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Characterisation and disintegration properties of irradiated starch

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Abstract

Irradiation treatment could provide a quick and simple way to modify the physical, chemical and pharmaceutical properties of biopolymers such as starch. Corn, potato and drum dried corn starch were exposed to X-ray and electron beam (e-beam) irradiation treatment at doses of 10, 50 and 100 kGy. The disintegration properties of these starches were compared using α-lactose monohydrate tablets containing 5% (w/w) starch as disintegrant. Starch solubility increased, while its swelling capacity decreased with increasing irradiation dose. The irradiation treatment caused fragmentation of the amylopectin fraction. Irradiation modified the different starches thoroughly, showing remarkable differences in disintegration properties after X-ray treatment and e-beam modification. The e-beam modification resulted in significantly higher disintegration times of the tablets. © 2001 Elsevier Science B.V. All rights reserved.

Keywords: Disintegration; Starch; Irradiation; Starch characterisation; X-ray; Electron beam

1. Introduction

Worldwide, starch is one of the most used excipients in pharmaceutical formulations. It is used mainly in oral solid dosage forms as a filler, binder or disintegrant. Next to plain starch, a variety of chemical and physical modification techniques are used to impart certain properties to the starches. These modified starches are used not only in the pharmaceutical industry, but also in the textile, glue and paper industries. The modification techniques are often complex and time consuming; however, irradiation can provide a cost-lowering and environment-friendly alternative to change the physical, chemical and/or biological characteristics of a product. This treatment requires limited sample preparation, is fast, does not require catalysts and does not induce a major temperature increase (Woods and Pikaev, 1994). Until now, irradiation of materials was mainly performed with the gamma rays of ^{60}Co sources. As a result the available literature data concerning the irradiation of starch focused on experiments conducted with photons of cobalt sources (Sokhey

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and Hanna, 1993). The effect of irradiation on the properties of pharmaceutical excipients has been investigated during the sterilisation of drugs (Basly et al., 1996), medical devices (Takehisa et al., 1998) and polymers used as drug carriers (Sintzel et al., 1997) or packaging materials (Spry, 2000). ElBagory et al. (1994) found no measurable differences between the tabletting properties of gamma-irradiated (5, 10 and 25 kGy) and non-irradiated powders (including pregelatinised starch). The effectiveness of corn starch as a disintegrant was not affected by gamma irradiation.

Over the last years due to the recent improvements of electron machines in the 5–10 MeV range, producing high beam power and high dose rates, the possible applications of irradiation have been expanded. Exciting new opportunities emerged in the field of the synthesis of advanced biomaterials, polymer chemistry and waste treatment (Mondelaers, 1998). The aim of this project was to evaluate the disintegrating properties of starch products irradiated by X-rays and electron beams.

2. Materials and methods

2.1. Materials

Corn starch, potato starch and drum dried corn starch (DDCS) were received from Eridania Béghin Say Cerestar (Vilvoorde, Belgium). The tablets contained 94% (w/w) α-lactose monohydrate (Pharmatose® 100 Mesh, DMV, Veghel, The Netherlands), 1% (w/w) magnesium stearate (< 90 μm) (Federa, Brussels, Belgium) and 5% (w/w) starch.

2.2. Methods

2.2.1. Irradiation facility and procedure

The disintegrants were exposed to either X-rays or electron beams produced with a 15 MeV linear electron accelerator (Mondelaers et al., 1996). This accelerator delivers 20 kW electron beams with a well-defined energy in the range between 3 and 15 MeV. The electron beams can be used directly or can be transformed into X-rays. For the production of X-rays, the electrons are stopped in a high-atomic-number absorber and part of the kinetic energy of the decelerated electrons emerges in the form of bremsstrahlung photons. This X-ray beam exiting from the high-power bremsstrahlung target is strongly forward peaked due to the angular cross-section of bremsstrahlung production. To produce X-radiation fields with high lateral dose uniformity, biconal shaped Pb dose flattening filters were developed and added to the converter target (Van Laere and Mondelaers, 1997). With this configuration homogeneous X-ray irradiation fields (homogeneity better than 2%) with a diameter of 20 cm are produced. Because of the radioactivity constraints, the electron beam energy for X-ray irradiations was limited to 5 MeV during these experiments. For the electron irradiations, 10 MeV electron beams from the 20 kW Ghent accelerator were used. The electron beam traversed a water-cooled aluminium window and 50 cm of air, so that the lateral dose distribution was flattened by scattering. The lateral and depth dose homogeneity for X-ray and electron irradiations was better than 5%. The samples were irradiated with doses of 10, 50 or 100 kGy at a dose rate of 0.1 (X-rays) and 1 kGy/min (electrons). The irradiations were performed at ambient conditions.

