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SYNTHETIC POLYMER MATERIALS AND THEIR POTENTIAL APPLICATIONS IN TREATING BATTLEFIELD INJURIES

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Abstract: In modern warfare, combat trauma can easily cause skin defects or loss of function, destroying the barrier function of the skin to the human body and affecting the stability of the internal environment of the body. Currently, there are various types of wound coverings available, but they have their own advantages, disadvantages and indications due to different performances. As an emerging product, biosynthetic polymer materials have huge application potential. This article provides a review on the research progress of biosynthetic polymer materials.
Keywords: Biosynthetic polymer materials; War trauma; Application; Progress

1 PERFORMANCE REQUIREMENTS AND CURRENT SITUATION OF WOUND REPAIR MATERIALS

An ideal wound repair material should have the following characteristics: (1) Adhesion. Can quickly and firmly adhere to the wound surface. (2) Permeability. It is semi-permeable and impermeable to water, but it can control water evaporation. (3) Barrier function. It can prevent the proliferation and invasion of bacteria on the wound surface. (4) Reduce pain. Protect nerve endings from external stimulation. (5) Security. Non-toxic, non-pyrogenic, no or low antigenicity, and sterilizable. (6) Compliance. Has good elasticity and flexibility. (7) Durability. It is stable on various types of wounds and suitable for different parts of the human body. (8) Does not interfere with the wound healing process. Does not hinder epithelialization and does not promote temporary excessive deposition of new matrix. In recent years, wound repair materials have developed rapidly, come in various varieties, and have a wide range of applications. According to their sources and related properties, they can be divided into the following three categories (Table 1).

Table 1 Classification of wound repair materials

type	Example
Natural biomaterials	Autologous tissue: skin, bone, aponeurosis, omentum, blood vessels, etc. Allogeneic tissues: cardiac valves, angular membranes, aponeurosis, amniotic membrane, peritoneum, blood vessels, etc. Xenogeneic tissue: pig, dog, monkey, rabbit, chicken skin, ten-heart valve, pig heart valve Artificial biological materials: animal materials to reconstruct protein (collagen), fibrin (fibrin membrane), silk protein/ silkworm (silk fibroin membrane)
Artificial biomaterials	Polysaccharides: cellulose, chitin, chitosan Plant-based materials: seaweed (sodium alginate), aloe vera (methylated polysaccharide), potato (sponge type wound dressing) Ceramic Material: Bioactive Glass Polymer plastics: polyurethane, silicone rubber, polyvinyl alcohol, polyisopropylene alcohol, polymethyl methacrylate, polytetrafluoroethylene, man-made fiber polypropylene mesh, nylon velvet, Teflon velvet
COMPOSITE biomaterials	Synthetic peptides, polypeptide membranes, polypeptide velvet, synthetic materials + synthetic materials / fully synthetic materials, synthetic materials + biological / synthetic materials, synthetic materials + biological / synthetic materials + active biological materials

However, the current wound repair materials have many defects and shortcomings: (1) The problem of infection caused by implantation in the body is serious. Infection of biological graft materials is a serious problem, especially intracorporeal grafts. Infection of the implantation center in the body is one of the most important reasons restricting the widespread application of biomaterials. After temporary or permanent biological materials and artificial organs (such as surgical suture materials, artificial joints, artificial valves, intraocular lenses, etc.) are implanted in the body, the incidence of central infection accounts for 45% of nosocomial infections, and the mortality rate is 5% to 60%. (2) Natural biological transplantation materials have strong antigenicity. Allogeneic or xenogeneic natural biological transplant materials (such as skin) have extremely strong antigenicity. The antigenicity of xenogeneic skin is stronger than that of allogeneic skin, and the antigenicity of other xenogeneic skins is stronger than that of pig xenograft skin. Therefore, human cadaver skin and pig skin are often used as transplantation materials. Covering areas of burn wounds. Low-temperature cryopreservation, glycerolization (80% concentration), glutaraldehyde, irradiation, and freeze-drying can reduce the antigenicity of natural biological transplant materials; immunosuppressants (such as cyclosporine A, prednisone, etc.) can delay the rejection time. (3) Natural biological transplant materials are difficult to preserve. Only some tissues can be stored at low temperatures for a long time, and other tissues are seriously damaged by freezing.

