SURGICAL SUTURE MATERIALS WITH ANTIMICROBIAL PROPERTIES

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Methods and manufacturing conditions were developed for giving ion-exchange properties to PCA fibres by graft polymerization of methacrylic acid to PCA fibres and styrene to PP fibres followed by sulfurization of the graft polystyrene. Antimicrobial surgical suture materials with fixation of antibiotics on the modified sutures by the ion-exchange mechanism were obtained. It was found that the duration and effectiveness of the antimicrobial action of the sutures are determined by the amount of antibiotic sorbed and the ionic bond strength of the latter with the ion-exchange groups in the sutures. The effect of the conditions of modification and methods of sterilization on the physicochemical properties of the sutures was investigated. Antimicrobial surgical PCA sutures with the gentamycin Caprogent are recommended for use in general clinical practice and are being manufactured.

One of the most effective methods of obtaining antimicrobial surgical suture materials is chemical modification of fibres with drugs [1]. Selection of this method predetermines a number of special requirements which must be considered in working with the initial materials and reagents.

The fibres used must not only be biologically inert and sufficiently strong, but also contain active functional groups which can react with the drugs either directly or after additional modification [2]. In turn, the drugs must not be inactivated as a result of chemical addition itself or under the effect of the modification conditions. In consideration of these requirements, polycaproamide (PCA) and polypropylene (PP) fibres were used for production of antimicrobial suture materials.

In view of the important losses (waste by oxidation) that take place in textile processing of fibres, chemical modification was conducted on finished textile articles. For this purpose, we made PCA and PP twisted surgical sutures with arbitrary numbers from 5/0 to 5 (metric size 1-7).

To give the PCA and PP fibres antimicrobial activity, the drugs were attached to them by the ion-exchange mechanism. We developed methods for preliminary incorporation of cation-exchange groups in the fibres by grafting methacrylic acid (MAA) to the PCA fibres and styrene to PP fibres, followed by sulfonation of the graft polystyrene (PS).

The reaction of grafting MAA to PCA fibre was initiated by peroxide and hydroperoxide groups obtained by mild oxidation with the Fe³⁺—H₂O₂ system. The advantages of this method are the important decrease in the probability of formation of homopolymer and preservation of the physicochemical properties of the fibres.

To incorporate peroxide and hydroperoxide groups in PCA, the fibre was successively treated with a solution of iron chloride in dilute hydrochloric acid and an aqueous solution of hydrogen peroxide. The oxidation process was monitored by the content of active oxygen in the PCA fibre.

It was found that the acid medium causes swelling of PCA so that the number of peroxide and hydroperoxide groups, probably formed due to deeper penetration of the reagents inside the fibre, is increased as a result. However, it is not useful to increase the concentration of the acid above 0.3 M, since hydrolytic decomposition and degradation of PCA are intensified, as the increase in the content of end carboxyl groups in the polymer and the decrease in the strength properties of the fibres indicate.

In studying the conditions of oxidation of PCA fibres, we found that the content of active oxygen in them, responsible for initiation of graft polymerization, increases continuously with an increase in the concentration of iron chloride. However,

TABLE 1. Effect of Graft Copolymerization Conditions on SEC of Modified PCA Fibre and Amount of Graft PMAA

<table>
<thead>
<tr>
<th>Duration of reaction, min</th>
<th>SEC, mmole/g, at different temperatures (°C)</th>
<th>Amount of PMAA in fibre, %, at different temperatures (°C)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>50</td>
<td>60</td>
</tr>
<tr>
<td>30</td>
<td>0.8</td>
<td>2.8</td>
</tr>
<tr>
<td>60</td>
<td>2.4</td>
<td>3.4</td>
</tr>
<tr>
<td>120</td>
<td>2.7</td>
<td>3.6</td>
</tr>
<tr>
<td>180</td>
<td>2.9</td>
<td>3.8</td>
</tr>
<tr>
<td>240</td>
<td>3.0</td>
<td>4.0</td>
</tr>
</tbody>
</table>

at a concentration of iron chloride greater than 5%, iron oxide hydrate forms intensively, so that its content is restricted by this value. Correspondingly, 60°C and 20 min were set as the optimum temperature and duration of the process, since increasing these parameters did not significantly increase the amount of peroxide and hydroperoxide groups in PCA. As for the effect of hydrogen peroxide on oxidation of PCA fibres, increasing its concentration above 10% and the treatment temperature above 40°C actually does not affect the active oxygen content in PCA. In these conditions, the reaction practically ends after 10 min. The active oxygen content in these conditions reaches 6.4·10⁻³ mg/g.

After carefully washing, MAA was grafted to the fibres treated in this way, conducting the reaction in 5-10% aqueous solutions of this monomer with pH of 4.0-4.2 in the presence of a promoter — divalent iron ions.

As indicated in [3], decomposition of hydroperoxide groups that initiate the graft polymerization reaction begins at 40°C. However, the rate of decomposition at this temperature is relatively low, since graft copolymerization of vinyl monomers almost does not take place. In this respect, it was interesting to determine the effect of the temperature and duration of the reaction on the static exchange capacity (SEC) of modified PCA fibre and the amount of graft PMAA. For this purpose, graft copolymerization was conducted in the 50-80°C temperature range for 0.5-4.0 h and with a batch ratio (BR) of 30.

The results obtained indicate (Table 1) that grafting of MA takes place most intensively in the first 30-60 min. A further increase in the duration of the reaction at 70 and 80°C does not significantly alter the amount of graft polymer, while at 50 and 60°C, the yield of graft copolymer also increases after treatment for 4 h. This is probably because intensive decomposition of the hydroperoxide groups in PCA begins at 70-80°C.

To determine the optimum conditions for graft polymerization that ensure the maximum strength of PCA surgical sutures, mathematical experimental design with processing of the data by regression analysis was used.

The following independent variables were included in the experimental program: \( X_1 \) — concentration of monomer in the solution, %; \( X_2 \) — concentration of promoter (Mohr’s salt), %; \( X_3 \) — reaction temperature, °C.

The output parameters were: \( Y' \) — SEC, mmole/g; \( Y'' \) — relative unit breaking load, cN/tex.

After estimating the significance of the regression coefficients with Student’s criterion, the regression equations were:

\[
Y' = 2.4075 + 0.48 X_1 + 0.109 X_2 - 0.0423 X_3
\]

\[
Y'' = 17.7125 - 1.0875 X_1 + 0.9125 X_2 + 0.1875 X_3
\]

These equations are linear, so that they can be optimized with the simplex method of searching for the extremum. Since it is necessary to find the optimum for two mutually contradictory functions in this case, one of them was used as restricting, and optimization was performed with the other using a standard program.

The optimum for function \( Y' \) is found in restriction of function \( Y'' \) by the value of 19.8 cN/tex, which corresponds to the unit relative breaking load of the initial PCA fibre of 65%. The values of the factors in the optimum regime were: \( X_1 = 5.3\%; X_2 = 2.5\%; X_3 = 70°C \).

The optimum value for function \( Y'' \) was found by restricting function \( Y' \) by the value of 3.0 mmole/g. The natural values of the factors in the optimum conditions are: \( X_1 = 10\%; X_2 = 2.5\%; X_3 = 66°C \).

PCA fibres were processed in each of the proposed regimes. It follows from Table 2 that the fibres modified in restricted function \( Y' \) had a SEC 25% higher than the calculated SEC, and strength that approached the mathematically expected strength, while in the second case, at SEC close to the calculated SEC, the strength loss is greater than 50% of the initial value, which is unacceptable in using such fibres as suture material.