did his best to prevent or retard this process without even getting an insight into its physical meaning. It is not therefore surprising that degradation and stabilisation of polymers were among the first subjects of investigation in polymer chemistry. However, the discoveries made in the past few decades enabled the utilisation of degradation processes in modern technologies.

The ecological equilibrium formed over the course of millenia was disturbed drastically in the past century as a result of anthropogenic activity, particularly due to conversions of natural substances (mineral oil, gas, carbon) into novel, non-natural materials, such as Teflon, polystyrene, polypropylene, *etc*. No efficient mechanisms of the degradation of these polymers exist in nature, therefore their stock on the Earth is steadily increasing, which threatens severe, hardly predictable changes in the environment. The ever increasing output of synthetic polymeric materials is a challenge to Mankind as regards the maintenance of the global equilibrium (sustainable development).

This review surveys the papers devoted to studies on the degradation of natural and synthetic polymers in the environment as well as the use of this process in modern technologies.

II. General concepts of polymer degradation

Deterioration of polymeric materials occurs much faster than that of other substances (metals, minerals, *etc*.) resulting in the loss of their strengths and elasticities up to spontaneous decomposition of polymeric articles even in the absence of external forces. Degradation of the constituent polymers is the reason for such behaviour of polymeric materials.

Degradation of polymers, *i.e*., cleavage of chemical bonds in the main chain of a macromolecule, is usually classified according to two parameters, *viz*., the mechanism of chain degradation and the type of energy that brings about the degradation. The former involves chain reactions (depolymerisation) where monomeric molecules are eliminated successively from the reactive site of the macromolecule under the action of energetic factors. An alternative mechanism consists of random degradation where those chemical bonds are cleaved under the action of energy factors, which experience the maximum strain by virtue of fluctuation.[2]

Virtually all energy types cause degradation of polymers. This can be induced by thermal, radiation-chemical (photochemical), chemical (hydrolysis, ammonolysis, oxidation), mechanochemical, *etc*., factors. In most cases, the degradation is induced simultaneously by several factors and the contribution of each of them cannot always be established. One of the most common types of polymer degradation, *viz*., biodegradation, occurs in polymers under the action of different enzymes. In a broad sense, biodegradation implies the destruction occurring under the influence of environmental factors, such as water, soil, bio-

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logical fluids, *etc*. Many synthetic polymers, especially carbochain polymers, *i.e*., those built exclusively of carbon atoms in the main chain, are not subject to biodegradation and remain in the environment over the course of years. In contrast, biopolymers (natural polymers and their synthetic analogues) undergo biodegradation being converted into low-molecular-mass compounds.

The degradation rate is an essential feature of the process. However, its true rate constant can seldom be established and this can be done only under model, strictly specific conditions. In real situations with numerous factors influencing the degradation, the rate of the overall process has to be determined by indirect methods.

The most popular methods for the estimation of the degradation rate are as follows:[2]

(1) Estimation of changes in masses and linear sizes of samples. This approach is used for determining the degree and rate of degradation by measuring the reduction of the mass per unit time. If the surface area is known, the reduction of the mass per unit area per unit time can easily be calculated and the corresponding rate constants can be determined. The dimensional characteristics of the samples can be established in a similar way.

(2) Estimation of changes in the average molecular mass and molecular-mass distribution of the polymer employed in the preparation of a sample. In this case, determination of molecular characteristics of the original sample (as a rule, by gel-permeation chromatography) is followed, after a definite period of time, by determination of molecular characteristics of the sample subjected to degradation. However, the heterogeneity of degradation over the bulk of the sample prevents correct interpretation of the results.

(3) Estimation of changes in the concentrations of the degradation products. This approach is used for the determination of diverse miscellaneous characteristics, *e.g*., total volume of gaseous products, concentration of the monomer or the degradation products of a particular polymeric material, changes in pH, *etc*. This method usually gives reliable results provided that the degradation of the tested sample is complete.

(4) Estimation of changes in the concentrations of low-molecular-mass products included into the tested sample. Dyes and radiolabelled substances are used as the most reliable 'markers'; in practice, drugs can also be employed.

(5) Determination of the rates of changes in the mechanical characteristics of degradable polymeric articles. As a rule, these studies are confined to films or fibres.

(6) Determination of the rates of changes in the thermal characteristics of polymers used as starting materials for the preparation of tested articles (*e.g*., melting and glass-transition temperatures).

The above-described methods are not absolute and the results obtained depend critically on the experimental conditions. Therefore, a comparison of experimental results obtained by different groups of researchers who employ different methods is not always justified. To make the experimental results comparable, the methods used for the study of polymer degradation should be standardised.

The methods for estimating the changes in the molecular masses or concentrations of degradation products in the tested samples provide the most reliable information about the rates of these reactions. Such characteristics can be used for the assessment of the average degree of degradation of the sample at large. However, taking into account the heterogeneous nature of the process the surface/volume ratio of the sample should be considered in each specific case

III. Natural polymers contributing the most to the formation of the biosphere

In nature, biopolymers are represented by several major classes which differ in the types of the chemical bonds in the main chains. These include hydrocarbons (rubber, gutta-percha), carbohydrates (cellulose, starch, chitin, *etc*.), proteins, nucleic acids, aliphatic polyesters and polyphenols (lignin).

Structure-forming polymers of plants and animals constitute the major part of high-molecular-mass organic substances synthesised on the Earth annually. The structural function of biopolymers underlies the ability of the living beings (from bacteria to higher organisms) to take definite shapes which is changed depending on the situation. In plants, the structure-forming function is fulfilled by polysaccharides, first of all, by cellulose. In animal organisms, this role is played by both polysaccharides (*e.g*., chitin, the main constituent of invertebrate's exoskeletons) and proteins (*e.g*., collagen and keratin, the main structure-forming elements of vertebrates). Biochemical conversions of these polymers are crucial for the formation of the biosphere.

1. Polysaccharides

Cellulose (poly-1,4-β-D-glucopyranose) is the main constituent of algae, herb and shrub stalks and stems. Biosynthesis of cellulose seems to be among the most ancient biochemical processes on the Earth. Recent studies have shown that cyanobacteria (blue-green algae), one of the oldest life forms on our planet, synthesise cellulose.[3,4] There is evidence [5] that cellulose can also be synthesised by some animal organisms. It is interesting to note that cellulose underlying a vast array of food chains of higher animals is not digested by their organisms due to the absence of the corresponding enzymes (cellulases). In herbivores, its primary degradation to easily digestible oligo- and monosaccharides is effected by symbiotic microorganisms.[6]

From the chemical point of view, cellulose degradation represents hydrolysis of the polysaccharide to oligo- and monosaccharides. In nature, this reaction is predominantly catalysed by the enzyme cellulase.

Studies of cellulose degradation are of special importance for a number of reasons.

— Owing to its large-scale synthesis in nature, cellulose represents the main material factor responsible for the formation of soils and deposits (carbon, shale oils). As to the origin of oil fields, this is still open to question. These problems constitute the subject of an interdisciplinary science, biogeochemistry.

— The cellulose-based articles (*e.g*., fabrics, wood) that came down to us from ancient times are of tremendous interest for archeochemistry, a science that evolved at the interfaces between archeology, history, chemistry, microbiology, mycology and some other sciences.

— Cellulose is a basic component of paper. Therefore, studies of cellulose degradation are underway on the (i) development of methods for conservation, protection and restoration of paper and articles thereof and (ii) determination of the rates and mechanisms of degradation of cellulose (including paper) under the action of external factors in compost, soil, river- and seawater, *etc*.

