

OPTIMIZATION OF THE PRODUCTION OF SODIUM ALGINATE DERIVATIVES

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Abstract: A natural polysaccharide sodium alginate, a salt of alginic acid, is widely used as a wetting and thickening agent in food, pharmaceuticals, cosmetics and other fields. Interest in the practical use of the derivatives of sodium alginate poses the problem of their convenient and cost-effective production.

Two methods applied for the synthesis of uronic acids from sodium alginate were studied. The previously created method of Prof. A. Mirshafiey (Mirshafiey & Lalander, 2024) has been tested in the laboratory. The method is based on the hydrolysis of sodium alginate with sulfuric acid followed by the separation of D-mannuronic acid (MA) and L-guluronic acid (GA), that included pH regulation and precipitation by centrifugation and quite long-time drying process. However, the method is rather complex, time-consuming and energy-intensive. To simplify and reduce the cost of uronic acids production, it was necessary to optimize the technology. Optimized in the laboratory method kept the previous step of sodium alginate hydrolysis unchanged. Further, the method differed in that the MA and GA mixture was precipitated, washed and filtered on membrane filter without prior separation. The obtained MA + GA gel composition may be used without drying in the creation of new innovative products for human health. The optimization of the method has greatly simplified the synthesis of sodium alginate derivatives and makes it possible to increase the economic efficiency of the process.

Key words: mannuronic acid, guluronic acid, production cost-effectiveness

Introduction

Alginic acid, a widely used natural polysaccharide, is generally derived from brown seaweed. It can also be produced by microbial fermentation using specialized bacteria (Goh et al., 2012). Alginic acid naturally exists in cytoplasm and plays an important role in strengthening the cell wall (Kloareg & Quatrano, 1988).

Alginic acid is a linear polysaccharide consisting of two forms of linked hexuronic acid residues D-mannuronic acid (MA) and L-guluronic acid (GA), Fig. 1.

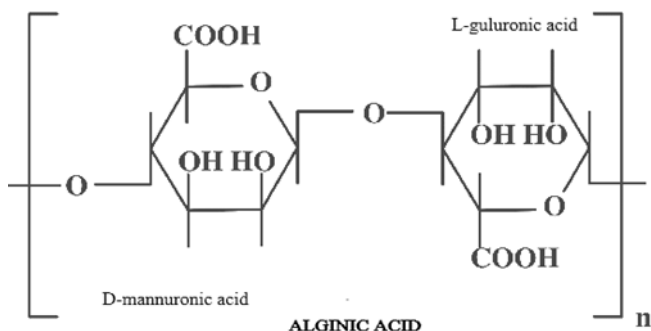


Figure 1. Structural formula of alginic acid.

One of the alginic acid forms in cells is sodium alginate, the extract of which is obtained from brown algae. Sodium alginate is a light powder, forming a highly viscous aqueous solution, which has the characteristics of thickening, suspending, emulsifying, stabilizing, forming a gel, forming a film and spinning fibres, and has a long and extensive use in the food, paper and cosmetic industries (Guo et al., 2020). Modern pharmacological studies have shown that alginic acid has antianaphylaxis effect (Jeong et al., 2006), immunomodulatory activities (Caipang et al., 2011; Fattahi, et al., 2015), antioxidant activities (Sarithakumari et al., 2013), and anti-inflammatory effects (Mirshafiey et al., 2007; Sarithakumari & Kurup, 2013). Alginate is a biocompatible and biodegradable natural product. Mannuronic and guluronic acids, as alginate hydrolysate components, are safe and non-toxic ingredients (Sharfi et al., 2024).

The biological activities of alginic acid and its derivatives are of interest for its practical production and further application. Technology for uronic acids production may have some problems including labor-intensive and unhealthy of the process as well as low productivity. Therefore, it is necessary to modify this product, considering the reduction in production costs. In other words, the technological process needs optimization to make it more efficient, productive and cost-effective. Streamlining activities provides improvement of process efficiency, ensures time, resources and financial savings (Miyambu & Seeletse, 2016). Process upgrades will improve technology and keep costs down.

To produce uronic acids from sodium alginate the original method (Mirshafiey & Lalander, 2024) was tested in the laboratory. It was established that the important indicators of the process – duration of the procedure and the cost of the final product – need to be corrected.

The purpose of the present study was to optimize the previously created method for the production of uronic acids and aimed at improving of the technology effectiveness and cost minimization.

Material and methods

Chemicals

1. Sodium alginate Type NA4012 (C. E. Roeper, German).
2. Sulfuric acid 95 % solution pure p. a. H₂SO₄ (Chempur, Poland).
3. Sodium carbonate, Na₂CO₃ (Chempur, Poland).
4. Hydrochloric acid, 35 % HCl (Chempur, Poland).