Prior to the irradiation, dose homogeneity of the radiation fields was verified with an ionisation chamber on a motor-driven scanning system. Absolute dose calibration was performed with a chemical dosimeter using a ferrous sulphate Fricke solution. Far West Technology dosimeters (FWT 60-00) calibrated against the Fricke dosimeter were used to measure the distribution of the absorbed dose within each irradiated sample.

2.2.2. Determination of the starch solubility

The solubility of non-irradiated and irradiated (28 days after irradiation) starch was measured according to the method described by Tollier and Guilbot (1970). A dispersion of 500 mg starch in 10 ml water was made in a test tube. After 48 h of stirring (Coulter Mixer, Electronics limited, Luton, UK), the samples were centrifuged. After

decantation of the supernatans, the aliquot was dried until no further weight loss was detected and finally weighed. The solubility was expressed as the percentage of powder dissolved related to the total amount of starting material. This test was run in duplicate.

2.2.3. Determination of the starch molecular weight distribution

The molecular weight distribution of the starch samples was obtained using gel permeation chromatography on three Shodex columns (Showa Denko, KK, Tokyo, Japan) placed in series: KS 806, KS 804, KS 802. The starch samples were dissolved in dimethylsulfoxide/ water (90/10; v/v).

The column was maintained at a temperature of 70°C, while the mobile phase (0.05% (w/v) sodium hydroxide) was used at a flow rate of 1 ml/min. The system was calibrated with pululan standards (Shodex P-82, Showa Denko, Japan). These reference standards were prepared by storing a 0.05% (w/v) aqueous solution for 24 h at 25°C. After 24 h the particles were completely swollen and the dispersion was shaken until all particles were dissolved. Before use, the solution was filtered through a 0.45 μm filter. The weight distribution profile, the weight average molecular weight (M_w), the number average molecular weight (M_n) and the polydispersity (M_w/M_n) were determined for all samples using the Caliber GPC software program (Polymer Laboratories/Lab Systems).

2.2.4. Preparation of tablets and determination of the tablet disintegration time

All components, except magnesium stearate, were mixed for 15 min in a Turbula mixer (System Schatz, Basel, Switzerland). After addition of magnesium stearate, the mixing procedure was continued for an additional 5 min. By direct compression using an excentric tablet press, 600 mg tablets were prepared (Korsch, type EK0, Berlin, Germany) at a compression force of 14.7 kN, equipped with 12 mm flat punches. The tablet disintegration time was measured in water at 37°C according to the Ph. Eur. III method using a Pharma Test PTZ-E (Hamburg, Germany) disintegration tester without disks. Immediately before the disintegration time was determined, tablets were prepared with irradiated corn starch stored for 1, 3, 7, 14 and 28 days after irradiation. The tablets containing irradiated potato and irradiated DDCS were prepared with starch stored for 28 days after irradiation.

The data are presented as a mean disintegration time ($n = 6$) and were further analysed with one-way Anova. Comparison in pairs was done using the Scheffé test at a level of significance of 0.05. The normality of the different data was first checked using the Kolmogorov–Smirnov test. To check the homogeneity of the variances, the Levene test was used. The variances of certain data were not homogeneous. In those cases, the results were transformed to fit the conditions for statistical analysis. If transformation did not result in homogeneity of the variances, a non-parametric Kruskall–Wallis test was conducted, followed by the Dunns-procedure for comparison in pairs with $P < 0.05$ (Rosner, 1995). The program SPSS (Statistical Package for the Social Sciences, version 9.0) for Windows was used for statistical analysis.