— Of particular importance is thermal degradation of cellulose concomitant with inflammation of degradation products. Studies in this area make the subject of thermochemistry and those branches of chemistry that are concerned with reduction in the combustibility of cellulose materials.

Among other polysaccharides, mention should be made of a structural isomer of cellulose, *viz*., poly-α-D-glucopyranose (starch, glycogen and amylose). They are synthesised in plants and animals as reserve sources of carbon and energy and are easily hydrolysed by the corresponding enzymes. Of tremendous importance in this group of biopolymers is starch, which has been widely used since the 1990's for the preparation of biodegradable polymeric materials as a constituent of mixtures with polyethylene, polypropylene and other large-scale non-biodegradable synthetic polymers.

Chitin [poly(*N*-acetyl-1,4-β-D-glucosamine)] occupies a special place in polysaccharides. It is present in small amounts in fungi and some algae. In the biosphere, chitin is predominantly localised in the external skeletons of invertebrates, particularly of

Arthropoda. It was calculated [7] that the total mass of chitin in the oceans amounts to 1.5×10^{12} kg. Its annual production by krill alone exceeds 10^8 kg. Enormous amount of chitin-containing waste products formed upon its processing is considered to be a valuable raw material for the commercial production of a vast array of chemical substances.[8]

A partly N-deacetylated chitin derivative chitosan presents particular interest for medicine. Chitosan is one of the few biopolymers that contain basic groups, which determines its ability to form interpolyelectrolyte complexes upon interaction with negatively charged biomacromolecules. The problems of biocompatibility, biodegradation and practical application of chitin and chitosan are considered in detail by Kumar.[9]

2. Proteins and polypeptides

This group includes both natural polymers (collagen, fibroin) and synthetic polypeptides based on one or several amino acids.

In mammalian tissues, collagen constitutes up to 30% of the protein mass. Collagen is an extracellular matrix protein and contains predominantly glycine, proline and hydroxyproline; three separate polypeptide chains form helical structures, which combine in more complex microfibrils. Being a constituent of connective tissues, cartilages and vascular walls, collagen plays the role of a structure-forming element in the organism. Besides, it is the main protein component of a bone tissue. More than 10 types of collagen can be distinguished depending on the type and function of the parent tissue.

3. Polyhydroxyalkanoates

Polymers pertaining to this group occur in nature as organelles of some fungi and bacterial cells and serve as the reserve energy and carbon sources.[10] The first compound of this series, poly(3-hydroxybutyrate) (PHB), was discovered in 1927. In its properties, it is similar to synthetic thermoplastics, such as polyethylene or polypropylene, but, in contrast to the latter, it is decomposed in biological media into non-toxic products. This property attracted keen attention of investigators in PHB and its structural analogues as promising biodegradable plastic materials for medical purposes. In addition, these polymers present substantial interest as biodegradable packaging materials. Although PHB is itself a brittle material, its mechanical properties can significantly be improved if employed as a co-polymer with other monomers, *e.g.*, 4-hydroxyvaleric acid.[11–14] The industrial production of PHB and a co-polymer of 3-hydroxybutyric and 4-hydroxyvaleric acids (PHBV) under the tradename Biopol by microbiological synthesis using the widepsread soil bacteria *Alcaligenes eutrophus* began in the 1980's. Whereas in 1980 the cost of PHB was $\sim$2000 USD per kilo, by 1995 it dropped to 10 USD per kilo (*cf.* the cost of ordinary polyethylene-type thermosets, 1 USD per kilo).[15]

The possibility to synthesise polyhydroxyalkanoates using transgenic plants was widely explored in the past decade. The first report on such a synthesis in a transgenic cruciferous plant (*Arabidopsis thaliana*) appeared in 1992.[16] It is expected that the cost of natural polyhydroxyalkanoates will soon reach that of large-scale products, such as sugar or starch.

Degradation of PHB and PHBV *in vivo* occurs under the action of intracellular and extracellular enzymes (depolymerases) to yield digestable hydroxybutyric and hydroxyvaleric acids. Their further aerobic conversions yield water and carbon dioxide. Under anaerobic conditions, methane is also formed. The metabolic pathways in organisms that produce polyhydroxyalkanoates and prospects of their biotechnological manufacture are discussed in detail.[17–19]

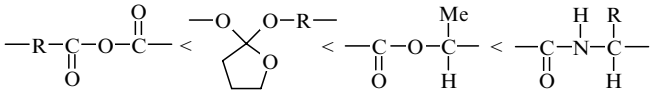
The problems related to environmental pollution by synthetic polymers and the increasing cost of crude oil the reserves of which will sooner or later be depleted have recently become especially acute. In this connection, special attention is given to the production of materials based on either natural polymers or polymers prepared from natural renewable raw materials. These include traditional natural polymers (wood, cotton, silk, wool, leather, *etc.*) and their analogues or hitherto unknown polymeric materials prepared by genetically modified microorganisms in common biosynthetic routes.[20] So far, these polymeric materials are much more expensive than the synthetic polymers. Moreover, studies in this area come up against the resistance of oil-producing companies which supply raw materials for the production of synthetic polymers.

4. Polyphenols

Lignin is the most important representative of this class of polymers. In addition to cellulose, it is an essential component of wood; in soft woods, its content reaches 50%. This amorphous non-toxic polymer is widely available as a side product from paper-making; however, it has a limited market [21] and it is mainly used as a fuel. Lignin macromolecules have complex structures: in softwoods, the main monomeric fragment of lignin is 2-methoxy-4-propylphenol (guaiacol), while that in hardwoods is 1,5-dimethoxy-4-propyl-phenol (syringol). In the environment, lignin is rapidly decomposed into low-molecular-mass phenols and is regarded as a very promising material for the preparation of biodegradable polyalkene-containing mixtures.

IV. Synthetic biodegradable polymers. Chemical structures and preparation features

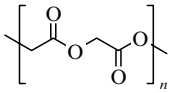
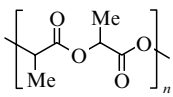
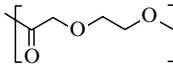
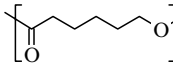
The onrush of the field of polymer chemistry related to the synthesis and utilisation of biodegradable polymers is observed in the past decades. As a rule, it is the ester and amide bonds that undergo hydrolytic degradation under biotic and abiotic conditions. Other bond types, *e.g.*, anhydrides, also cleave easily. The stabilities of the corresponding chemical groups against hydrolysis increase in the following order:



The discovery of bacterial polyhydroxyalkanoates stimulated the search and synthesis of novel polymers related to this class.[22] Polymers of glycolic and lactic acids (polyglycolides and polylactides, respectively) are the most known and most abundant representatives of synthetic polyhydroxyalkanoates. High-molecular-mass polymers were obtained for the first time in the 1950's.[23] They are usually synthesised by ionic polymerisation in a melt of a monomer under the action of organometallic catalysts, *e.g.*, tin octanoate.[24–26] Properties of the polymers thus prepared strongly depend on the nature of the catalyst;[27,28] therefore, a search for novel efficient catalysts is a topical trend in studies aimed at the synthesis of biodegradable polyhydroxyalkanoates.[29–40]

Some examples of polyhydroxyalkanoates prepared by chemical synthesis are listed in Table 1.[22]

Table 1. The main synthetic polyhydroxyalkanoates.

