

Miscibility Study of Chitosan/Polyethylene Glycol Fumarate Blends in Dilute Solutions

Azadehsadat Hashemi Doulabi,¹ Hamid Mirzadeh,¹ Mohammad Imani²

¹Polymer Engineering Department, Amirkabir University of Technology, Tehran, Iran

²Novel Drug Delivery Systems Department, Iran Polymer and Petrochemical Institute, Tehran, Iran

Correspondence to: H. Mirzadeh (E-mail: mirzadeh@aut.ac.ir)

ABSTRACT: Solution miscibility of chitosan/polyethylene glycol fumarate blends dissolved in acetate buffer solution was investigated in different blend compositions by viscosity, density, and refractive index measurement techniques at 30, 40, and 50°C. In order to quantify the miscibility of the polymer pair, degree of miscibility was studied by means of two criteria known as interaction parameters i.e., μ and α . On the basis of the sign convention involved in these criteria, these values revealed that the blend solution was miscible when the chitosan content was more than 80% (w/w) of the composition. The results were confirmed by density, and refractive index measurements. Furthermore, the results showed that the miscibility window of chitosan/polyethylene glycol fumarate blends was independent with respect to the changes in solution temperature. Therefore, these results suggested due to intermolecular hydrogen-bonding interaction between amino and hydroxy groups of chitosan and hydroxy groups of polyethylene glycol fumarate which play an important role in the formation of miscible phase. © 2012 Wiley Periodicals, Inc. *J. Appl. Polym. Sci.* 000: 000–000, 2012

KEYWORDS: miscibility; polymer blends; solution properties; chitosan; polyethylene glycol fumarate

Received 16 June 2011; accepted 5 March 2012; published online 00 Month 2012

DOI: 10.1002/app.37637

INTRODUCTION

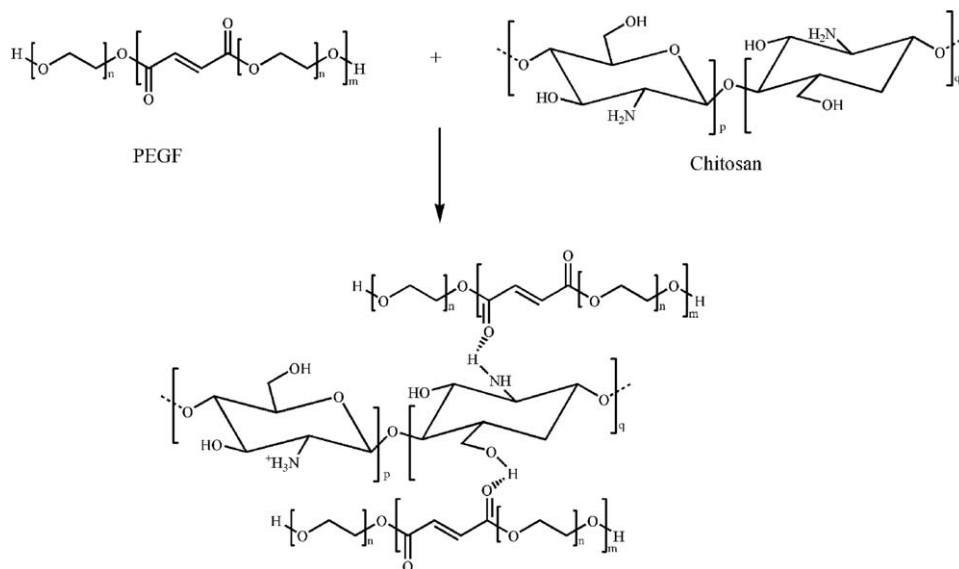
During the recent years there has been a growing interest in modifying the existing polymers rather than synthesizing new ones to improve both mechanical and physical properties. Polymers blending, making composites, and synthesizing copolymers and interpenetrating polymer network (IPN) can be named as some of different modes of polymers modification.^{1–3} Polymer blends are physical mixtures comprising of structurally different polymers that interact through secondary forces with no covalent bonding though the best method of enhancing miscibility of a polymer blend is to introduce specific weak molecular interactions.^{4,5}