3. Results and discussion

Disintegration times are shown in Tables 1 and 2, divided in columns showing homogeneous subsets. For each disintegrant, data belonging to one subset are not significantly different from each other, while data given in different subset are significantly different. Table 1 shows the disintegration time of α-lactose monohydrate tablets formulated with 1% (w/w) magnesium stearate and 5% (w/w) starch as a function of X-ray irradiation dose. An increasing irradiation dose resulted in a decrease of the disintegration time of the tablets. For the tablets formulated with corn starch, a significant decrease (compared to tablets containing the original corn starch) was found at an irradiation dose ≥ 50 kGy. When analysing formulations containing non-irradiated and irradiated potato starch or DDCS, a significant difference was observed at an irradiation dose ≥ 10 kGy, but no significant differences were detected between the different irradiation doses.

Table 2 shows the disintegration time of tablets formulated with corn, potato and DDCS as a function of e-beam irradiation dose. Tablets formulated with irradiated corn starch had a significantly lower disintegration time at an irradiation dose of 100 kGy; irradiation at lower doses had no significant effect on the disintegration time. No correlation was observed between the irradiation

Table 1
Mean disintegration time ($n = 6 \pm$ SD) of tablets containing α-lactose monohydrate, magnesium stearate (1%; w/w) and corn, potato or DDCS (5%; w/w) as a function of X-ray irradiation dose[a]

Starch type	Irradiation dose (kGy)	Mean disintegration time (s) (± SD)		
		Subset 1	Subset 2	Subset 3
Corn	0	280 (20)		
	10	216 (44)	216 (44)	
	50		156 (14)	156 (14)
	100			88 (4)
Potato	0	84 (8)		
	10		20 (0)	
	50		20 (5)	
	100		18 (0)	
Drum dried corn	0	87 (12)		
	10		24 (1)	
	50		29 (1)	
	100	34 (2)	34 (2)	

[a] Irradiated starch was stored for 28 days before tabletting. Data are presented in columns showing homogeneous subsets. Disintegrant data belonging to one subset are not significantly different from each other, while the data of different subsets are significantly different.

Table 2
Mean disintegration time ($n = 6 \pm$ SD) of tablets containing α-lactose monohydrate, magnesium stearate (1%; w/w) and corn, potato or DDCS (5%; w/w) as a function of electron beam irradiation dose[a]

Starch type	Irradiation dose (kGy)	Mean disintegration time (s) (± SD)		
		Subset 1	Subset 2	Subset 3
Corn	0	280 (20)		
	10	319 (40)		
	50	323 (30)		
	100		168 (29)	
Potato	0	84 (8)		
	10		168 (40)	
	50		160 (14)	
	100	56 (7)		
Drum dried corn	0	87 (12)		
	10		64 (0)	
	50		69 (9)	
	100			514 (85)

[a] Irradiated starch was stored for 28 days before tabletting. Data are presented in columns showing homogeneous subsets. Disintegrant data belonging to one subset are not significantly different from each other, while the data of different subsets are significantly different.

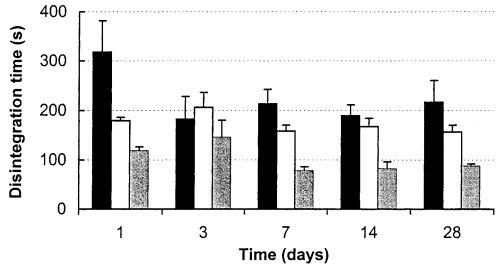

Fig. 1. Mean disintegration time ($n = 6 \pm$ SD) of tablets containing α-lactose monohydrate, magnesium stearate (1%; w/w) and X-ray irradiated corn starch (5%; w/w). The corn starch was irradiated at different doses and used at different time intervals after irradiation (Black box, 10 kGy; White box, 50 kGy; Grey box, 100 kGy).

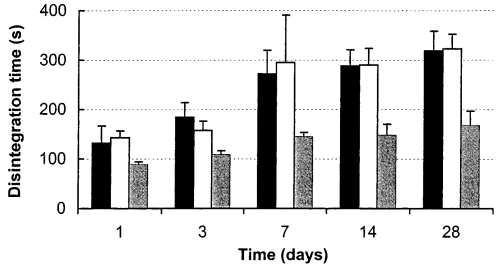

Fig. 2. Mean disintegration time ($n = 6 \pm$ SD) of tablets containing α-lactose monohydrate, magnesium stearate (1%; w/w) and e-beam irradiated corn starch (5%; w/w). The corn starch was irradiated at different doses and used at different time intervals after irradiation (Black box, 10 kGy; White box, 50 kGy; Grey box, 100 kGy).

dose and mean disintegration time of the tablets containing irradiated potato starch. At an irradiation dose of 10 and 50 kGy the disintegration time increased, while it dramatically decreased at 100 kGy. Using DDCS as a tablet disintegrant, a dramatic increase of the disintegration time was found at an irradiation dose of 100 kGy, while the disintegration time of these tablets irradiated at lower doses was similar to non-irradiated samples.