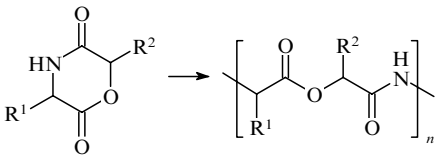
Name	Structure
Poly(oxymethylenecarbonyl) (polyglycolide, polyglycolic acid)	
Poly(oxyethylidenecarbonyl) (polylactide, polylactic acid)	
Poly(oxymethyleneoxyethylenecarbonyl) [poly(1,4-dioxanone)]	
Poly(oxypentamethylenecarbonyl) [poly(6-caprolactone)]	

Polyglycolide is a crystalline polymer with the melting temperature 225–230 °C.[41] Its half-life varies from 60 to 90 days depending on the shape and size of the tested sample and the degradation conditions.[42–49]

In contrast to polyglycolide, polylactides differ in structures and, correspondingly, in properties. The presence, in lactic acid, of a chiral carbon atom points to the existence of two stereoisomers (D and L); therefore, polylactide chains can be built of D- or L-isomers or of a racemic mixture of both. Poly-D-lactide and poly-L-lactide are crystalline polymers. Poly-D,L-lactide is an amorphous polymer; its properties are determined by the microstructures of its chains, namely, by the distribution of the D- and L-isomers,[50–54] which varies from random to highly blockwise. This, in turn, determines physical (crystallisability) and chemical (degradation rate) properties of the polymer.[55]

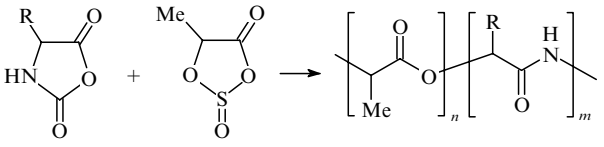
Both polyglycolide and polylactides can be regarded as the basic polymers of a family of polymeric products; in their hydrolysis, the —O—C(O)— bond is cleaved. One of the groups of this family is represented by polyhydroxyalkanoates with a long-chain side alkyl substituent at the α-carbon atom.[56–67] Yet another prominent group contains linear ω-polyesters among which poly(6-caprolactone) presents the greatest practical interest.[68–73]

In addition to polyesters containing only ester hydrolysable groups, of great industrial importance are polymers containing other functional groups in the main chain, *e.g.*, ether groups, obtained by polymerisation of dioxanones.[74–78] Such polymers are more hydrophilic than polyhydroxyalkanoates. Mention can be made of polymers containing alternating ester and amide bonds in their chains. They are prepared by polymerisation of morpholine-2,5-diones.[79–83] Essentially, these compounds represent alternating copolymers of α-hydroxy and α-amino acids. They possess enhanced hydrophilicities; in addition, side functional groups that can undergo polymer-analogous transformations can be incorporated into the polymeric chains.



Synthesis of such polymers is rather complicated and labour-consuming; therefore, copolymers of lactide with the corresponding morpholinediones are prepared instead.[84–91]

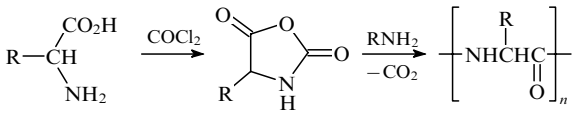
An interesting and efficient approach to the synthesis of copolymers of hydroxy and amino acids has been developed by Deng and co-workers.[92] It is based on the copolymerisation of amino acid *N*-carboxy anhydrides with α-hydroxy acid anhydrosulfites.



The physical and chemical properties of polymers (including degradation rates) can be changed substantially by varying their chemical structures. The degradation rate depends critically on the nature of the monomers. Thus polyesters derived from oxalic acid are characterised by the highest degradation rates and are rapidly (within several hours) decomposed in weakly alkaline media (*e.g.*, in saturated solutions of sodium bicarbonate).[93–95] Polyanhydrides[94–104] prepared by polycondensation of aliphatic dicarboxylic acids in the presence of acetic anhydride[105] or by polymerisation of cyclic anhydrides[106,107] undergo very fast hydrolytic degradation. However, polyoxalates and polyanhydrides have one common disadvantage: their degradation yields abiogenic products.

Yet another type of biodegradable polymers is represented by polyamides including synthetic protein analogues, *viz.*, poly-α-amino acids (polypeptides). Their degradation rates in biological media are significantly lower than the degradation rates of structurally similar polyesters. As a rule, the degradation of polyamides requires the presence of the corresponding proteases in the reaction medium.[108–112]

Polypeptides are prepared by various methods, among which polymerisation of *N*-carboxy anhydrides of α-amino acids has been studied in detail.



Recently, procedures for the polymerisation of these monomers have been developed that yield living polymers. This allowed preparation of polypeptides with a very narrow molecular-mass distribution.[113,114]

The amino acid units in synthetic polymers based on natural amino acids can be linked into polymeric chains in both α- and other positions. Along with amino and carboxylic groups, other functional groups (*e.g.*, the hydroxy groups of serine, threonine or tyrosine) can be involved in the chain formation, which enables the access to polymers with predetermined properties.[115]

V. Degradation of natural and synthetic polymers in the environment

Studies of degradation of natural and synthetic polymers in the environment may conventionally be classified into several groups:

— 'Archeochemical' studies of polymeric articles dating back to ancient times. As a rule, such investigations are concerned with archeological finds. Thus the paper[116] describes the results of an analysis of more than 6000-year-old wood specimens from some Egyptian tombs in comparison with other ancient specimens discovered in different parts of the world. Special attention is given to the dependence of the action of fungi and microorganisms on the specimens in the local environmental conditions (humidity, soil characteristics, *etc.*).

— 'Full-scale' studies of polymer degradation in soil, sea- and river water, compost, *etc.* Such studies usually have only limited, regional significance, since the factors responsible for the degradation of polymers are highly region-specific. The objects for such studies include newsprint paper, natural and synthetic packaging materials, *etc.*[117–122]

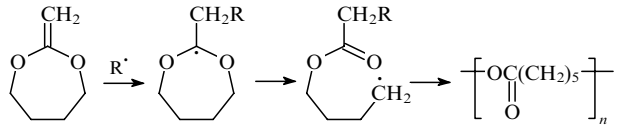
— Laboratory studies where the effects of one or several quantitatively describable factors able to induce degradation of polymers in nature (light, oxygen, water, definite bacterial strains, *etc.*) are simulated.[123–125]

Studies of polymer degradation *in vivo* occupy a prominent place.

The search for synthetic polymeric materials that are decomposed in the environment at fast rates without the formation of large amounts of harmful products are underway in many countries. A key trend is the increase in the degradation rates of materials based on carbochain polymers, such as polyethylene, polypropylene, poly(vinyl chloride), which contribute the most to the environmental pollution, since they are not very prone to oxidative and photochemical degradation, nor they are decomposed by enzymes, microorganisms or fungi. Polyethylene, which is especially dangerous for soils, is an example. It was calculated[120] that the decomposition of low-density 60 μm-thick polyethylene films lasts 300 years! IR spectroscopic studies have shown that the main degradation mechanisms of this material include oxidative and photooxidative degradation, which is accompanied by the introduction of hydroxy groups and double bonds in the polymeric chain. Enhanced hydrophilicity of polymeric films favours their attack by microorganisms.

The main pathways to increase the decomposition rates of polyethylene and related polymeric compounds include the incorporation, into the polymeric chain, of units susceptible to degradation. This can be performed by copolymerisation of the basic monomer with a small amount of a 'degradable' co-monomer or by preparation of composite biodegradable materials from blends of carbochain polymers with natural biodegradable polymeric compounds, *e.g.*, starch.

2-Methylidene-1,3-dioxepane, which is easily homo- and copolymerised under various conditions, is a promising degradable co-monomer. Upon its incorporation into polyethylene [126] or other vinyl polymers,[127] the monomeric units are formed that contain an aliphatic ester bond which undergoes cleavage in the hydrolytic degradation of the copolymer macromolecule.



