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GAMMA IRRADIATION INDUCED CHANGES IN THE BIOADHESION PROPERTIES OF CALCIUM ALGINATE GELS

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Abstract: The controlled release of substances and their administration to a specific substrate (tissue, epitel, etc.) often is facilitated with polymer gels that increase the bioadhesion force. One way for modification of the bioadhesion properties of polymer gels is through gamma irradiation. In this work, calcium alginate hydrogels were gamma irradiated with different absorbed doses (nonirradiated, 2.74 kGy, 5.47 kGy and 8.21 kGy or equivalent of 0h, 48h, 96h, and 144h of irradiation) for inducing changes of its bioadhesion properties. Mechanical compressibility tests (Zwick Z010 universal testing machine) and bioadhesion pull tests (DCAT tensiometer) were conducted on the irradiated hydrogels. We worked with three different types of sodium alginates from which hydrogels were prepared. $CaCO_3$ was used as a source of Ca^{2+} ions for crosslinking and GDL as an Ca^{2+} ions activation agent. The results showed that high absorbed doses of gamma irradiation reduced the structural integrity of the hydrogels (becoming softer) with small increase of the bioadhesion force.

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1. INTRODUCTION

Alginates are natural occurring polysaccharides found in substantial amounts in brown seaweeds. They are unbranched binary co-polymers of (1–4)-linked residues of b-D-mannuronic acid (M) and a-L-guluronic acids (G). Alginic acid and its water-soluble sodium salt form have a great ability to give highly viscous solutions even at moderate concentrations. Aqueous solution of sodium alginate forms stable gels in the presence of multivalent cations such as Ca^{2+} and Mg^{2+}. Gel formation occurs due to the ionic interaction between guluronic acid residues from two or more alginate chains and cations, yielding a three-dimensional network of alginate molecules well described by the ‘‘egg-box" model [1]. Functional and physical properties, mechanical strength, porosity, gel uniformity, biocompatibility, and influence on encapsulated cells and other incorporated substances in the alginate gels vary widely depending on ratio of

mannuronic to guluronic acids, the frequency and size of guluronic acid blocks and the molecular weight of the polymer [2].

Currently Ca2+ is preferred to crosslink alginate for biomedical applications because of the mild reaction conditions compared for example to the cellular toxicity of both Ba2+ and Sr2+ [3,4]. Two methods of gelation have been extensively described and used to create alginate hydrogels: diffusion gelling and in-situ gelling. Diffusion gelling is an ideal approach that is widely used for rapidly encapsulating cells in microspheres of alginate used for controlled released methods where polymer gels swell in a medium in order to release a given substance. In this method calcium ions diffuse through the liquid alginate boundary, cross-linking alginate strands as the ions move through the volume of alginate. However, cross-links are not uniformly distributed throughout the gel [5,6].

On the other hand, in recent years there has been a very big interest in the preparation of homogeneous alginate gels in different forms by using in-situ gelling methods. In this method $CaCO_3$ is mixed with alginate to create a homogeneous mixture. D-Glucono-d-lactone (GDL) is added to acidify the solution and release calcium ions, making them available for cross-linking. The resultant hydrogel has an uniform distribution of cross-links [7].

Bioadhesion is the special case of adhesion in which the substrate is of biological origin (for example, skin or a mucous membrane). Bioadhesion is crucially important for pharmaceutical applications to design and develop biomaterials with optimal mucoadhesive properties. In the past few decades, several theories have been developed to describe the adhesion phenomena. Such theories include the electronic theory, [8] the adsorption theory, [9] the wetting theory, [10] and the diffusion theory [11].

2.MATERIALS AND METHODS

Sodium alginate samples were obtained from FCM Biopolymers Company, Norway and used as received. The initial molecular weights of NaAlgs (number-averaged M_n and weight-averaged M_w), guluronic to mannuronic ratio G/M are given in Table 1. Calcium carbonate and D-glucono-δ-lactone (GDL) were obtained from Aldrich. The polymer samples were placed in tightly closed containers, and irradiated for given time (48h, 96h, 144h or equivalent dose of, 2.74 kGy, 5.47 kGy and 8.21 kGy) in a Gammacell 220 type 60 Co-gamma irradiator at room temperature in air.

Table 1.

Alginate type	$\bar{M}_n$, g/mol	$\bar{M}_w$, g/mol	G/M
LF120M	340×10^3	670×10^3	70/30
LF200M	310×10^3	690×10^3	50/50
LF240D	275×10^3	500×10^3	45/55

2.1 Preparation of Alginate Gels

A $CaCO_3$-GDL system was used to activate controlled gellation. Calcium carbonate ($CaCO_3$) was used as a source of calcium ions to initiate gellation and GDL was used as a weak

acid for the activation of calcium ions from the carbonate. To achieve a neutral pH value, the molar ratio of $CaCO_3$ to GDL was maintained at 0.5. A molar ratio of calcium ion to GDL of 0.36 was used in order to secure preparation of an uniform gels from 1.5% sodium alginate solution as follows: 0.105g of sodium alginate was dissolved in 7 ml of deionized water and 0.0158 g $CaCO_3$ was put into the sodium alginate solution and the mixture was vortexed for 60 seconds. 0.056 g of GDL was dissolved in 0.02 mL of deionized water and added into alginate solution immediately and vortexed for 45 seconds and then put to rest. After 24 hours the gels are formed. Through the same method calcium alginate activated solutions were prepared from irradiated sodium alginates. In figure 1.1 and 1.2 we see a bulk prepared alginate gel and a 5 mm thick slice prepared for compressibility and bioadhesion tests [12]. Because of the fact that the compressibility and bioadhesion test are with destructive nature we noticed some small differences in values with slices from different bulk samples but the results are reproducible in a given range.

