

## POSTER PRESENTATIONS

### OPTIMIZATION OF POLYLACTIDE MICROSPHERE COMPOSITION FOR CONTROLLED PROLONGED RELEASE OF BETAMETHASONE ACETATE

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Rheumatoid arthritis (RA) is one of the most common autoimmune diseases, characterized by chronic inflammation, pain syndrome and destruction of cartilage and bone tissue of synovial joints, which leads to a decrease in the quality of life of patients and a high risk of disability. At the same time, the need for lifelong systemic administration of high doses of glucocorticoids acts as a serious limitation that reduces the effectiveness of RA therapy [1]. An effective solution is the development of injectable depot forms based on polylactide (PLGA) microspheres that provide local prolonged action of glucocorticoids. Thus, in our previous work [2], we obtained PLGA microspheres with betamethasone acetate (BA) with a size of  $53 \pm 13$   $\mu\text{m}$  and a BA loading of about 4%.

The aim of this study is to optimize the composition of PLGA microspheres to increase BA loading and control the release rate.

The solid-in-oil-in-water (S/O/W) multiple emulsion method and the oil-in-water (O/W) emulsification method with the addition of benzyl alcohol (BA) were used to increase BA loading. The concentration of BA in the organic phase was increased from 30 to 50 mg/mL. Microspheres were prepared based on PLGA (75:25, 42 kDa, carboxyl end groups, Novokhim LLC, Tomsk). As a result, both approaches allowed increasing BA loading from 4% to 30%. At the same time, in the case of the S/O/W method, the microsphere size increased from  $53 \pm 13$   $\mu\text{m}$  to  $85 \pm 16$   $\mu\text{m}$ , whereas in the case of the O/W method with the addition of benzyl alcohol, the microsphere size did not change.

In addition, the effect of polymer composition (molecular weight 42 and 58 kDa, L/G ratio 50/50 and 75/25, end group COOH and COOR) on microsphere characteristics and the release rate of BA was investigated. All obtained microspheres had a size of 57–65  $\mu\text{m}$  and a BA loading of 25 to 32%. It was noted that an increase in PLGA molecular weight from 42 to 58 kDa and the replacement of the COOH group with the COOR ester group led to a decrease in the BA release rate: the difference in release reached 44% (56% vs 12%) by day 65. However, the most uniform BA release rate was achieved from microspheres with the following composition: 58 kDa, L/G 75/25, -COOH group. Over 60 days, about 50% of BA was released.

Thus, the optimized PLGA microsphere composition (58 kDa, L/G 75/25, -COOH group) with a BA loading of 30% and a size of  $59 \pm 19$   $\mu\text{m}$  allowed controlled release of BA over 60 days. The obtained microspheres may open up the possibility for the development of a prototype long-acting form.

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#### References:

1. Singh H, Dan A, et al // Biomaterials. 2023. Vol. 303. P. 122390.
2. Ulianova Y.V. et al // Industrial laboratory. Diagnostics of materials. 2025. V. 91. № 9. P. 19-27.