However, the majority of these studies are aimed at the production of blends of carbochain polymers with biodegradable (both natural or synthetic) polymers. A prominent position among natural polymers used as additives to polyethylene or polypropylene is occupied by starch. Blending of starch with polyethylene in certain proportions under various conditions affords thermoplastic polymeric materials. The articles prepared from them are only slightly inferior to those prepared from the free polymer in mechanical characteristics, but they decompose in the environment by factors of tens faster.[119] A series of such polymeric materials (Mater-Bi) have been developed recently in Italy.[128] The interest in their manufacture is especially high in southern countries where the production of starch from various local sources, *e.g.*, rice, is especially well-established.[129] In some cases, hydrophilic polysaccharides are subjected to chemical modification in order to enhance their hydrophobic properties and to improve their compatibilities with hydrophobic polyolefins.[130]

Composite degradable polymeric materials were also developed on the basis of other polymeric combinations, *e.g.*, poly(vinyl alcohol) – starch [131] and polycaprolactone – lignin.[132] The main advantages of this approach include relative simplicity, low cost and possibility to use basic polymers produced on a large scale and inexpensive degradable additives (starch, lignin). The disadvantage consists of low mechanical characteristics of ready articles, predominantly due to the poor compatibility of the components.

The manufacture of polymeric articles that preserve high mechanical characteristics throughout the operation period and undergo rapid degradation afterwards without release of harmful products is yet another promising trend in the design of environmentally friendly polymeric materials. As regards their functions, this group refers primarily to packaging materials. The aliphatic polyesters of synthetic and microbiological origin described above present the greatest practical interest in this respect. Such polymers can be used as such in single-component systems and as degradable components in blends with large-scale manufactured polymers.

VI. Biomedical technologies based on polymer degradation

Natural polymers (*e.g.*, cellulose and silk fibres) have been used in medicine as suture and dressing materials since the time of its origin by virtue of their high durability, flexibility and ability to absorb moisture. The advent of novel polymeric materials (natural rubber and gutta-percha) favoured the development of novel medical products. The discovery of the macromolecular origin of polymers and the subsequent explosive development of the synthetic polymer chemistry has led to closer interactions between these areas of knowledge. Biodegradable polymers were also in great demand in clinical medicine. A variety of novel, in principle, biomedical technologies developed in the past decades are based on degradation of polymers in aqueous physiological media.

The biodegradable polymeric materials used in the medical practice differ in the phase states of their constituent polymers (solutions, gels, solids), shapes [*viz.*, one-dimensional (fibres, tubes), two-dimensional (films, fabrics), three-dimensional (large-size articles some of which have rather complex shapes)] and in decomposition rates in biological media. This Section deals with the description of three lines of research in this area, *viz.*, preparation of biodegradable suture and dressing materials, development of biodegradable polymers for the targeted delivery of medicinal drugs and the use of biodegradation in tissue engineering.

1. Biodegradable polymeric suture, fastening and dressing materials

The problem of bioresorbable (biodegradable) suture materials is as old as the surgery itself. Whereas suture removal after external wound healing does not present significant difficulties, in the case of intracavitary operations this procedure may require additional surgical intervention.

Traditionally, fibrous materials of cellulose fibres are used in the clinical practice as dressings due to their high moisture-absorbing properties. Filaments of cellulose and natural silk have been used as suture material; they do not induce rejection, but are resorbed in the organism for a time exceeding manifold that required for the regeneration of tissues. Therefore, practitioners in medicine are on a continuous search for bioresorbable suture materials. The catgut, *i.e.*, a filament prepared from dried intestinal membranes of young cattle, is now forbidden for use in the surgical practice in many countries of the world because of the problem of 'mad cow disease' (bovine spongiform encephalopathy).

Suture materials (fibres and filaments) prepared from polylactide, polyglycolide and their copolymers are currently widely used in intracavitary operations. These polymers are readily converted into fibres by extrusion at temperatures below their thermal degradation temperature, which excludes the presence of foreign degradation products in the extrudates. The time required for the complete decomposition of these materials in the human organism can be controlled by the composition of the copolymers. Commercial production of such suture materials (mono- and polyfilamentous fibres) [133] is currently underway in some European companies. Each type of filaments has advantages and disadvantages of its own. Monofilamentous threads have smoother surfaces and are sterilised more easily. Their main disadvantage is higher stiffness, which creates additional problems during the operation. Polyfilamentous threads are more convenient, however their less smooth surfaces create complications and do not always meet the requirements for high sterility.[133–138] In Russia, surgical suture filaments based on biodegradable polymers (Vycril, Dexon) are mainly produced from imported raw materials.

The adequate use of ware for union and fastening of bone fragments in reconstructive surgery presents a serious problem. While metallic (titanium) staples, pins and screws are very convenient surgical tools, their removal after consolidation of fractured bones demands additional surgical operation. Therefore, leaving metallic fasteners in the patient's organism is considered admissible. Within the organism, these are gradually overgrown with connective tissue and after a while they are no longer recognised by the organism as foreign bodies. However, the difference in the deformation characteristics of the bone tissue and titanium may create serious problems for patients. Moreover, redistribution of load in favour of the metallic element increases the risk of osteoporosis.

Some manufacturers produce polylactide fasteners for bone fragments. The adequate choice of chemical structures of poly-

mers enables the synchronisation of the time of their degradation and that of bone consolidation, which varies from several weeks to several months. Such materials are usually made of poly-L-lactide, a polymer with a regular structure and high degree of crystallinity. Due to the regular crystalline structure, the diffusion coefficients of the destructive reagents inside the fasteners decrease, which makes the latter more stable than those made of amorphous materials. Of particular importance is the sizes invariability of polymeric fastenings in the earliest steps of bone consolidation, *i.e.*, these materials should not swell in biological media.[139]

2. Biodegradable polymers for targeted delivery of medicinal drugs

The problem of drug formulations is one of the main challenges to modern pharmacology. On entering the organism (especially, upon oral administration) drugs are exposed to the action of highly active biological media containing enzymes. This results in partial or complete inactivation of the drug before it reaches the small intestine and is absorbed by blood. Therefore, one has to increase the drug dose, which increases the risk of side effects. Direct administration of medicinal drugs into the circulating blood is not always efficient due to functioning of protective mechanisms from drugs as foreign compounds. Therefore, the therapeutic effects of drugs administered in this way are short-lasting (Fig. 1).

In the 1950's, it has occurred to use polymers for the modification of medicinal drugs. Initially, biologically active substances were chemically immobilised on polymeric macromolecules as supports.[140] This approach was thought to prevent drug inactivation in the organism (especially, upon oral administration) and to prolong their therapeutic effects. Studies aimed at perfecting the functioning of drugs follow two major lines, *viz.*, (i) maintenance of constant drug levels over sufficiently long periods of time and (ii) efficient (without inactivation) delivery of drugs to damaged cells, tissues or organs with subsequent release of the active substance in the target organ or tissue (targeted drug delivery).