Fig. 1.1.

Fig. 1.2

Fig. 1.3.

Fig. 1.4.

2.2 Experimental setup for structural integrity tests

For compressibility tests we used Zwick Z010 with universal one axial mode of work. We use a 1kN cell and movement speed of 5 mm/min.

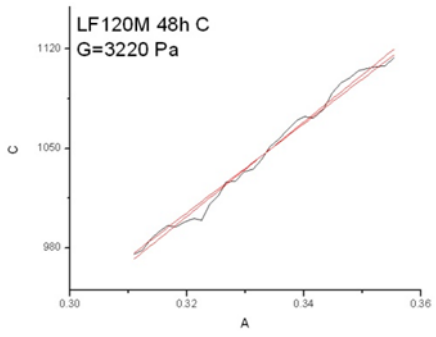

Fig. 1.5.

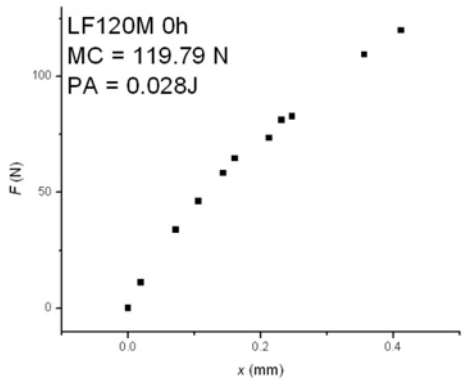

Fig. 1.6.

The instrument is show in figure 1.3.The results further shown are an average of four measurements for every type of sample. On figure 1.5 we give a graphical example of the compressibility tests and on figure 1.6 we give a graphical example of the bioadhesion tests.

2.3 Experimental setup for bioadhesion

For the bioadhesion measurements we used DCAT 11 from DataPhysics, Germany. This instrument has a movable lover part and a fixed upper end that is connected to the measurement sensor. We use two-composite instant glue to attach the gel on the lower side with the movable part. To the sensor we attach a flat surface holder where we place poly(ethyleneterephthalate) foil as the contact surface that mimics mucosa layer. The whole system is presented on figure 1.4. Contact between the gel and the surface is detected as a load change of 8 mg on the sensor. Then the gel is pushed up to exert a force equivalent to 5g on the gel. We measure two parameters of bioadhsesion. Force at detachment (FD) and work of adhesion (WA).

3. RESULTS AND DISCUSSIONS

We do bioadhseion and compressibility tests for all types of alginates for nonirradiated and irradiated samples. In table 3.1, 3.2,and 3.3 we give the results for the elastic modulus of the alginate gels from the compressibility tests made for LF120M, LF200M and LF240D alginate. In table 3.4, 3.5, and 3.6 we give the results from the biadhesion pull tests for alginate gels made from LF120M, LF200M, LF240D alginate.

Table 3.1: Mechanical tests for alginate LF120M

Dose (kGy)	0	2.74	5.47	8.21
G (N/m^2)	3491	2647	2735	2312

Table 3.2: Mechanical tests for alginate LF200M

Dose (kGy)	0	2.74	5.47	8.21
G (N/m^2)	3223	2810	2971	2333

Table 3.3: Mechanical tests for alginate LF240D

Dose	0	2.5 kGy
G (N/m^2)	2320	2069

Table 3.4: Bioadhesion tests for alginate LF120M

Dose (kGy)	Force of detachment (N)	Work of adhesion (J)
0	119,79	0,028
2.74	73,28	0,036
5.47	71,80	0,045
8.21	115,84	0,049

Table 3.5: Bioadhesion tests for alginate LF200M

Dose (kGy)	Force of detachment (N)	Work of adhesion (J)
0	108,74	0,031
2.74	99,34	0,039
5.47	100,27	0,031
8.21	109,52	0,049

Table 3.6: Bioadhesion tests for alginate LF240D

Dose (kGy)	Force of detachment (N)	Work of adhesion (J)
0	110,95	0,103
2.74	83,72	0,068
5.47	106,56	0,098
8.21	87,14	0,078

The results presented in the above tables 3.1, 3.2 and 3.3 show that by the increase of the absorbed dose of gamma irradiation the elastic modulus decrease. That indicated mechanical weakness of the gels influenced by the irradiation scission effect of the polymer chains in the gel network. The results of the bioadhesion tests (tables 3.4, 3.5 and 3.6) show changes of the force of detachment and the work of adhesion, mainly at 2.74 kGy and 5.47 kGy. This findings show that gamma irradiation of the alginate gels can yield more soft gels with decreased bioadhesion in comparison to the nonirradiated gels. In other words, applying gamma irradiation at desired doses to alginate gels can produce changes in mechanical and bioadhesion properties that can be of interests for some specific application of the gels.

4. CONCUSION

With this work we show that gamma irradiation of the calcium alginate gels has an influence on their bioadhesion and mechanical properties, especially at some medium doses. We conclude that gamma irradiation on calcium alginate gels at specific doses can produce gels with changed properties – strong bioadhesive gels can become less bioadhesive and more elastic. That can be of interest for applications where bioadhesion need to be less pronounced. Furthermore, we see that alginate that has lower rigidity or has a lower G/M ratio has a higher work of adhesion, because of its week gel structure funded on less specific ionic interactions between the Ca^{2+} ions and the ionic groups in the alginate polymer.

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