The importance of blending has increased in the recent years because it has become a useful approach for preparing materials with tailor-made properties different from those of the constituent polymers.⁶ Blending polymers may result in reducing their basic cost, improving their processing efficiency, and maximizing their important properties. The gain in properties of the blend depends on the degree of compatibility or miscibility of the blended polymers at the molecular level. At first sight, depending upon the degree of molecular mixing, blends may be categorized into three groups including: totally miscible (compatible), semimiscible (semicompatible), or immiscible (incompati-

ble) blends.⁶ Due to the fact that the Gibbs free energy of mixing is positive because of negligible change in entropy as a result of high molecular weight of polymers and with enthalpy term being positive so totally miscible blends are rather rare.⁴ A literature survey reveals a variety of techniques of studying the miscibility of polymer blends such as Fourier-transform infrared spectroscopy (FTIR), positron annihilation lifetime spectroscopy (PALS), thermal analysis e.g., differential scanning calorimeter (DSC), scanning electron microscopy (SEM), dynamic mechanical studies and viscometric techniques, and so on.^{7–10} Some of these techniques are rather costly and sophisticated, or time-consuming. Hence, it is worthwhile to identify some simple, inexpensive, and rapid techniques to study the miscibility of polymer blends.

Using a solvent system that is thermodynamically favorable for both components is the simplest method to mix two or more chemically different polymers in solution state. Upon evaporation of the solvents, a homogeneous blend will be obtained. In particular, interesting observations on the blends of chitosan (Ch) with different polymers such as polyvinyl pyrrolidone (PVP),^{7,11} polyvinyl alcohol (PVA),¹ collagen,¹² alginate,¹³ hydroxypropylmethyl cellulose,¹⁴ and polyethylene oxide (PEO)¹⁵ have been reported in solution state. Miscibility among

© 2012 Wiley Periodicals, Inc.



Scheme 1. Chemical structure of Ch/PEGF blend and possible interactions between their functional groups.

the components showed a marked influence on some characteristic properties of the polymer blends such as mechanical, morphological, physicochemical ones.

The compatibility or miscibility of the parent polymers at the molecular level is of utmost importance for the blends. Many experimental and theoretical methods have been developed to investigate the polymer-polymer miscibility and the interaction between the polymers. Early works on using dilute solution viscometry to evaluate the interactions occurred in polymer systems was reviewed by Olabisi et al.¹⁶ Chee,¹⁷ Sun et al.,¹⁸ and Jiang and Han¹⁹ have described dilute-solution viscometry (DSV) as a simple, reliable, and low-cost alternative which provides very useful information about the bulk structure of a polyblend. Rajulu and Sab²⁰ and Sajal et al.²¹ have suggested the use of ultrasonic velocity and viscosity measurements for investigating polymer miscibility. Also other researchers have shown that the variations in viscosity and refractive index of blend solutions are linear for miscible blends and nonlinear for immiscible blends.^{22,23} The mixing of solutions of interacting polymers produces an immediate precipitation or turbidity or homogeneity, indicating strong, weak, and no or very small interaction between the polymers, respectively.²²

Ch and its derivatives have been increasingly applied to biomedical, pharmaceutical, food, industrial, and agricultural sectors to tap its potential properties including biocompatibility, biodegradability, film forming, renewability, ability to time release of fertilizers and nutrients into the soil.^{24–26} Ch is generally blended with other hydrophilic polymers to overcome some disadvantages such as loss in mechanical strength or adjust hydrophilic character of the finally blended solid compound.^{8,27}

Polyethylene glycol fumarate (PEGF) is a biocompatible and biodegradable unsaturated polyester based on polyethylene glycol and fumaric acid which have been previously synthesized and reported for different applications, for example, nerve regeneration, bone substitutes, cements, cartilage wound healing and drug delivery.^{28–31}

In the present investigation, the aqueous solutions of Ch and PEGF blends are studied extensively over a wide range of solution temperatures and compositions. When Ch and PEGF polymer molecules collided, the amine, residual amide, and hydroxyl groups of Ch can interact with hydroxyl ending groups of PEGF via weak secondary interactions like hydrogen bonds as shown in Scheme 1. Such intermolecular interactions regulate the miscibility among the component polymer molecules. The main message and rational behind of this work is to assay miscibility properties of the blends in order to evaluate some important characteristics of them for biomedical applications such as wound healing. To the best of our knowledge there is no work reported in the literature dealing with Ch and PEGF blends miscibility.