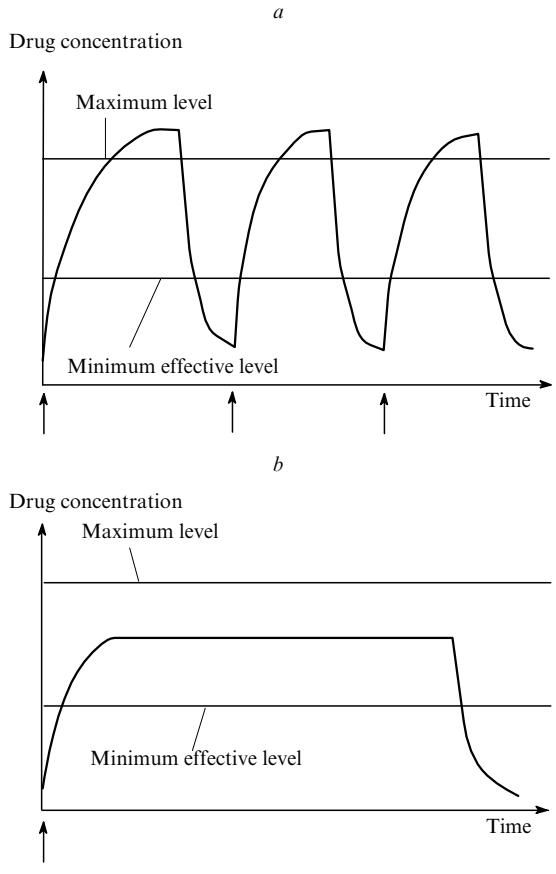


Figure 1. Time dependences of the concentration of a free drug (*a*) and of a drug included into biodegradable polymeric microgranules (*b*). The time of drug administration is marked by arrows.

Various approaches are known to reach this goal, including the use of thermo- and pH-sensitive hydrogels [141] and biodegradable polymers. Chemical and physicochemical aspects of drug design for targeted delivery of active substances based on the use of biodegradable polymers are considered below. The main principle in the design of such formulations consists of the encapsulation of medicinal drugs into matrices of biodegradable polymers and administration of these compositions. In the organism, the polymer undergoes gradual degradation with liberation of the active substance. Obviously, invariability of the drug upon the production of such compositions is a necessary condition.

Biodegradable films and macroscopic plates are among the simplest formulations of this kind where the active substance is dispersed more or less uniformly in the bulk. Such articles are implanted into the area of the injured tissue or organ and function as 'drug depots'. The controlled release of the drug from the polymeric matrix occurs continuously, in the course of its degradation.

The methods for the manufacture of such articles depend on the physicochemical properties of the constituents. If the drug and the polymer are soluble in the same solvent (*e.g.*, dichloromethane), films of required thickness are cast from a solution of the components and are cut into plates or rods. If the components have no common solvent, they are finely dispersed into a mechanical blend and thermal compacting affords films, plates or rods. In the case of thermal inactivation of a drug, an inert solvent is added to the dispersed blend until a thick paste is formed. This is dried to give plates of a biodegradable polymer–drug composite. This method was used [142] to obtain composites of the antibiotics Sulperazone or Duocide with a copolymer of 3- and 4-hydroxybutyric acids employed in the therapy of osteomyelitis.

Microencapsulation is a more complex process for the production of compositions of biodegradable polymers with drugs. Usually, it includes emulsification of a solution of a biodegradable polymer in water in the presence of a surfactant or a stabiliser, *e.g.*, partly hydrolysed poly(vinyl acetate). In these technologies it is important that the polymer and the drug be soluble in the same solvent. In this case, the polymer and the drug are dissolved in this solvent (*e.g.*, dichloromethane) and are emulsified in water in the presence of a surfactant (an 'oil-in-water' emulsion) using vigorous stirring or sonication. On gentle heating, the solvent is evaporated from the emulsion droplets to afford a suspension of microgranules. Their sizes depend on the stirring rate, the surfactant concentration and other factors; they vary from 10 to 60 μm. Such granules represent homogeneous systems the active drug in which is evenly distributed in the bulk.

This method was used by Langer and co-workers [143] for the preparation of microgranules from copolymers of lactic acid with lysine containing side polypeptide chains grafted to the NH_2 groups of lysine. Rhodamine B was used as a model of the encapsulated drug. Such copolymers present considerable interest, since the presence of side amino acid functional groups and the active substance in the grafted polypeptide chains allows covalent binding of this or any other drug to the surface of the microgranules (in addition to encapsulation) or its binding through electrostatic forces.

The situation is more complex where the drug is water-soluble and the polymer is soluble in a low-polar solvent. In this case, microgranules are prepared by the double emulsion method ('water-in-oil' in water). The first step includes the preparation of an emulsion of an aqueous solution of the drug in a solution of the polymer in a low-polar solvent ('water-in-oil'). In the second step, the resulting emulsion is poured into an aqueous solution of a surfactant with vigorous stirring or sonication (Fig. 2) to yield a double emulsion ('water-in-oil' in water). The last step includes

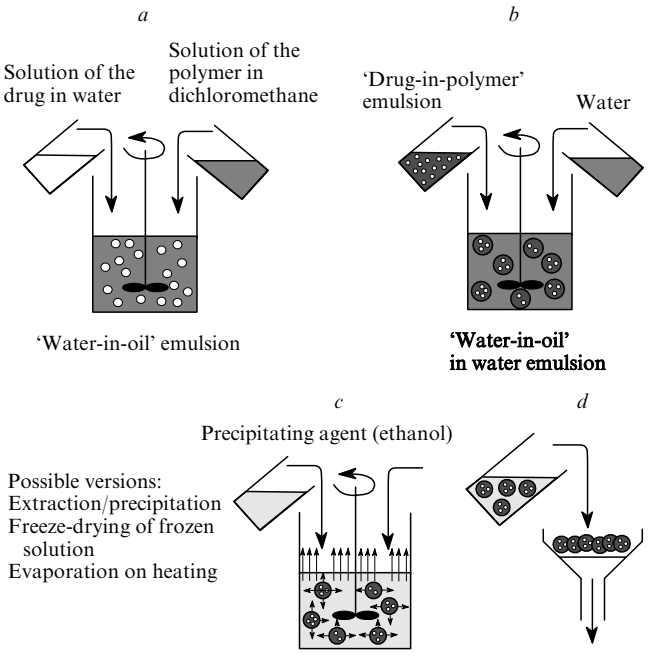


Figure 2. A chart of manufacture of drug-loaded polymeric microgranules.
(*a*) Loading of the polymer with the drug; (*b*) preparation of a polymer dispersion; (*c*) removal of an organic solvent; (*d*) isolation of the microgranules.

removal of the low-polar solvent and solidification of the microgranules with the encapsulated droplets of the aqueous drug solution by evaporation of the solvent with constant stirring or by addition of a solvent that precipitates the polymer. The microgranules can be filtered off or isolated by centrifugation. If required, water can be removed from the frozen granules by lyophilisation. The product obtained represents a microheterogeneous system where the drug (as an aqueous solution or as such) is dispersed in the bulk of the degradable polymer. Surface erosion of such granules results in the release of the drug into the organism.

The features of the manufacture of microgranules based on a copolymer of D,L-lactide with glycolide by the double emulsion method is described in detail.[144] In this study, ^{14}C-mannitol was used as the included compound; its content in the granules and the rate of its liberation upon polymer degradation were established by radioactivity measurements.

More sophisticated techniques for the manufacture of microgranules with drugs included have been developed. For example, according to the ProLease® technology,[145] a solution of a polymer in dichloromethane containing dissolved or dispersed additives is sonicated in a vessel with liquid nitrogen. On the vessel bottom, frozen ethanol is present meant for polymer precipitation. Thawing of ethanol as the temperature is increased results in extraction of the solvent from the granules. This approach was used [146] for the manufacture of polylactide microgranules containing human growth hormone; their degradation and the concomitant liberation of the hormone were studied both *in vitro* and *in vivo*.