Previously created method of sodium alginate derivatives production

The method of Prof. A. Mirshafiey (Mirshafiey & Lalander, 2024) was tested in the laboratory. To produce MA and GA according to this method the following technological steps were used. Hydrolysis of sodium alginate with 20 % H₂SO₄ at 85–90 °C during 3–4 h. Hydrolysate (mixture of MA and GA) was produced. Separation of the mixture of uronic acids. This step includes precipitation, centrifugation (4000 g), following re-dissolution by neutralization (using 1M Na₂CO₃). After pH regulation till 2.99 and next centrifugation (4000 g), the collected precipitate of L-GA washed with distilled water and spread over a smooth surface following long-term drying at room temperature. The supernatant of GA was adjusted to pH 1.0 by 0.5 M HCl, and MA precipitated by centrifugation (4000 g). The final precipitate (D-MA) washed with distilled water, also spread over the smooth surface, and dried out for 5–6 h. Separated uronic acids GA and MA can be mixed and used as a final product.

Optimized method of sodium alginate derivatives production

The described above method of alginate - based synthesis of MA and GA was updated in the laboratory. The process of sodium alginate hydrolysis remained unchanged. However, the next step of the procedure was significantly optimized. The produced hydrolysate of sodium alginate (as precipitated MA + GA mixture) was filtrated on membrane filter without prior separation of uronic acids. The received uronic acid mixture washed with distilled water and filtered again. The obtained final gel product of MA + GA composition is a result of technological process optimization and may be used without drying.

Results and discussion

The laboratory study showed that the previously created method of sodium alginate derivatives (MA and GA) production is rather complex, time-consuming and energy-intensive (Mirshafiey & Lalander, 2024). The activity of these two uronic acids was assessed separately. Having compared the biological effects of MA and GA, only non-essential differences between them were established (Fattahi, et al., 2015). At the same time, MA was the main necessary product, while GA almost was not used (Sharfi et al., 2024). This suggested the possibility of practical use of a mixture of MA and GA without prior separation. This final composition is used for gel production.

Comparison of two represented methods procedures is offered in Table 1. When using the previously created method, the yield of the product was 53.8 ± 3.1 %, while the optimization of the procedure made it possible to raise this parameter by 21.9 %. Besides it should be noted that the reduction of technological process duration by 5 h is due to the omission of uronic acids separation step. In addition, there was observed a decrease in the consumption of components and the formation of waste requiring special disposal. Thus, it is obvious that the optimized method is simpler and cheaper.

Table 1. Manipulation algorithm for preparing a mixture of mannuronic and guluronic acids in two ways.

| Steps of technological procedure | |
|---|--|
| Previously created method | Optimized method |
| Weighing and loading the sodium alginate into the reactor | Weighing and loading the sodium alginate into the reactor |
| Addition of 20 % H ₂ SO ₄ | Addition of 20 % H ₂ SO ₄ (reduced acid volume by 50 %) |
| Precipitation of mannuronic and guluronic acids mixture | Precipitation of mannuronic and guluronic acids mixture (final product) ready for gel production |
| Dissolution of precipitate in alkaline solution (1M Na ₂ CO ₃) | Was not carried out |
| Separation of guluronic acids precipitate | Was not carried out |
| Washing the received precipitate twice and centrifugation | Washing the received precipitate of mannuronic and guluronic mixture and filtration |
| Drying of guluronic acid precipitate | Was not carried out |
| Precipitation of mannuronic acid | Was not carried out |
| Separation of mannuronic acid, twice washing and centrifugation | Was not carried out |
| Drying of mannuronic acid precipitate, mixing of both uronic acids (final product) | Gel composition of mannuronic and guluronic does not require drying (final product) |
| Final product yield in g per 100 g of initial sodium alginate 53.8 % | Final product yield in g per 100 g of initial sodium alginate 65.6 % |

The Table 1 demonstrates the technological advantages of the optimized method. The final product (MA + GA composition) obtained by the improved procedure is a result of technological process parameters correction and does not require pre-drying before subsequent use.

The comparison of two final products – separated, dried and mixed MA + GA and optimized gel composition of MA + GA revealed the advantage of the last one. It has convenient consistency and improved consumer properties for further using. The comparative cost and economic efficiency of the studied methods for obtaining sodium alginate derivatives are presented in Table 2.

