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KINETIC STUDY OF CHITOSANE/GENIPIN SYSTEM USING DSC

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Knowledge of the the kinetic study of chitosan/genipin allow to know the different effects that time and temperature have on the cure reaction of the material.

The total enthalpy of reaction, the glass transition temperature and the partial enthalpies have been determined using DSC in dynamic mode. Two models, one based on chemical kinetics and the other accounting for diffusion were used. The incorporation of the diffusion factor in the second model allowed for the cure kinetics to be predicted the whole range of conversion.

Keywords: *curing kinetics, DSC, epoxy network, resins*

Introduction

Chitosan is a biopolymer with low cytotoxicity and good biocompatibility composed on units of N-acetylil-*D*-glucosamine and *D*-glucosamine. It is obtained by the alkaline deacetylation of chitin, a homopolymer of N-acetyl-*D*-glucosamine. Chitosan is a naturally occurring polymer soluble in acidic medium or in water in its salt form [1]. In many studies chitosan has been found to be a good candidate for diverse applications as in food industry, wound dressing, and support material for drug delivery. In this field, chitosan has been used specially in systems for controlled release of drugs [2, 3], antigens [4], enzymes [5], or even for gene delivery [6]. Encapsulation of drugs in polymeric drug devices based on this polysaccharide is usually carried out by different techniques (emulsion, coacervation, spray-drying, etc.) [7].

A drawback of microparticles obtained with pure chitosan or gelified with polyanions is need to cross-link them covalently to exclude premature dissolution or disintegration [8]. Various approaches have been proposed to cross-link chitosan microparticles, the most usual compounds have been glutaraldehyde, formaldehyde and other dialdehydes. However, all kind of these compounds present certain cytotoxicity when they were used in in vitro studies using cell culture [9, 10].

An alternative molecule to be used as cross-linker with chitosan may be genipin. Genipin is a glucone of geniposide which is isolated from gardenia fruits (*Gardenia jasminoides Ellis*). Genipin has been used in the past as cross-linker of molecules with primary amino residues as proteins or chitosan [9]. In in vivo studies genipin has been shown a superior biocompatibility and slower degradation rate on chitosan implants those glutaraldehyde-cross-linked microspheres [10]. Polymerization reactions of chitosan-genipin system are induced in the presence of oxygen radicals, it is affected by temperature and it is inhibited by the presence of H^+ [11]. Cross-linking mechanism between polymers with primary amino groups (as chitosan) and genipin takes place in two different reactions which lead to the cross-linking between two primary amines from N-acetylglucosamine of chitosan [11]. The fastest is a nucleophilic attack of one of aminogroups of chitosan to carbon 3 of genipin which results in a heterocyclic compound of genipin linked to glucosamine unit. The second reaction and slowest is a nucleophilic substitution of the ester group of genipin to form an amide and produce methanol. Simultaneously, the polymerization of genipin might be produced between genipin molecules already linked to amino groups of chitosan which could lead to the cross-linking of amino groups by genipin molecules or even by genipin copolymers [9].

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Because of the good properties of the chitosan with several polymer blends recently have been used for drug release and drug-excipient [12, 13].

The objective of this paper was to calculate the total enthalpy of reaction ΔH_t and the glass transition temperature T_g using DSC in dynamic mode for the system chitosan and genipin as curing agent. In the second experimental step, the partial enthalpies ΔH^T have been determined using DSC in dynamic mode. From these experimental data, the conversions α and the reaction rates $d\alpha/dt$ have been calculated. These data allowed determining the kinetic coefficients of the Sourour and Kamal model [14] and the global order of the cure reaction. In addition, a diffusion factor was added to model that predicts the behaviour of the system for high values of conversion, where the kinetic no longer is the controller phenomenon. For it, a semiempirical model proposed by Chern and Polheim [15] based on free volumes considerations has been used, and successfully applied by other authors to several epoxy systems [16–19].

Experimental

Sample preparation

Chitosan dispersion (0.5 mass/mass%) was prepared in distilled water and it was stirred during 12 h. Genipin was incorporated at concentration of 1 mM and the solution was incubated during 30 min and 18 h. Chitosan microparticles were prepared by spray dryer. The chitosan dispersion was sprayed through the nozzle (0.5 mm diameter) of a spray dryer (model Büchi 190, Büchi Labortechnik AG, Flawil, Switzerland). The process parameters were set as: inlet temperature=90±5ºC, outlet temperature=70±3ºC, aspirator setting: 100%, pump setting=3 mL min^{-1} and air flow rate 600 L h^{-1}.

The obtained chitosan microspheres were collected and dried in vacuum oven under reduced pressure (20 mbar) for 24 h. The final product was stored under dry conditions at room temperature.