Production of nanoparticles with included medicinal drugs was the next step in the miniaturisation of degradable polymer granules. These technologies are based on the formation of micelles of diphilic block-copolymers, one of the blocks being biodegradable. Immobilisation of lipophilic drugs is achieved by their solubilisation in micelle cores. The structures of micelles can be stabilised by polymerisation of the functional groups localised either in the micelle core or on its surface. A series of papers devoted to polymeric core-shell micelles were published by Kataoka and co-workers.[147, 148] One of the first reports on 'surface cross-linked' micelles was published by Wooley and coworkers.[149] Micellar 'nanodepots' for drug delivery are reviewed in detail.[150, 151]

3. The use of biodegradable polymers in tissue engineering

Tissue engineering is a novel, rapidly developing trend in the biomedical science which is concerned with the methods for the growth of fragments of tissue or organ injured as a result of a disease or an accident, from patient's own cells and further implantation of the tissues into the organism. Quite naturally, the immunocompatibility problem is not critical in this case. This approach was developed in the 1980's by the American surgeon Vacanti in collaboration with the chemist Langer. The first publications on this subject appeared in the early 1990's.[152, 153]

Currently, cell therapy is often used for the treatment of some severe diseases resulting from injuries of tissues of internal organs and including myocardial infarction. A suspension of living cells of the corresponding tissue are commonly administered to the patient, they find the target site themselves and favour fast healing of the injured tissue. Unfortunately, this approach is not always efficient; moreover, it demands the use of a large excess of cell cultures.

In the approach developed by Langer and Vacanti, the cell culture of the corresponding tissue is plated onto a special porous scaffold made of a biodegradable polymeric material. After adsorption on the inner surface of the scaffold pores, the cells begin to proliferate, which results in fusion of an integrated tissue. In a biological medium, the scaffold undergoes gradual degradation (Fig. 3). After a while, a fragment of the integrated tissue is formed instead of the polymeric scaffold with sown cells. Its shape is the same as the shape of the original scaffold and is not foreign for the organism.

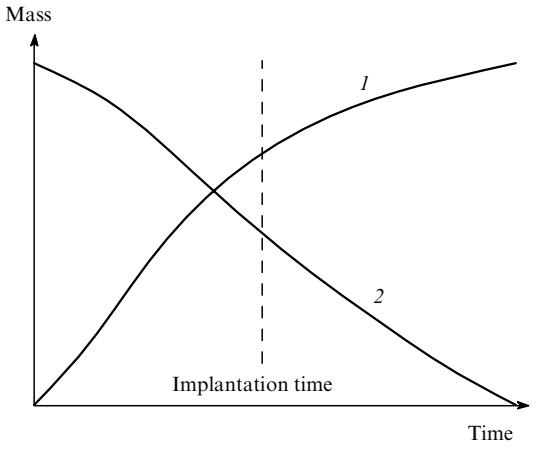


Figure 3. Time dependences of the mass of an integrated cultured tissue (*1*) and the polymeric material of the scaffold (*2*).

At present, the muscle, bone and connective tissue engineering has reached the clinical level.[154–159] Studies on culturing of skin,[160, 161] nerve,[162–165] parodentium [166, 167] and eyeball (including crystalline lens) tissues [168–170] are in the research stage. Needless to say, each tissue type has its own peculiarities and requires original approaches. Thousands of papers devoted to tissue engineering have appeared since the first publication (see, for example, Refs 171–187). The use of polymeric materials in tissue engineering has been reviewed [188, 189] (the data are as of 2000).

Further progress in this area depends on the solution of a great number of diverse problems. Here we briefly discuss the major problems related to the use of biodegradable polymers in tissue engineering (for the design of scaffolds) and their interactions with the cellular material, *viz.*,

— chemical nature of the polymer;
— types of polymeric scaffolds and technologies for their manufacture;
— dependence of cell behaviour on chemical, energetic and morphological characteristics of the polymer surface;
— cell interaction with the polymeric surface of the scaffold and the principles for improving its efficiency by surface modification.

a. Chemical nature of polymers used in scaffold manufacture

Polymers used for the manufacture of scaffolds should meet a number of demands:

(i) they should not be toxic, nor induce rejection, *i.e.*, be biologically compatible with body tissues;

(ii) their degradation rates should correlate with the rates of formation of the integrated tissue;

(iii) their degradation products should not be toxic; moreover, it is desirable that these products served as nutrients for the growing tissue cells;

(iv) the chemical structures of the polymers should create the most favourable conditions for the cell growth on the scaffold surface.

A series of natural and synthetic biodegradable polymers meet these requirements. Among the natural polymers, various types of collagens, chitosan, hialuronic acid, starch and some other polysaccharides can be distinguished. Being a matrix protein formed by living cells sown onto a foreign surface, collagen would be an ideal material for the scaffolds. However, its physicochemical properties do not always match the technology of scaffold manufacture. In addition, the rate of its degradation in the organism is often too low for the solution of many practical tasks of tissue engineering. Chitosan is a product of partial or complete deacetylation of chitin. Its physicochemical properties are determined by the degree of deacetylation, which allows their adaptation for the solution of specific tasks.[9, 190] For this reason, chitosan and its derivatives can be regarded as promising polymeric materials for the manufacture of scaffolds.[191–195]

However, the majority of studies aimed at the design of scaffolds deal with synthetic biodegradable polymers, predominantly polyhydroxyalkanoates and related materials. Poly-D,L-lactide, poly-L-lactide and their copolymers are used as the basic polymers; they are the most thoroughly studied as regards their synthesis, degradation and behaviour *in vivo*. The use of polylactides for the preparation of medicinal products is authorised in the majority of industrially developed countries. Non-toxicity of these polymers and their degradation products is their main advantage.

The degradation rate of poly-D,L-lactide meets the requirements for the polymeric materials used for the manufacture of scaffolds. These materials are easily processed by molding from melts or casting from solutions in organic solvents.[196] The broad range of properties of lactide-based copolymers allow their extensive use in the design of macromolecular constructions.

A family of novel copolymers based on polylactide have been developed.[197] These include depsipeptides with side groups containing ionogenic groups; comb-like and branched polylactides; polylactides grafted to polysaccharide chains. Polylactide copolymers grafted to dextran as the main chain have been described.[198]

b. Types of polymeric scaffolds and technologies of their manufacture

A key problem in the construction of a tissue or an organ fragment is related to the structure of the polymeric scaffold used as a biodegradable matrix for cell seeding. As a rule, they are two- or three-dimensional constructions containing an array of interconnected pores of definite sizes and configurations. These may include truly porous (*e.g.*, foam-like or sponge-type) or quasi-porous objects made of woven or non-woven moulded materials with fibres of various diameters prepared from biodegradable polymers. The manufacture of the latter type of scaffolds utilises the most advanced technologies, such as, for instance, multilayer deposition of fused fibres with the help of a special programming device (Fusion Deposition Modelling). The approaches to the formation of such scaffolds are given in detail in a review.[155]

Of particular interest are the technologies used for the manufacture of genuinely porous scaffolds where the cells are bound to the polymer on the inner surface of a pore rather than on the outer surface of a fibre or a disc. In contrast to foams where the pores are isolated from one another, sponges contain a well-developed system of interconnected pores. Sponge-like systems are the most suitable for tissue engineering, the bimodal pore size distribution being optimal, with large pores having diameters $\geqslant 100$ μm and small ones having diameters of tens to hundreds nanometres. It is on the inner surface of large pores that the cells attach to the polymer, proliferate and then integrate into the tissue. The supply of nutrients and the removal of metabolites occur through the biological fluid that circulates through the system of small pores. Porosity, *i.e.*, the ratio of the pore volume to the total volume of the polymeric article, is an important characteristics of a scaffold. This is directly related to its mechanical properties including the ability to preserve its shape during the time required for the formation of an integrated tissue. In this situation, it is important to maintain the balance between the mechanical strength and the resistance of the scaffold to external factors, on the one hand, and the minimum content concentration of the structure-forming polymer in the total volume of the scaffold, on the other hand. The main methods for the manufacture of porous scaffolds and their characteristics are listed in Table 2.[155, 199]

Table 2. The main approaches to the manufacture of polymeric scaffolds.

