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Preparation and characterization of alginate/hyaluronate hydrogel incorporating zoledronic acid-loaded chitosan/alginate microparticles for osteoarthritis therapy

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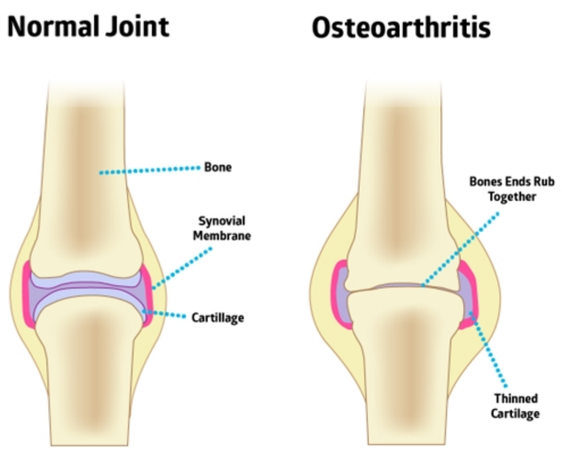
INTRODUCTION & AIM

OSTEOARTHRITIS is a joint disease characterized by cellular stress and degradation of the extracellular matrix. These processes are initiated by macro- or micro-injuries that trigger abnormal adaptive repair responses, including the activation of pro-inflammatory immune pathways [1].

A key factor in joint functionality loss is the impaired synthesis of synovial fluid components, leading to a reduction in its viscoelastic properties.

However, current standard therapies primarily focus on symptom management. Therefore, the aim of our work is to develop an injectable hydrogel system capable of restoring the viscoelastic properties of synovial fluid and preventing the development of joint tissue inflammation.



METHOD

Materials

- Sodium alginate (SA);
- Sodium hyaluronate(SH);
- Chitosan (Cs);
- Crosslinking agent (CA) – $CaSO_4$;
- Crosslinking inhibitor (CI).

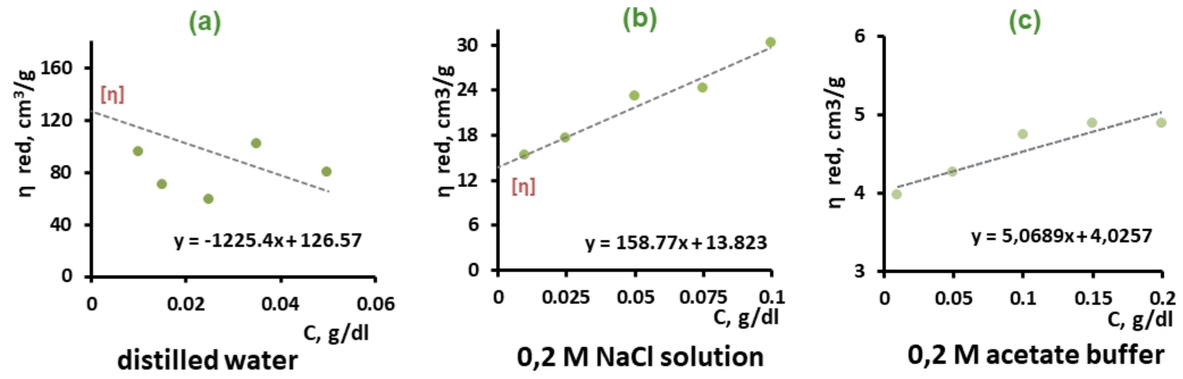
Methods

- Capillary viscometry;
- Dynamic vibroviscometry;
- *In vitro* cytotoxicity studies of samples;
- FTIR;
- SEM.

RESULTS & DISCUSSION

Characterization of the initial components (molecular weight)

Dependence of η_{red} on the concentration of SA (a), SH (b) and Cs (c):



K = 1,99·10⁻⁴ ml/g α = 0,96 M_w = 692,6 kDa	K = 1,23·10⁻⁴ ml/g α = 0,82 M_w = 1832,1 kDa	K = 1,38·10⁻⁴ ml/g α = 0,85 M_w = 179,1 kDa

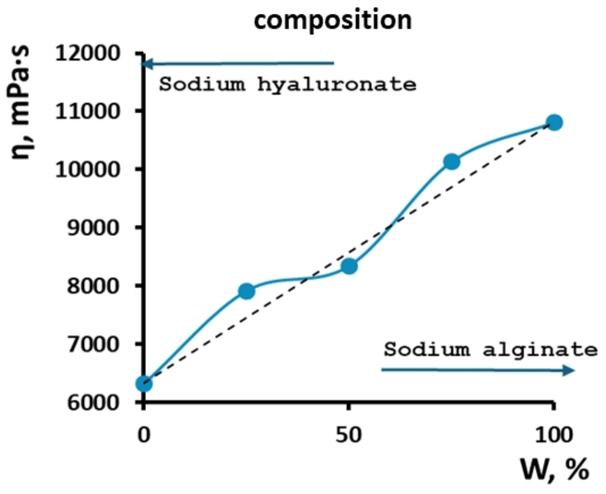
Concentration dependences

Dependence of polymer viscosity on concentration

	η, mPa·c	
C, %	HA	SA
0,5	71,8	45,7
1	471,3	140,1
2	2084,7	782,3
3	6331,8	3374,2

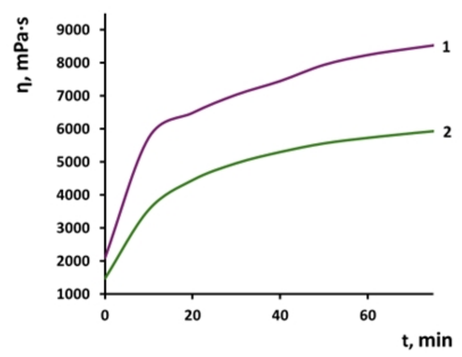
A composition with an SA/HA ratio of 75/25 was selected for 5% SA and 3% HA, respectively