Table 2. Consumption and cost of source materials expended per 100 g of dry matter of uronic acids

| Materials | Previously created method | | Optimized method | |
|--------------------------------------|---------------------------|---------------|---------------------|---------------------|
| | per 100 g | Eur per 100 g | per 100 g | Eur per 100 g |
| Sulfuric acid, conc., g | 349.3 | 2.20 | 142.5 | 0.90 |
| Sodium carbonate, g | 157.6 | 0.68 | 129.3 | 0.55 |
| Hydrochloric acid, conc., ml | 25 | 0.15 | Was not carried out | Was not carried out |
| pH calibration standard solution, ml | 80 | 1.50 | Was not carried out | Was not carried out |
| Sodium alginate, g | 185.8 | 4.19 | 158.7 | 3.57 |
| | | Total: 8.72 | | Total: 5.02 |

The ratio of the cost of raw materials to the cost of 100 g of the final product is 2.08 and 1.41 for the old and new methods, respectively. This allows us to conclude that the cost effectiveness of the modified technology is 32.3 % higher than for the previously developed version of production. In other words, the cost of producing the same amount of final product using the modified method will be one-third lower.

Conclusion

The optimization of the technology for the synthesis of sodium alginate derivatives makes it possible to increase the economic efficiency of the process and significantly reduce the cost of final product. The gel composition of manuronic and guluronic acids obtained in this way is safe and may be used in the creation of new innovative products for human health.

References

- Caipang, C. M. A., Lazado, C. C., Berg, I., Brinchmann, M. F., Kiron, V. 2011. Influence of alginic acid and fucoidan on the immune responses of head kidney leukocytes in cod. *Fish physiology and biochemistry*, 37, 603–612.
- Fattahi, M. J., Abdollahi, M., Agha Mohammadi, A., Rastkari, N., Khorasani, R., Ahmadi, H., et al. 2015. Preclinical assessment of β -d-mannuronic acid (M2000) as a non-steroidal anti-inflammatory drug. *Immunopharmacology and immunotoxicology*. 37, 535–40.
- Goh, C. H., Heng, P. W. S., Chan, L. W. 2012. Alginates as a useful natural polymer for microencapsulation and therapeutic applications, *Carbohydrate polymers*, 88: 1–12.
- Guo, Xi., Wang, Yan., Qin, Yuimin., Shen, Peili., Peng, Qiang. 2020. Structures, properties and application of algic acid: A review. *International journal of biological macromolecules*, 162, 618–628.
- Jeong, H. J., Lee, S. A., Moon, P. D., Na, H. J., Park, R. K., Um, J. Y., Kim, H. M., Hong, S. H. 2006. Alginic acid has anti-anaphylactic effects and inhibits inflammatory cytokine expression via suppression of nuclear factor-kappa B activation. *Clinical and experimental allergy*, 36, 785–794.
- Kloareg, B. & Quatrano, R. S. 1988. Structure of the cell walls of marine algae and ecophysiological functions of the matrix polysaccharides, *Oceanography and marine biology: an annual review*, 26, 259–315.

- Mirshafiey, A. & Lalander, J. 2024, Mannuronate Guluronate and Gulumannuronate gel or cream and method for its preparation. (EP 4393479A1) European Patent Office, <https://www.epo.org/en>
- Mirshafiey, A., Rehm, B., Abhari, R. S., Borzooy, Z., Sotoude, M., Razavi, A. 2007. Production of M2000 (β -d-mannuronic acid) and its therapeutic effect on experimental nephritis. *Environmental toxicology and pharmacology*, 24, 60–66. doi: 10.1016/j.etap.2007.02.002. Epub 2007 Feb 16. PMID: 21783790.
- Miyambu, G. R. & Seeletse, S. M. 2016. Numeric measurement of business process optimization. *Environmental Economics*, 7, 20–24. doi:10.21511/ee.07(4).2016.02
- Sarithakumari, C. H., Renju, G. L., Kurup, G. M. 2013. Anti-inflammatory and antioxidant potential of alginic acid isolated from the marine algae, *Sargassum wightii* on adjuvant-induced arthritic rats, *Inflammopharmacology*. 21, 261–268.
- Sarithakumari, C. H., Kurup, G. M. 2013. Alginic acid isolated from *Sargassum wightii* exhibits anti-inflammatory potential on type II collagen induced arthritis in experimental animals, *International Immunopharmacology*, 17, 1108–1115.
- Sharfi L., Nowroozi M. R., Smirnova G., Fedotova A., Babarykin, D. & Mirshafiey A. 2024. The Safety Properties of Sodium Alginate and its Derivatives. *British Journal of Healthcare and Medical Research*. 11, 263–274.