EXPERIMENTAL

Materials

Low viscosity chitosan (Ch, 20–200 mPa s, DDA = 80%, Fluka, Germany) was purified by dissolving in 0.2N HCl solution and consequent centrifugation at 9000 rpm for 20 min to separate nondissolved impurities. The solution was then neutralized using 1N NaOH to precipitate the polymer. The precipitate was separated by vacuum filtration (Wattman, 11.0 cm, UK) and washed extensively with dionized water and subsequently vacuum dried at 40°C for 2 days. Polyethylene glycol (PEG, 3000 g mol⁻¹ nominal molecular weight, Sigma) was dried by azeotropic distillation using toluene. Fumaryl chloride (FuCl, 99.99%, Aldrich) was used after distillation at 161°C under ambient pressure. Propylene oxide (PO, 99.99%, Merck, Germany) was used as received. Acetate buffer (pH = 5, I = 0.3) was prepared by mixing equal volumes of acetic acid (0.1M) and sodium acetate (0.2M) solution. All other chemicals, HCl, NaOH, dichloromethane (DCM), toluene, sodium acetate, and acetic acid (HAc) were purchased from Merck Chemicals Co., (Dusseldorf, Germany) and used without further purification.

Methods

PEGF Synthesis. The unsaturated polyester i.e., PEGF was synthesized as described elsewhere.³² Briefly, PEGF macromer was

Table I. Molecular Characteristics and Physical Properties of PEGF in this Study Including T_c , T_m , ΔH_m , χ_c , T_{onset} , T_{max} , $[\eta]$, M_n and M_w

Characteristics for	T_c^a (°C)	T_m^b (°C)	ΔH_m^c (J g ⁻¹)	χ_c^d (%)	T_{onset}^e (°C)	T_{max}^f (°C)	$[\eta]^g$ (dL g ⁻¹)	M_n^h (g mol ⁻¹)	M_w^i (g mol ⁻¹)
PEGF	25.91	55.43	87.85	42.67	200	300	0.0838	10,000	17,200

^aCrystallization temperature, ^bMelting temperature, ^cHeat of fusion, ^dCrystallinity was measured by DSC, ^eOnset temperature of degradation, ^fMaximum temperatures of degradation were determined by TGA, ^gIntrinsic viscosity in acetate buffer at 30°C was measured by capillary viscometer, ^hNumber-average (M_n) is calculated by GPC, ⁱWeight-average (M_w) molecular weight is calculated by GPC

synthesized by condensation polymerization of PEG with FuCl (0.995 : 1) in DCM in the presence of PO as a catalyst and proton scavenger. Upon completion of the reaction, the product was washed several times with 0.1N NaOH to extract the resulted byproducts i.e., chlorinated propanols then PEGF macromer was obtained by rotavaporation. The characterization results are summarized in Table I.

Dilute Solution Viscometry. For the Factorial design, the statistical software named Minitab 16 (Minitab Inc., State College, PA) was used. It has two factors (temperature and Ch composition in the blend) which have 3 and 9 levels, respectively. Dilute solutions (<1% w/v) of polymers were used for viscometric studies. Stock solutions of Ch, PEGF and the blends in different compositions i.e., 10/90, 20/80, 30/70, 40/60, 50/50, 60/40, 70/30, 80/20, 90/10 of Ch/PEGF were prepared in filtered acetate buffer solution.⁶ Viscosity measurements at 30, 40, and 50°C were made using an Ubbelohde suspended level viscometer (SCHOTT Geräte GmbH, Germany) of appropriate internal capillary diameter to provide the flow time of approximately 100 s for the buffer solution. The kinetic energy and shear corrections were negligible. The different temperatures were maintained in a thermostatic bath with a thermal stability of $\pm 0.01^\circ\text{C}$. The total weight of the two dissolved polymer components in the solution was always maintained at 1 g/dL. Ch and PEGF and their blends were studied in a concentration range of 0.1 to 1.0 g/dL. Average flow times were determined for at least five times for each sample. The density of the solutions was measured via pycnometry (5 mL, Gay-Lussac, Germany). The accuracy of the density measured by pycnometry was $\pm 0.03\%$.