Dependence of the η of an aqueous solution on the volume fraction of SA in the SA/HA composition

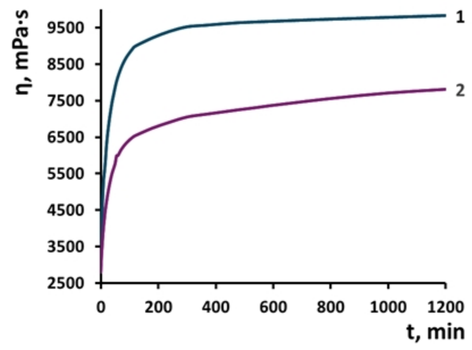


Kinetics of ionic crosslinking of SA solution

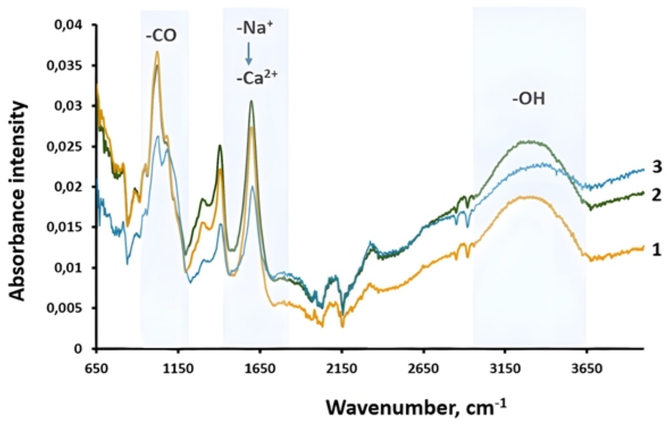
Comparison of the cross-linking kinetics of the SA solution (1) and the SA/HA system in a 75/25 ratio (2)



Comparison of the cross-linking kinetics of the SA/HA 75/25 system without inhibitor (1) and with inhibitor (2)

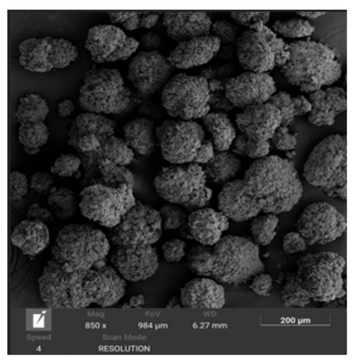


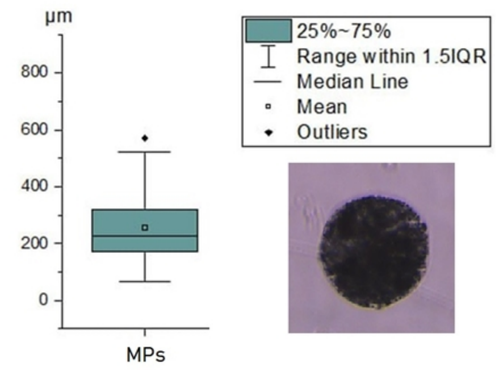
FTIR



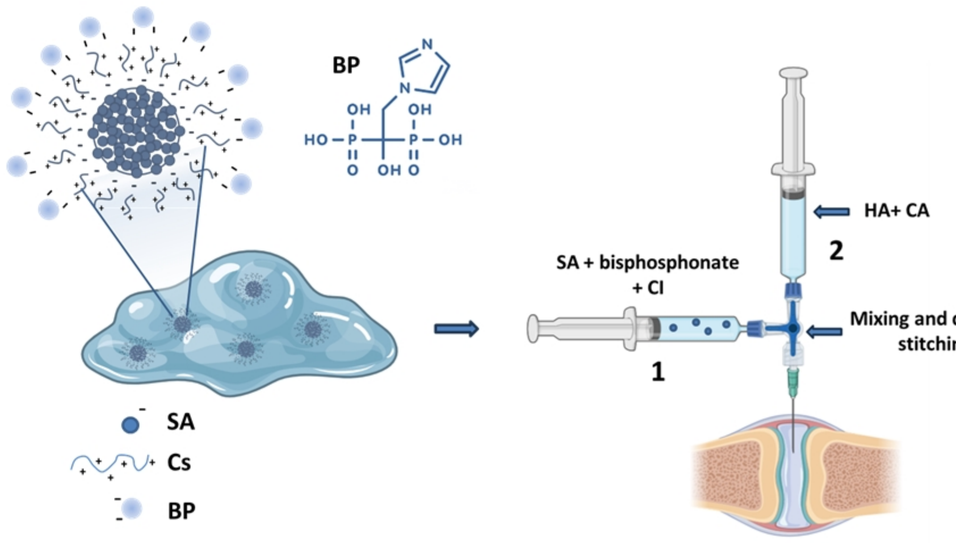
1 SA/HA 75/25
2 SA/HA - CaSO4
3 SA/HA - CaSO4 - CI

Alginate/chitosan MPs obtained by emulsification





Conceptualization of current research



CONCLUSION

The data obtained indicate the prospects of the developed hydrogel system with microparticles, but later another biologically active substance was chosen, therefore, further testing of the system with other bisphosphonates is planned.

REFERENCES

1. Allen, K.D.; Thoma, L.M.; Golightly, Y.M. Epidemiology of Osteoarthritis. *Osteoarthr. Cartil.* **2022**, *30*, 184–195. https://doi.org/10.1016/j.joca.2021.04.020