Differential scanning calorimetry

A differential scanning calorimeter DSC Q100 V6.19 Build 227 of TA Instruments was used to obtain all the experimental data. In order to determine the total heat of reaction ΔH_t a first scan was carried out in dynamic mode from –30 to 250ºC at constant heating rate of 10ºC min^{-1}. A second scan from 15 to 250ºC at constant heating rate of 10ºC min^{-1} was carried out to determine the glass transition temperature T_g of epoxy system.

In the second phase of the experimental investigation, the partial enthalpies ΔH^* have been determined using DSC in dynamic mode.

Results and discussion

In the first experimental step we realize calorimetric scans in dynamic mode that allow observing endothermic peaks that corresponds to the melting point of water. Due to large area of the endothermic peaks can not be seen the exothermic curve of the reticulation of the system. So the endothermic peak of water was eliminated to deduct graphically the reticulation curve of the curves of chitosan and genipin.

In the second experimental step, the total heat of reaction and the glass transition temperature of the system were performed in quintuplicate for the following incubated times: 30 and 1080 min. Table 1 shows the average values and their standard errors corresponding to different preparation times. It can not been observed differences between the values of ΔH_t and the values of T_g for the incubated times, so for the microparticles formation already took place before 30 min.

Table 1 Total heat of reaction and the glass transition temperature at different incubated times

Incubated time/min	ΔH/J g^{-1}	s.d.*	T_g/°C	s.d.*
30	161.96	2.46	61.29	1.28
1080	157.56	0.48	61.07	1.15

*s.d. – standard deviation

The values of partial enthalpies were determined from calorimetric scans in dynamic mode at different times. The total degree of conversion α of this system can be calculated using the following expression:

$$\alpha = \frac{\int_{t_0}^{t<t_f} dH/dt}{\Delta H_t} = \frac{\Delta H^*}{\Delta H_t} \quad (1)$$

where ΔH^* is the heat evolves up at a certain time.

Figure 1 shows the conversion *vs*. time at different incubated times. It can be seen that the reticulation begins at 17 min for the different incubated times.

From dynamic calorimetric scans also can be determined the instantaneous heat flow dH/dt and the correspondence reaction rate $d\alpha/dt$

$$\frac{d\alpha}{dt} = \frac{dH/dt}{\Delta H_t} \quad (2)$$

The reaction rates $d\alpha/dt$ allowed determining the kinetic coefficients and the global order of the cured

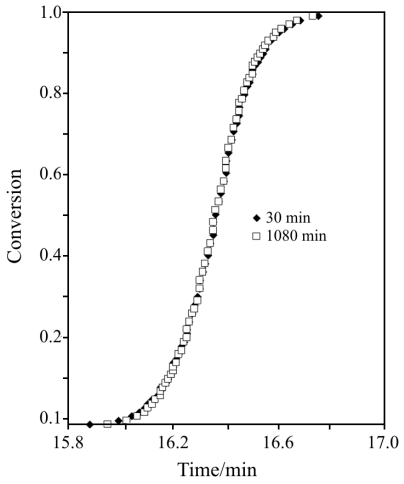

Fig. 1 Degree of conversion *vs*. time at different incubated times

reaction from the Sourour and Kamal [14] kinetic model assuming stoichiometric proportions and equal reactivity for all amine hydrogens

$$\frac{d\alpha}{dt}=(k_1+k_2\alpha^m)(1-\alpha)^n \quad (3)$$

This model expresses the contribution of two mechanisms: autocatalytic and *n* order. The constant rates of two reactions are k_2 and k_1, and *m* and *n* are the parameters related to the two orders of reaction.

The used kinetic model does not fit to experimental plots of reaction rate *vs*. conversion. The same behaviour can be observed with the *n* order model. An autocatalytic model was choosing to fit experimental results.

$$\frac{d\alpha}{dt}=k_2\alpha^m(1-\alpha)^n \quad (4)$$

Table 2 shows constant rate and reaction orders for the autocatalytic model at different incubated times. Values listed in this table suggest a value of 2 for the overall reaction order (*m*+*n*), in good agreement with values reported by Núñez *et al*. [18, 19] and Zvetkov [20] for epoxy systems. In Figs 2a and b are showed the reaction rate *vs*. conversion at different incubated times where experimental results are compared with those obtained to a chemical kinetic model. At higher conversion the deviations between theoretical and experimental data from a critical conversion (58% typically) [21] are due to a gradual decrease in the reaction and the curing kinetic becomes diffusion controlled. A semiempirical model based on free volume considerations proposed by Chern and Polheim [15] and used by Cole *et al*. [16], Khanna and Chanda [17] and by Núñez *et al*. [18, 19, 22] was used to study the diffusion-controlled reaction rate. In this model a diffusion factor is defined as

Table 2 Constant rate and reaction orders for the autocatalytic model at different incubated times