Refractive Index Measurements. The refractive index of the same blend solutions were measured using a DR 5000 KRÜSS refractometer (A. KRÜSS OPTRONIC GmbH, Germany) with a thermostated water circulation system at 30, 40, and 50°C. The accuracy of the refractive index measurement was $\pm 0.02\%$.

RESULTS AND DISCUSSION

Ch dissolved in acidic media, exists in an extended rigid-rod conformation and exhibits characteristic behaviors of polyelectrolyte solution properties due to an enlarged effective volume resulting from charge repulsion of quaternary ammonium functional groups in the backbone of this polycation which stretches out of the molecule.³³ This causes a significant deviation from the classical Huggin's equation in turn, therefore in order to suppress the repulsion of the same charges in dilute solutions and overcome this difficulty, a mixture composed of acetic acid (0.1M) and sodium acetate (0.2M) buffer solutions was chosen as the solvent.¹⁵ In a buffer solution, the polyelectrolyte approaches a ran-

dom-coil conformation due to the screening effect of the counter ions on the cationic centers of the polymer backbone.³³ In contrast, PEGF is a flexible and uncharged hydroxyl-terminated polymer which completely obeys classical Huggins equation.

The principle of using dilute solution viscometry to trace polymers miscibility is based on the fact that the repulsive or attractive intermolecular interactions between two different polymers in solution should make different contributions to the viscosity of the polymer mixture solution.³⁴ It has also been assumed that polymer-polymer interactions usually dominate over polymer-solvent ones. Attraction between the two component molecules may cause expansion of macromolecular coils, resulting in an increase in viscosity and a positive deviation from additivity, or otherwise, repulsion may cause shrinkage of the macromolecular coils giving a negative deviation from viscosity additivity.¹² As a result, the viscosity of a ternary system may be either lower or higher than the one calculated from viscosities of both pure blend components assumed on the additivity law.^{35,36}

Basically, miscibility parameters obtained by dilute solution viscometry are derived from classical Huggins equation, which expresses the specific viscosity η_{sp} of a single-solute solution as a function of concentration c :^{36,37}

$$\eta_{sp} = [\eta]c + bc^2 \quad (1)$$

where $[\eta]$ is intrinsic viscosity, c is a concentration and b is related to the Huggins coefficient, K_H reflects binary interactions between polymer segments.

$$b = K_H[\eta]^2 \quad (2)$$

The value of Huggins coefficient is a measure of the interpenetration of polymer coils, the extent of which depends upon the segment-segment and segment-solvent interactions. This in turn affects the intermolecular hydrodynamic interaction and molecular dimensions. An analogue of eq. (1) proposed by Huggins can be adapted to a ternary system (polymer 1/polymer 2/solvent). Equation (1) extended by Krigbaum and Wall can be applied to polymer mixtures in a common solvent. The total concentration ($c = c_1 + c_2$) is introduced,³⁸

$$\eta_{spm} = [\eta]_m(c_1 + c_2) + b_m(c_1 + c_2)^2 \quad (3)$$

Subscripts 1, 2, and m represent polymer 1, polymer 2, and polymer blends, respectively. b_m is related to the Huggins parameter by

