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## The Effect of Chemical Composition on Crosslinking Kinetics of Methylcellulose/Agarose Hydrogel

Beata Niemczyk, Paweł Sajkiewicz, Arkadiusz Gradys

Laboratory of Polymers and Biomaterials, Institute of Fundamental Technological Research,  
Polish Academy of Sciences,  
Pawińskiego 5b St., 02-106 Warsaw, Poland  
[bniemczyk21@gmail.com](mailto:bniemczyk21@gmail.com)

### INTRODUCTION

Currently, injectable thermosensitive in-situ gelling hydrogels are investigated as polymeric scaffolds directed toward tissue engineering applications. Their attractiveness is connected with minimally invasive effect of injection to body, solidification within injured tissue providing complete filling of the lesion and effective delivery of therapeutics [1].

Methylcellulose (MC) and rather unique methylcellulose/agarose (MC/AGAR) systems were investigated. The aim of this study was to investigate the kinetics of cross-linking, and mechanical properties of MC and MC/AGAR systems in order to find optimal conditions for tissue engineering applications.

### EXPERIMENTAL METHODS

Methylcellulose METHOCEL A15LV (Sigma Aldrich) was obtained in various concentrations (3; 5; 7 % (w/v)) in demineralized water [2]. The MC aqueous solution was mixed in 1:1 w/w ratio with agarose SEAPREP (Lonza) aqueous solution (1,5%(w/v)) [3, 4].

The cross-linking kinetics of MC and MC/AGAR aqueous solutions were carried out by dynamic mechanical analysis (DMA), using Anton Paar Physica MCR301 rheometer. The oscillatory analysis was performed utilizing small-amplitude sinusoidal deformation. In the temperature range 33-39°C, under isothermal conditions, time dependence of the storage modulus,  $G'$ , the viscous modulus,  $G''$ , and complex viscosity were determined. Observing, that there is no intersection of  $G'$  and  $G''$  curves, the kinetics of cross-linking was deduced from the time derivative of the  $G'$ , providing, as parameters of cross-linking, the time position and the height of the maximum of the time derivative of  $G'$ . Approximation and extrapolation beyond the registered time range with asymmetric double sigmoidal function as well as integration, allowed estimation of the final modulus and complex viscosity of hydrogels, which is crucial from the practical perspective.

Additionally, thermal effects of cross-linking were studied by differential scanning calorimetry (DSC). Measurements were carried out using Pyris 1 DSC (Perkin Elmer). To avoid water evaporation, hermetic pans were used.

### RESULTS AND DISCUSSION

DMA studies revealed that addition of agarose, generally, improves mechanical properties of methylcellulose, what agrees with the data reported in [3].

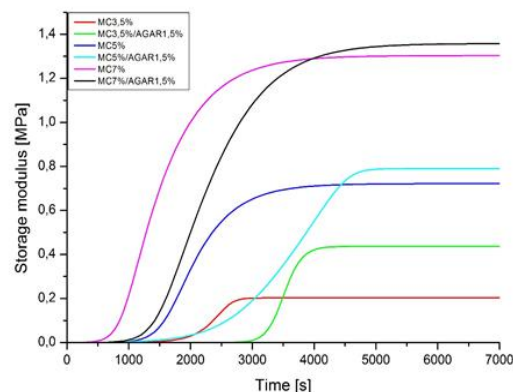


Fig. 1. Storage modulus vs. time for various concentrations of MC and MC/AGAR aqueous solutions at 37°C.

However, as oppositely to [3], it also considerably increases the time of cross-linking, what may be explained as due to the presence of long agarose molecules, which act as steric barriers on the way of methylcellulose crosslinking. As reported in [3], addition of agarose accelerates dehydration of methylcellulose, thereby improves hydrophobic interactions between MC chains. As shown in the Fig 1, the higher the concentration of MC and MC/AGAR, both  $G'$  increases and cross-linking accelerates.

### CONCLUSION

Addition of agarose considerably extends the cross-linking time and improves mechanical properties of methylcellulose hydrogel, making this approach attractive for soft tissue engineering applications as injectable hydrogels.

### REFERENCES

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