	30 min	1080 min
k_2/min^{-1}	0.178±0.008	0.193±0.011
m	1.071±0.023	1.130±0.027
n	0.850±0.045	0.943±0.057
R^2	0.9981	0.9977

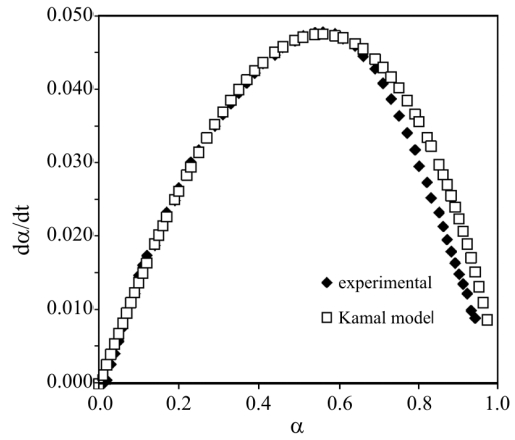

Fig. 2a Reaction rates *vs*. conversion at the incubated time of 30 min

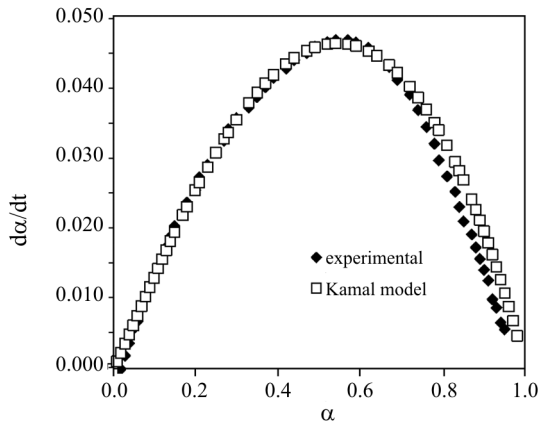

Fig. 2b Reaction rates *vs*. conversion at the incubated time of 1080 min

$$F(\alpha)=\frac{1}{1+e^{A_1(\alpha-\alpha_c)}} \quad (5)$$

where α_c is the critical conversion, and A_1 is an adjustable parameter.

Using the diffusion factor $F(\alpha)$ the reaction rate can be expressed in the following form to account for effects of diffusion:

$$\frac{d\alpha}{dt}=(k_1+k_2\alpha^m)(1-\alpha)^n F(\alpha) \quad (6)$$

In Figs 3a and b are showed the reaction rate *vs*. conversion where experimental results are compared with those obtained to a chemical kinetic model and

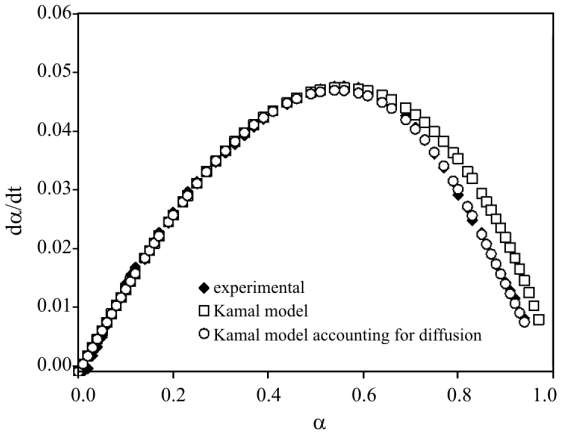

Fig. 3a Reaction rates *vs.* conversion for experimental data. Data obtained to a chemical kinetic model and to the kinetic model accounting for diffusion at the incubated time of 30 min

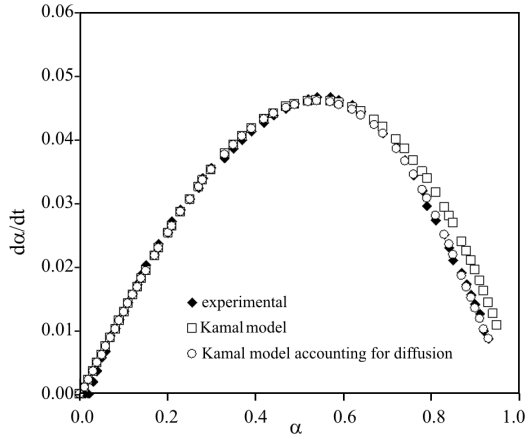

Fig. 3b Reaction rates *vs.* conversion for experimental data. Data obtained to a chemical kinetic model and to the kinetic model accounting for diffusion at the incubated time of 1080 min

to the kinetic model accounting for diffusion. It can be seen that the agreement is extremely good between experimental results and kinetic model accounting for diffusion.

Conclusions

The chemical kinetic model predicts properly the experimental results at low conversions. At high conversion it is necessary to add a diffusion factor that predicts properly the behaviour of the system.

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