The e-beam modification of corn, potato and DDCS resulted in significantly higher disintegration times compared to X-ray irradiation, indicating that X-ray treatment was the most effective modification method.

The different starch types were influenced at different rates by X-ray and e-beam treatment indicating that the starch origin and the pregelatinisation process affected the sensibility of starch towards X-ray and e-beam treatment.

Fig. 1 shows the disintegration time of tablets formulated with X-ray irradiated corn starch as a function of storage time after irradiation. The disintegration times measured 7, 14 and 28 days after irradiation were not significantly different, regardless of the irradiation dose used. Disintegration times measured 1 and 3 days after e-beam treatment were significantly lower than the ones detected after 7, 14 and 28 days (Fig. 2); however, the system was stabilised after 7 days.

Molecular weight distribution and solubility were determined for all original and irradiated starches in order to find an explanation for the phenomena observed.

The molecular weight distribution profile of non-irradiated starch is composed of two fractions. Fraction I consists of the branched and higher molecular weight amylopectine, while fraction II represents the mainly linear and lower molecular weight fraction of amylose (Sokhey and Chinnaswamy, 1993).

Tables 3 and 4 show the molecular weight distribution of corn, potato and DDCS modified by X-ray and electron beam, respectively, as a function of irradiation dose. Irradiation clearly caused fragmentation of the amylopectin fraction as these molecules became smaller in molecular weight with irradiation dose and merged with the amylose fraction. Polydispersity decreased with irradiation and finally, one fraction was eluted from the column. As an example, the molecular weight distribution of corn starch before irradiation and after X-ray irradiation at 50 kGy is shown in Fig. 3. This is in accordance with the literature data on the influence of gamma irradiation on the molecular weight distribution of starch. Rayas-Solis (1987) reported a decrease of molecular weight of both the amylose and amylopectin fraction of gamma irradiated (2.5–20 kGy) great northern beans, although fragmentation of the amylopectin fraction was more pronounced. This observation was confirmed by other studies (Roushdi et al., 1983; Sokhey and Chinnaswamy, 1993). An increase of the amylose-like fraction was also reported by Rayas-Duarte and Rupnow (1993). Only Esteves et al. (1997)

reported a significant increase of the amylopectin-like fraction (which could be attributed to the formation of crosslinks between amylose chains), while a decrease of the amylose-like fraction was evident from the elution pattern of the irradiated samples of both white and black pepper.

As the swelling behaviour of starch is attributed to the amylopectin fraction (Tester and Morrison, 1990), the decreased swelling capacities of irradiated starch could be explained by the marked decrease in concentration of the amylopectin fraction.

The solubility data (Table 5) indicated that both X-ray and electron beam irradiation have a profound effect on the soluble fraction of the different starches. Generally, solubility increased with increasing irradiation dose for all three starches after X-ray and electron beam irradiation. Minor differences are found between both irradiation treatments. No data are available on the solubility of starch modified by high-intensity electron linear accelerators, although some authors reported on the effects of gamma-irradiation on starch solubility. Hebeish et al. (1992) found

Table 3
Molecular weight distribution of X-ray irradiated corn, potato and DDCS as a function of irradiation dose [a]

Starch type	Irradiation dose (kGy)	M_w (10^5)	M_n (10^4)	DP_i
Corn	0	28.76	11.96	24.04
	10	1.62	2.50	6.49
	50	0.37	1.92	1.90
	100	0.20	0.52	3.93
Potato	0	38.75	24.11	16.07
	10	12.90	6.77	19.04
	50	1.67	1.41	11.83
	100	0.48	0.86	5.60
Drum dried corn	0	32.36	21.52	15.04
	10	4.43	3.36	13.21
	50	1.29	1.13	11.38
	100	0.80	0.77	10.39

[a] M_w: weight-average molecular weight, M_n: number-average molecular weight, DP_i: polydispersity.