Method	Average pore size /μm	Degree of porosity (%)	Structural features
Foaming with a gas	0.1 – 1000	—	open and closed isotropic pores
Phase stratification in the system polymer – solvent induced by temperature changes with subsequent removal of the solvent (by lyophilisation or extraction)	< 200	97	open isotropic pores
Preparation of a 'water-in-oil' emulsion with subsequent freezing and lyophilisation (removal of water)	< 200	97	the same
Preparation of mechanical blends of a polymer and fractionated salt crystals with subsequent extraction of the latter with water	< 100	85	closed and open pores having the shapes of porogen particles (cubic in the case of NaCl crystals)
Construction of a pore system using a three-dimensional template with subsequent removal of the latter	45 – 150	60	open pores of any predetermined shape
Phase stratification of two incompatible polymers with subsequent removal of one of the polymers by selective solubilisation or degradation	200 – 300	80 – 90	open pores

A novel approach to the formation of porous structures based on the use of blends of two incompatible polymers and subsequent selective degradation of one of them has been developed by the authors of the present review.[95] Its essence is as follows:

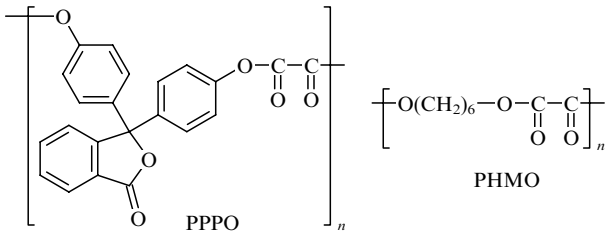
(1) The degradation rates of two polymers one of which is a matrix-forming component and the other is a pore-forming component should be essentially different (by no less than 1 to 2 orders of magnitude).

(2) The polymers should undergo phase separation in solution or in a melt to form biphasic continuous systems.

(3) The heterogeneous structure formed is stabilised by precipitation of the polymer or by cooling of the melt.

(4) The pore-forming polymer should be selectively extracted.

The feasibility of this approach was demonstrated in experiments with blends of a polylactide (PLA) and polyoxalates [poly(phenolphthaleine oxalate), PPPO and poly(hexamethylene oxalate), PHMO], which possess high degradation rates in alkaline media.



Highly porous polylactide discs (the degree of porosity $\sim 90\%$) were prepared by sedimentation of a heterogeneous polymeric blend from a solution with subsequent compacting and degradative removal of the polyester.[200] The micrographs show the general view of a porous disc (optical microscopy) (Fig. 4) and its microstructure (electron microscopy) (Fig. 5).

Porous films prepared by casting from both the melts and the solution with subsequent degradative polyester removal are shown in Fig. 6.[201] A similar approach to the formation of porous structures was developed recently by Favis and co-workers [202, 203] and by Langer and co-workers.[204]

Other characteristics of inner surfaces of the scaffold pores including the character of the inner surface of pores and its topography, free surface energy, charge, the presence of functional groups, hydrophobicity – hydrophilicity ratio, *etc*., also play a prominent role.

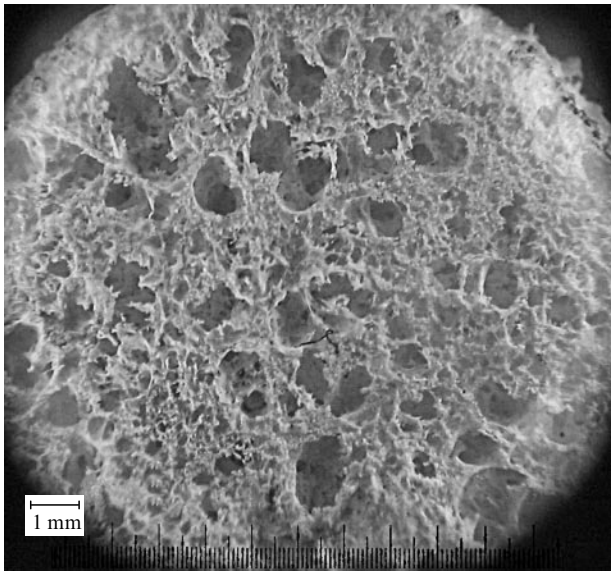


Figure 4. A porous disc manufactured from a heterogenous system PLA – PPPO in the solution by precipitation of the emulsion, extrusion and degradative removal of PPPO.

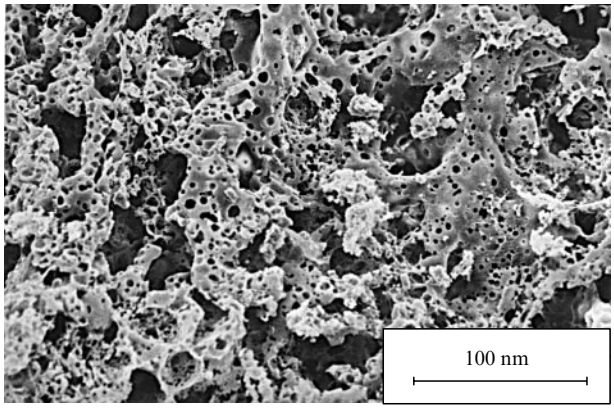


Figure 5. Microstructure of a porous disc (× 300 magnification).

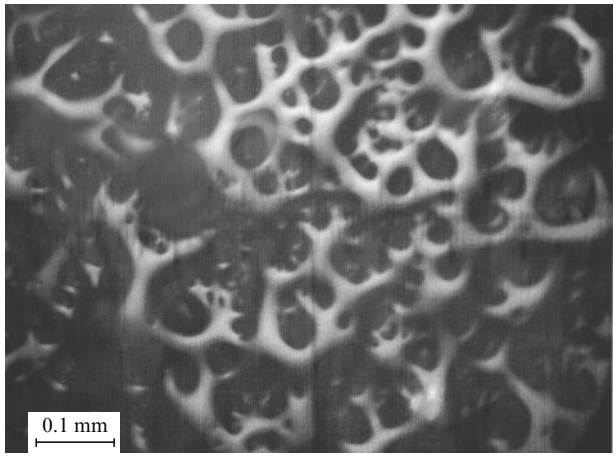


Figure 6. A porous film manufactured from the PLA – PHMO melt after the degradative removal of PHMO.

c. Cell interactions with scaffold polymeric surfaces

The interactions of living cells with polymer surfaces present a serious problem in many areas of biology and medicine, particularly with respect to donor blood storage, organ and tissue prosthesis, *etc*. However, it is in tissue engineering that the interactions of cells designed for tissue growth with polymer surfaces are especially critical. These cells ought to manifest specific behaviour over the whole period of tissue growth beginning with the plating of the cells onto the scaffold up to the moment of their implantation into the organism. In the first step, the cells are to be adsorbed on the surfaces of polymeric articles. In this step, the forces that determine their adsorption should be strong enough to ensure their binding to the surface without causing their deformation. In subsequent steps, the cells begin to synthesise extracellular matrix proteins (collagen, fibronectin, *etc*.) and thus create convenient surfaces for subsequent active proliferation and formation of integrated tissues. These processes occur in parallel with the disintegration of the polymeric material of the scaffold.

