

Esterification of Dextrine by the N-derivatives of Glutamic Acid Using Steglich Reaction

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Abstract – Was investigated the esterification of dextrin using Steglich reaction. Such modification allows obtaining a functional product with an extensive structure of macromolecules, capable to form self-stabilized dispersions in an aqueous environment. To ensure the branching, the modification was performed using the functional agents – N-derivatives of glutamic acid. The substitute in the N-position provides the introduction of the required function.

Keywords – dextrin, glutamic acid, cross-link, Steglich esterification, modification of polysaccharides.

I. Introduction

A number of natural properties of the polysaccharides do not allow their direct use for medical and biomedical purposes.

To create biomaterials based on them they need to be modified. Very often modification is made by controlled cross-linking of the polysaccharides macromolecules [1]. But, despite the modification, should not forget the advantages of this natural polymer. The materials, obtained by the modification, should stay polysaccharides and preserve the property of being tolerant to the human body.

Steglich reaction takes place in mild conditions, and the obtained polyester, as shown by the relevant studies, is non-toxic, depyrogenized and biodegradable material. It is also important fact that the products of decomposition of the polymer in the live organism are also non-toxic. [2, 3]

In light of this, the considerable interest represents the modification of polysaccharides by N-derived of dicarboxylic acid using Steglich reaction to produce polymer materials for medical and biomedical purposes.

II. Dextrine modification

In general, the interactions between the hydroxyl group of dextrin and carbonyl group of 2-(stearoylamino) pentane dicarboxylic acid (Glu(St)) can display the Fig. 2.

The degree of substitution of hydroxyl groups determined by the efficiency (selectivity) of the reaction and by the ratio between the reagents. Because the Glu(St) is a dicarboxylic acid, it is possible the cross-linking reaction between dextrin macromolecules, under conditions of sufficient process efficiency, in any ratio of the reagents. This process is reflected on the Fig. 3.

With moderate increase of quantities of cross-links will be formed modified dextrin with significantly increase of

molecular weight and a dendrite structure of macromolecules. The modified product, with the dendrite structure of macromolecules, should not lose solubility in water and, by introducing the residues of Glu(St) and the formation of ester group must obtain the ability to dissolve in some organic solvents, particularly in methanol.

On the other side, the formation of a significant amount of cross-links between the macromolecules of dextrin should lead to the formation of spatial net. The modified dextrin, which macromolecules formed cross-linked spatial nets, loses its ability to dissolve in solvents, including water, and it can only restricted swell. Furthermore, if to the process of creating a three-dimensional net will be involved a critical amount of macromolecules of dextrin it will lead to the gel formation, which, observed with a rapid increase of the viscosity of the environment.

Confirmation, that in the investigated system observed the progress of described above processes, can be seen on Fig. 1, which shows the change of viscosity of the reaction mixture during the process at the ratio of carboxyl groups of Glu (St) to the hydroxyl groups of dextrin as 1 to 1. As it can be seen from the curve, the viscosity of the mixture increases during the whole process of the reaction and when the process reach a certain conversion, occurs its rapid magnification and the reaction environment transformed into the gel. The processes of structuring passes during all the time of the reaction, and when it reached a certain molecular weight, at the point of percolation, it begins a mass interaction between the cross-linked macromolecules, leading to the formation of the gel. Chemical processes of structuring also occur and after percolation point.

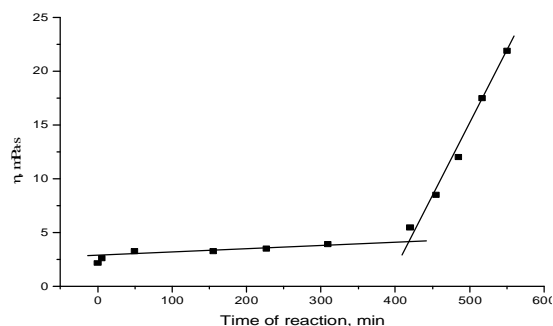


Fig 1. The change of viscosity over time.

Time of the percolation point achievement depends from the ratio of the reagents and from the conversion. The percolation point is observed at 6,5 ÷ 7,5 hour after beginning of the process, which corresponds to approximately 80 ÷ 90 % conversion.

Conducted research showed that the ratio, provided to the achieving of the 92÷95% conversion, is the determining factor for obtaining modified products of the different molecular weight and composition.