Table 4
Molecular weight distribution of electron beam irradiated corn, potato and DDCS as a function of irradiation dose[a]

Starch type	Irradiation dose (kGy)	M_w (10^5)	M_n (10^4)	DP_i
Corn	0	28.76	11.96	24.04
	10	2.18	3.69	5.89
	50	0.71	1.14	6.23
	100	0.40	6.27	5.90
Potato	0	38.75	24.11	16.07
	10	5.43	4.38	12.40
	50	1.52	1.54	9.90
	100	0.47	0.88	5.37
Drum dried corn	0	32.36	21.52	15.04
	10	4.35	2.17	20.05
	50	2.08	1.41	14.52
	100	0.67	0.75	9.04

[a] M_w: weight-average molecular weight, M_n: number-average molecular weight, DP_i: polydispersity.

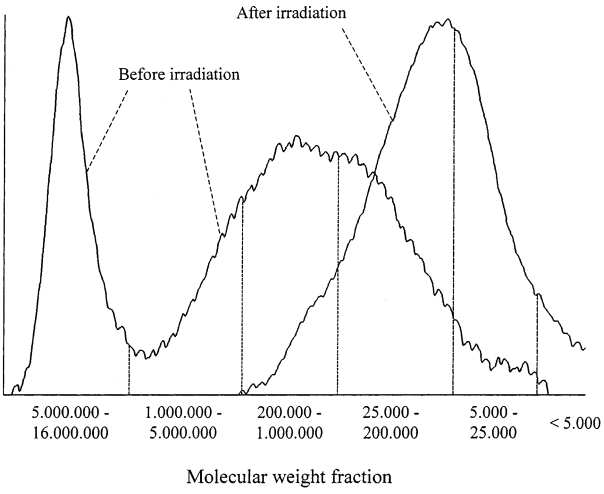

Fig. 3. Molecular weight distribution of corn starch before irradiation and after X-ray irradiation at 50 kGy. Molecular weight distributions were determined using gel permeatioin chromatography.

Table 5
Solubility ($n = 2$) of corn, potato and DDCS 28 days after irradiation treatment as a function of irradiation dose and irradiation source

Starch type	Irradiation dose (kGy)	Solubility (%)	
		X-ray	Electron beam
Corn	0	5.2–6.0	5.2–6.0
	10	6.6–7.4	8.0–8.4
	50	8.4–8.0	9.4–9.0
	100	9.6–9.6	10.6–10.8
Potato	0	12.6–11.8	12.6–11.8
	10	12.6–11.8	12.4–12.2
	50	12.8–12.8	12.6–13.0
	100	14.4–13.2	14.0–13.6
Drum dried corn	0	29.0–37.0	29.0–37.0
	10	32.2–30.6	35.8–33.8
	50	56.0–59.0	60.4–64.0
	100	64.0–65.8	69.2–64.6

similar results for both corn and rice starch: an increase of the soluble fraction when the gamma ray dose was varied between 10 and 250 kGy. In this study irradiation doses of 10, 50 and 100 kGy increased the soluble fraction of corn starch from 24% (non-irradiated) to 30, 70 and 75%, respectively. Sokhey and Chinnaswamy (1993) reported that the water soluble fraction of 70% amylose starch increased from 0.03 to 0.18%, when the irradiation dose was increased from 0 to 30 kGy. Other authors reported similar results (Michel et al., 1980; Roushdi et al., 1983; Rayas-Solis, 1987; Sabularse et al., 1992).

Several questions remain unanswered as to the prolonged disintegrating time of tablets formulated with 10 and 50 kGy e-beam irradiated potato starch and to the very long disintegration time observed with 100 kGy e-beam irradiated DDCS.

Clearly, other modifications and reactions are taking place during X-ray and e-beam irradiation of starch. Pregelatinised starch behaved differently in comparison to native starches, indicating the influence of pretreatment on the reactivity of starch molecules when irradiated with X-rays and e-beams. The time after irradiation treatment must also be taken into consideration, indicating that chemical reactions are still ongoing after irradiation. After e-beam treatment stabilisation of the system was noticed 7 days after irradiation.

4. Conclusions

It can be concluded that X-ray and electron beam irradiation have an important effect on the properties of starches. Clearly the reaction pattern seems complex and cannot be related to degradation of starch molecules alone. The disintegrating properties of some irradiated starches are promising, but a careful characterisation of the irradiated products and a validation of the process are required before this technique can be used as an alternative modification technique in comparison to chemically modified starches.

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