The interactions that determine the adsorption of cells on the scaffold surface can be classified into several groups:

(1) non-specific weak non-covalent interactions that are largely determined by the free surface energy of the polymeric material (or, more exactly, by the free interphase energy at the polymer – physiological medium interface);

(2) electrostatic interactions of negatively charged cells with the polymer surface;

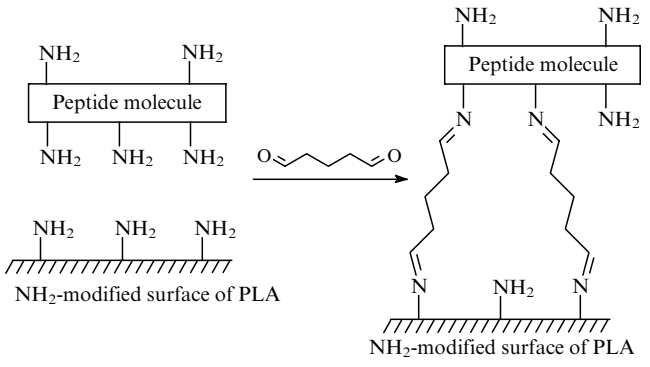
(3) highly specific interactions of cell receptors with binding chemical structures, most commonly, of the peptide nature, immobilised on the surface of the polymeric material.

In addition to physicochemical and biospecific factors, cell binding to polymeric surfaces strongly depends on their morphology.[205–208] The majority of cell adsorption experiments were carried out with films, since three-dimensional samples present problems as regards formation of certain surface structures and their analysis. Polymeric materials with predetermined surface morphology can be obtained in different ways, *e.g.*, using various combinations of a polymer and a solvent (or solvent mixtures)[209] or by preparing films from polymer blends followed by thermal or chemical treatment of the preformed films.[210,211] It was found[207] that polyhydroxyalkanoate films prepared under special conditions had coral-like surfaces with low cell adsorption. The structures of such surfaces become smoother upon treatment of films with lipase, which increases cell adsorption 40-fold.

The free energy of a surface is largely determined by the nature of the polymeric material. The lowest values of this parameter are characteristic of perfluorinated polymers. For example, the free surface energy of Teflon is 18 mJ m^{-2}. The interactions of such surfaces with cells are negligibly weak, which allows their use for the storage of donor blood and for other similar purposes. Higher values of free energy are required for more efficient adsorption of cells on the scaffold surface.[212] Surface hydrophilicity is yet another important related factor, since the majority of cells (with the exception of adipose tissue cells) function in aqueous media and possess high affinity for hydrophilic surfaces. Polyhydroxyalkanoates, the most popular scaffold material, have hydrophobic surfaces, which reduces cell adsorption on them.

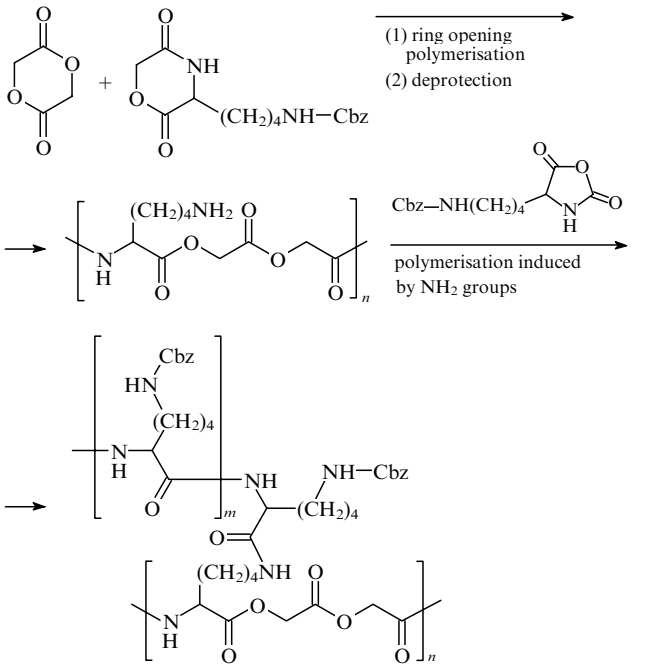
The hydrophilicities of polyhydroxyalkanoate-based scaffold surfaces can be increased by different methods. One of the most popular techniques includes treatment of scaffold surfaces with solutions of extracellular matrix proteins. This procedure has a dual effect, since it increases both the hydrophilicity and the biocompatibility of the scaffold surface. The use of collagen-treated films for cell adsorption allows one to increase significantly the number of cells adsorbed per surface unit.[213,214] Moreover, these cells are able to proliferate spontaneously (without additional adaptation). The main disadvantage of this approach is that collagen and other matrix proteins are very quickly desorbed from the polymer surface in physiological media. To prevent desorption, these proteins are covalently bound to the polymer, *e.g.*, using glutaraldehyde (Scheme 1).[184]

Scheme 1



However, the practical realisation of this approach requires the use of polymeric materials with surface amino groups, *e.g.* chitosan the number of amino groups in which is easily controlled by the extent of hydrolysis of the acetamido groups.[215] Lysine units can be introduced into polyhydroxyalkanoates, the most suitable material for the manufacture of scaffolds, by copolymerisation of the lactide with the corresponding morpholinedione.[88] Removal of the protective benzyloxycarbonyl groups in the side chains liberates amino groups.

Scheme 2



Cbz is benzyloxycarbonyl.

The role of positively charged amino groups on the scaffold surface is not confined to the covalent binding of matrix proteins. These groups enhance cell adsorption due to electrostatic interactions with the negatively charged cell surface.[216] In order to further enhance this interaction, Langer and co-workers[89] employed the amino groups of lysine in the copolymer chains for graft-polymerisation of N^{α}-carboxy-N^{ε}-benzyloxycarbonyl lysine (Scheme 2).

Covalent attachment of the so-called binding peptides is one of the most interesting approaches to increasing the affinity of the scaffold surfaces to the cells to be adsorbed. The tripeptide arginyl–glycyl–aspartyl (RGD-peptide) able to interact with cell-binding receptors has been studied in most detail.[217–221] The incorporation of even very small amounts of this peptide resulted in a significant increase in the surface adsorption of the cells. The works devoted to biospecific adsorption of cells on the surfaces of polymeric materials under the action of binding peptides were published quite recently. There is still no data on which of the methods for grafting of the peptide to the scaffold surface ensures the best results. However, further studies may culminate in significant achievements in the physicochemistry and biochemistry of interactions of living cells with various surfaces.

Obviously, very soon novel tissue engineering technologies will occupy a prominent place not only in reconstructive surgery, but also in treatment of diseases that are still beyond the control of modern medicine. The development of novel biodegradable polymeric materials will surely make a weighty contribution to the attainment of this goal.

VII. Conclusion

In the past few decades, the branch of chemistry of high-molecular-mass compounds concerned with the degradation and stabilisation of polymers has developed into a vast area of knowledge that involves diverse sciences and technologies — from chemistry to microelectronics, biogeochemistry, ecology, medicine and even archeology. The conventional views on the polymer degradation and its role in nature and in modern technologies also changed considerably. For a long time, the main efforts were focussed on the protection of polymeric articles from degradation;

however, more recent trends are towards investigation of the role of polymer degradation in sculpturing the appearance of our Planet and functions of living organisms, natural transformations of low-molecular-mass compounds into polymers and *vice versa* and the 'fate' of polymeric articles that have served their time in the environment. However, the most important result in studies of polymer degradation is that this phenomenon has found novel, quite unexpected applications in the most advanced technologies.

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