For example, the liver can only be stored at above-zero temperatures (4°C) for a few hours, and the kidneys can only be stored for about 2 days. (4) The research and application of traditional concepts and new biological transplantation materials need to be reconciled. Traditional concepts often affect the research, promotion and application of new biological transplantation materials. It is a big problem to transform the concept of new biological transplantation materials into actual products.

2 THEORETICAL BASIS OF MICROBIAL SYNTHESIS TECHNOLOGY

In recent years, studies have found that certain microorganisms in nature, under restrictive growth conditions, accumulate carbon sources and store energy substances in the form of granules in their cells, forming intracellular polyesters with molecular weights generally ranging from tens of thousands to millions. [1-4]. Polyhydroxyalkanoate is a type of intracellular polyester that can be completely degraded by microorganisms in nature. As a new bioengineering material, it has good plasticity and biocompatibility. It is widely used in human tissues represented by artificial skin. The field of engineering materials has extremely broad application prospects [5-7]. Common types of polyhydroxyalkanoate include: poly 3-hydroxypropionate [8], poly 3-hydroxybutyrate [8-9], poly 3-hydroxypropionate 4-hydroxybutyrate [10], poly 3-hydroxybutyrate 4-hydroxybutyrate [11-12], poly-3-hydroxybutyrate 3-hydroxyvalerate [13], poly-3-hydroxycaproate 3-hydroxyoctanoate [14], poly-3-hydroxybutyrate Caprylic acid 3-hydroxydecanoate [15] and so on.

Polyhydroxybutyric acid lactate is a new type of polyhydroxyalkanoate recently discovered. The polymerized monomers are derived from 3-hydroxybutyric acid and lactic acid [16]. Taguchi et al.[17] introduced β-ketothiolase derived from Alcaligenes eutropha, reduced nicotinamide adenine dinucleotide phosphate-dependent acetoacetyl CoA reductase, and 61-3 pseudomonas into Escherichia coli. Polyhydroxybutyric acid lactate was successfully synthesized for the first time using a polyhydroxyalkanoate synthase mutant derived from Mycobacterium spp. and a propionyl-CoA transferase derived from Megasphaeria escherichia. The molar ratio of 3-hydroxybutyric acid to lactic acid was 94: 6, and the average molecular weight is 199.5. When the culture conditions are anaerobic, the molar ratio of lactic acid in polyhydroxybutyrate lactate increases to 47% [18]. Changing the carbon source can affect the molar ratio of 3-hydroxybutyric acid lactate in polyhydroxybutyric acid lactate. The molar ratio of lactic acid in polyhydroxybutyric acid lactate synthesized with xylose as the carbon source is that of glucose as the carbon source. 1. 28 times [19]. Yang et al. [20] introduced β-ketothiolase derived from Cupria hookworm, reduced nicotinamide adenine dinucleotide phosphate-dependent acetoacetyl CoA reductase, and Pseudomonas 6-19 into Escherichia coli. Polyhydroxyalkanoate synthase mutants derived from Clostridium propionicum and propionyl-CoA transferase derived from Megasphaeria escherichia, and using methods such as error-prone polymerase chain reaction and saturation mutation to increase Clostridium propionicum The substrate specificity of propionyl-CoA transferase derived from Megasphaeria escherichia for lactic acid, enhances the synthesis level of 2-hydroxypropionyl-CoA, and improves the 6-19 polyhydroxyalkanoate synthase derived from Pseudomonas The mutant's substrate specificity for 2-hydroxypropionyl-CoA ultimately enabled the biosynthesis of polyhydroxybutyrate lactate. 6-19 The difference in substrate specificity of polyhydroxyalkanoate synthase mutants derived from Pseudomonas for 2-hydroxypropionyl CoA can change the molar ratio of lactic acid in polyhydroxybutyrate lactate [20]. The genetic background of the host bacteria was further modified to knock out acetate kinase, phosphoenolpyruvate carboxylase and alcohol dehydrogenase, and at the same time replace the promoters of lactate dehydrogenase and acetate synthase to obtain polyhydroxybutyrate. The molar ratio of lactic acid in lactate-producing strains is as high as 70% [21]. The above research mainly focuses on changing the enzymatic properties or modifying the primary metabolic pathway to achieve the biosynthesis of polyhydroxybutyrate lactate, combined with dissolved oxygen control during the culture process and exogenous addition of 3-hydroxybutyric acid or lactic acid to change polyhydroxybutyrate. By adjusting the molar ratio of polymerized units in acid lactate, polyhydroxybutyrate lactate with different compositions and physical and chemical properties can be obtained. However, in large-scale industrial fermenters, the method of adding exogenous polymer units to control the polyhydroxybutyrate lactate component will increase production costs. Different molar ratios of 3-hydroxybutyric acid and lactic acid are synthesized through precise control of the cell's own metabolism., and then obtaining polyhydroxybutyrate lactate with different compositions and physical and chemical properties is the key to obtaining different properties of biosynthetic polymer materials.

