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ANTI-ADHESIVE COMPOSITE BARRIER FILMS BASED ON POLYSACCHARIDES AND EVALUATION OF THEIR EFFECTIVENESS ON THE MODEL OF ALKALINE NECROSIS

The formation of postoperative adhesions is a serious clinical problem for the present-day cardiac and general surgery. It is characterized by a pronounced abnormal tissue growth caused by the proliferation of fibrous tissues that stick to the nearby normal organs, thus impairing their function and potentially leading to severe clinical complications [1].

A large variety of methods have been conducted aiming at the alleviation of surgery associated complications. For the past 30 years, biocompatible and biodegradable polymers have attracted wide attention in treating postoperative adhesions as promising physical barriers among tissues [2].

As anti-adhesion material, carboxymethyl cellulose (CMC) possesses outstanding characteristics, including good biocompatibility, high thermal stability, and good affinity with body tissue, for which reason CMC-based material can act as a local barrier. Alginate dressings in the dry form absorb wound fluid to re-gel, and the films then can supply water to a dry wound, maintaining a physiologically moist microenvironment and minimizing bacterial infection at the wound site. Alginate is selectively ionically crosslinked with calcium ions to maximize its performance as a barrier.

In this work, three kinds of polymer films based on the natural polysaccharides blends were prepared to study their antiadhesive properties.

Prior the surgery, fourteen rats were randomly divided into five groups (n=8 in each): the sham group, the control group without any treatment, and three experimental groups treated with polysaccharide-based film I, II, and III, respectively. Then all the rats were anesthetized by intraperitoneal injection of 300

mg/kg of Chloral hydrate and 1 mg/kg of Xylazine. After shaving and sanitizing, a 3-cm long median laparotomy was performed. In the sham group animals underwent only laparotomy without any injury and/or suturing. In the other experimental groups, the cecum was delivered and the cecum wall was injured by 1 minute application of a cotton pad soaked in 1 N sodium hydroxide solution. Then the cecum was thoroughly washed with saline water. In the experimental groups, the investigated anti-adhesive films were trimmed into pieces 2×2 cm and then applied in-between the abdominal wall and the injured cecum. The cecum was put back into the abdominal cavity and fixed to the abdominal wall. The abdomen was closed using two-layer closure technique. To prevent infections 50 mg/kg Tylosin was injected intraperitoneally once daily for 5 days after the surgery. Until the rats were euthanized, they were observed every day and the postoperative wound was cleaned with ethanol, if necessary.

At day 14 after surgery, the animals were euthanized with lethal doses of Chloral hydrate. The abdominal cavity was opened via a U-shaped incision and examined macroscopically by a surgeon, who was blinded with respect to the animals. Adhesion formation was evaluated macroscopically according to the adhesion rating scale from 0 to 5 [3]. Grade 0: no adhesions; grade 1: loose filmy adhesions separating by blunt dissection; grade 2: adhesions requiring <50% of sharp dissection for separation; grade 3: adhesions requiring >50% of sharp dissection for separation; grade 4: serosal injury, grade 5: full-thickness injury.

In the sham group (without prior adhesion-induced operation), six animals had no adhesions, while the other two had grade 2 adhesions. Severe grade of adhesion for the control group was 4.4. The animals treated with implanted film I had severe grade 1.6 adhesions. In the group treated by film II, the severe adhesion grade was 1.21, while in the third treated group the adhesion grade was 1.20. The overall significantly lower severity grade in the groups, where the polysaccharide-based films under study were applied, indicates the effectiveness of the chosen approach and materials for reducing the formation of tissue adhesion.

The results obtained demonstrated that the novel polysaccharide-based films were effective in reducing the formation of tissue adhesion. A correlation between the tendency to slow down biodegradation in vitro and the effectiveness of films in vivo was also established. With an increase in the concentration of sodium alginate in the test samples, the level of adhesion formation in animals decreased [4].

All experiments were carried out in compliance with the recommendations of the European Convention on Humane Treatment of Laboratory Animals [5].

References

1. Postsurgical intrapericardial adhesions: Mechanisms of formation and prevention. Vol. 95 / A. Cannata [et al.]. – Elsevier, 2013.
2. Polymer materials for prevention of postoperative adhesion / J. Li [et al.] // Acta Biomater. – 2017. – Vol. 61 – P. 21-40.
3. Oncel, M. et al. Comparison of a novel liquid (Adcon-P®) and a sodium hyaluronate and carboxymethylcellulose membrane (SeprafilmTM) in postsurgical adhesion formation in a murine model. Dis. Colon Rectum 46, 187–191 (2003).
4. Kanunnikava, A. The prevention of postoperative peritoneal adhesions in a rat model by the novel anti-adhesion polysaccharide-based films / A. Kanunnikava, V. Gureev, A. Nesterov, E. Patrakhanov, V. Pokrovsky, V. Tilikin. // Open Readings 2020 63nd International Conference for Students of Physics and Natural Sciences, Vilnius, Lithuania, P. 544
5. European Convention for the protection of vertebrate animals used for experimental and other scientific purposes. Strasbourg: Europ. Treaty Series, 1986. № 123. P. 48.