The investigation of the structure and composition of significantly structured product, that was obtained after percolation point, is complicated by the loss of its solubility. Therefore, within this work, conducted studies

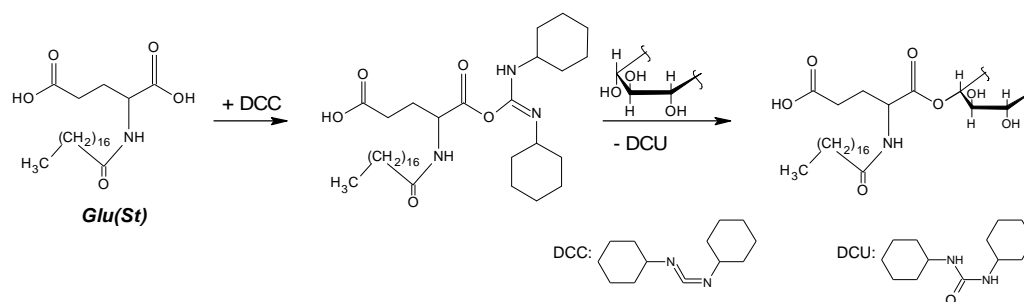


Fig. 2. Schematic image of the interaction between Glu(St) and dextrin by the Steglich reaction.

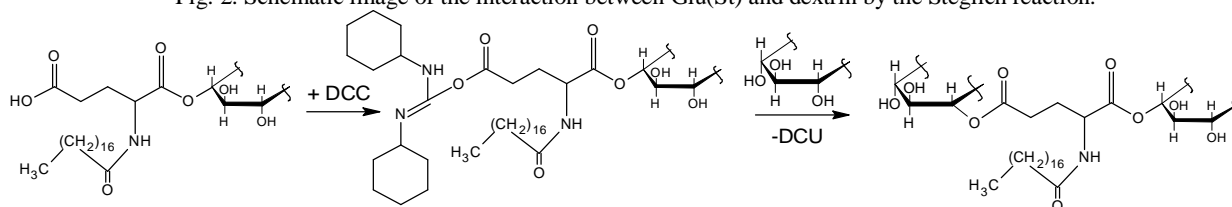


Fig. 3. Cross-linking of the dextrin macromolecules.

of modified dextrin, that formed before percolation point was reached, but under the condition of high conversion.

According to the methodology of the research, the resulting product was separated by extraction of samples with methanol and distinguished the product soluble in methanol and insoluble in it. Several additional observations such as swelling of methanol separated products in a variety of solvents showed that the fraction that soluble in methanol endlessly swells in DMF and product that insoluble in methanol has a limited swelling in some solvents. We can conclude that in the methanol dissolved the modified and heavily branched product, and insoluble in methanol fraction is a cross-linked product that during modifications forms the spatial net.

Fig. 4 shows the NMR spectrum of methanol soluble fraction of the product with referring of basic signals. This spectrum confirms the reaction of grafting Glu (St) to dextrin macromolecules.

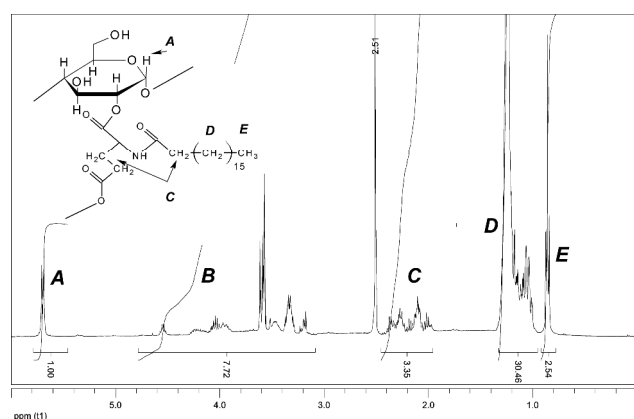


Fig. 4. NMR spectrum of the dextrin esterification product.

The resulting products were tested for the ability to form in water environments polymer dispersions. These studies have shown that modified dextrin with a dendrite structure of macromolecule formed in an aqueous environment, a self-stabilized dispersion with particles of nanometric size.

Conclusions

As a result of conducted studies was found that modification of the dextrin, by N-derivatives of the glutamic acid using the Steglich reaction, proceeds with high efficiency and provide the substitution of 50 to 75% of the hydroxyl groups from possible, at a given proportion of reagents. As a result of the modification it is formed the products with branched and cross-linked structure of macromolecules. These products can be separated and the ratio between them determined by the ratio of reagents at the stage of synthesis. The practical interest represents the product with branched structure of macromolecules, as it is able to form the self-stabilized aqueous dispersion, stable in time, with nano- and micro-metric size of the particles.

References

- [1] K. Ganguly, "Polysaccharide-based micro/nanohydrogels for delivering macromolecular therapeutics," *Journal of Controlled Release*, vol. 193, pp.162-173, Nov. 2014.
- [2] M. I. Nagornyak, "Reactivity of hydroxyl groups of sucrose in the Steglich reaction," *Visnyk of NU"LP"*, vol. 69, pp.812-818, Sep. 2015.
- [3] S. M. Varvarenko, "Synthesis and colloidal properties of polyesters based on glutamic acids and glycols of different nature," *Chemistry and Chemical Technology*, vol. 7, pp.164-171, 2013.