Through the control mode of adjusting the concentration of key substances at the level of the respiratory chain, the molar ratio of lactic acid to acetic acid in the glucose metabolism of E. coli can be adjusted. For the entire carbon metabolic flow, the synthesis of key substances requires only an extremely small amount of carbon source. This regulatory model based on the modification of the E. coli respiratory chain can precisely control the synthesis of E. coli metabolites lactic acid and acetic acid. The respiratory chain is an important pathway for cellular energy metabolism and redox regulation. Under aerobic respiration conditions, cells have high energy production efficiency and fast growth, but the accumulation of reducing equivalent nicotinamide adenine dinucleotide in the cell is small; during anaerobic respiration, the intracellular reducing equivalent nicotinamide adenine dinucleotide pool accumulates The reservoir accumulation is large, but the productivity is low and the growth is slow. Although microaerobic culture methods have been successfully used in many bio-based chemical production processes, they require precise control of oxygen concentration levels and have limitations in process scale-up. Coenzyme Q8 is an important electron transfer carrier in the respiratory chain of Escherichia coli. Isopentenyl pyrophosphate and 4-hydroxybenzoic acid are two important substrates for the synthesis of Coenzyme Q8 by Escherichia coli. By introducing geranyl transferase derived from

shikonin, it catalyzes isopentenyl pyrophosphate and 4-hydroxybenzoic acid to synthesize geranyl 4-hydroxybenzoic acid, which has no in vivo electron transfer ability, and competes for the isopentene required for the synthesis of coenzyme Q8. Pyrophosphate and 4-hydroxybenzoic acid[22-23]. The regulation of the intracellular expression level of geranyltransferase derived from shikonin can directly regulate the intracellular trace coenzyme Q8 concentration, thereby regulating the entire carbon metabolism flow distribution of the cell by controlling the level of the cellular respiratory chain [24]. During the aerobic fermentation process, as the concentration of coenzyme Q8 decreases, the activity of the cellular respiratory chain weakens, the ability of E. coli to use glucose to produce lactic acid increases, the accumulation of acetic acid decreases, and the final lactic acid yield reaches the theoretical yield [25-26]. The E. coli control mode can finely regulate the production of monomers (3-hydroxybutyrate CoA and 2-hydroxypropionyl CoA) required for the synthesis of polyhydroxybutyrate lactate within the cell, and obtain different 3-hydroxybutyric acid and lactic acid. The molar ratio of polyhydroxybutyrate lactate. Systematic fermentation experiments were conducted on the constructed metabolic engineering strains, and fermentation conditions (dissolved oxygen, rotation speed, pH, etc.) and fermentation methods (batch, continuous or interval feeding, etc.) were optimized, combined with analysis of transcription levels and intracellular metabolite concentrations. Measurement, metabolic flux analysis, comprehensive enzymatic activity and metabolite change rules, elucidate the dynamic change rules of cellular metabolic network, determine the key factors affecting the synthesis of polyhydroxybutyrate lactate, and break the bottleneck of the synthetic pathway (such as knockout The key enzyme of the competition pathway), and finally constructed an engineering strain that can efficiently synthesize polyhydroxybutyrate lactate containing different molar ratios of 3-hydroxybutyrate and lactic acid.

3 CONSLUSION

Different molar ratios of polyhydroxybutyrate lactate obtained using E. coli control mode have different chemical structures and physical and chemical properties. They can not only be used in the research of war wound repair materials, but also can be used as artificial tissue replacement in the field of military medicine. Paving the way has important military and civilian value.

COMPETING INTERESTS

The authors have no relevant financial or non-financial interests to disclose.

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