$$b_m = K_m[\eta]_m^2 \quad (4)$$

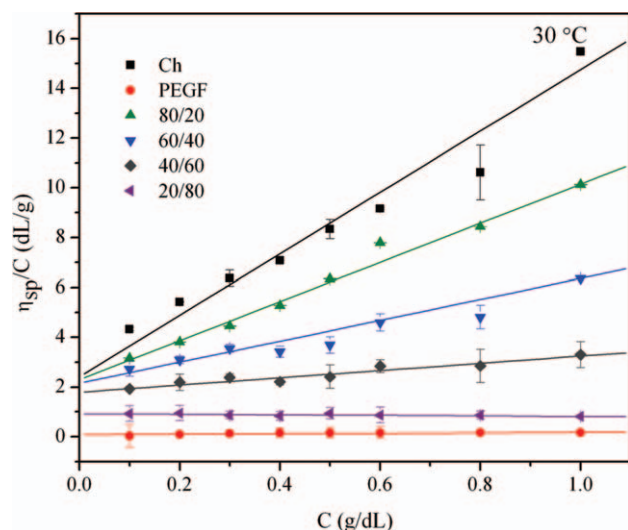


Figure 1. Huggin's plots for 1% (w/v) Ch/PEGF blend in buffer at 30°C. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

The plot of reduced specific viscosity of polyblend $\eta_{sp,m}/(c_1 + c_2)$ versus total polymeric concentration yields a straight line, and the intercept and gradient corresponds to $[\eta]_m$ and b_m respectively. Theoretically, $[\eta]_m/(c_1 + c_2)$ is the total effective specific hydrodynamic volume, which is the addition of the effective specific hydrodynamic volume of constituent polymers, and $b_m(c_1 + c_2)^2$ reflects to total molecular interaction.^{35,36}

The Huggin's plots for the pure components, Ch and PEGF, and their blends at the different temperatures are shown in Figures 1–3.

Figures 1–3 indicate considerably higher slopes for 80/20 and 60/40 Ch/PEGF blend compositions than PEGF-rich compositions. This may be attributed to the mutual attraction between

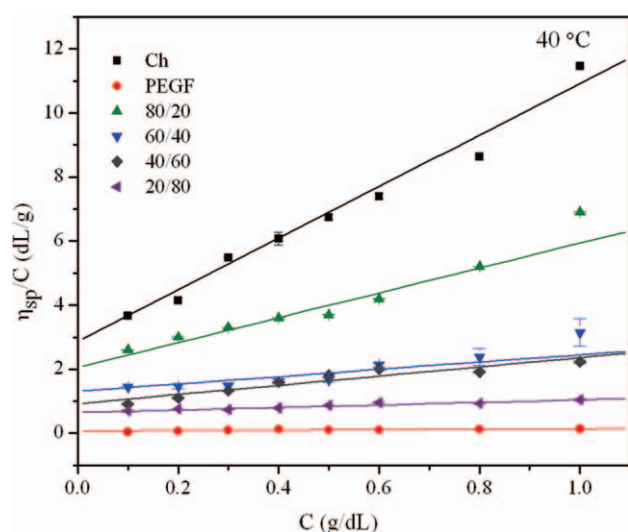


Figure 2. Huggin's plots for 1% (w/v) Ch/PEGF blend in buffer at 40°C. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

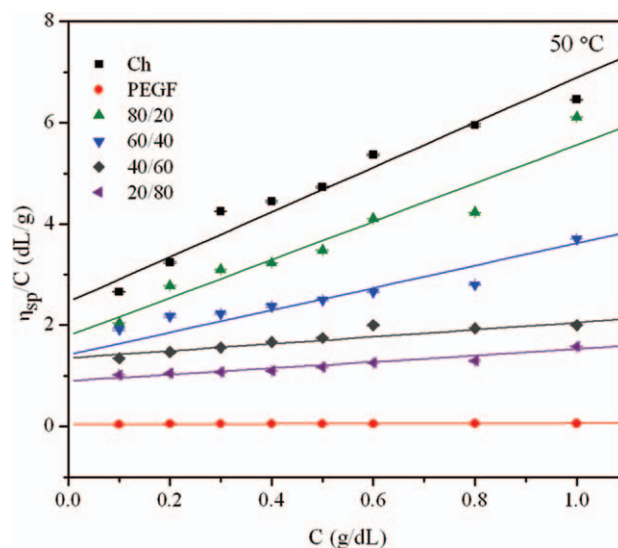


Figure 3. Huggin's plots for 1% (w/v) Ch/PEGF blend in buffer at 50°C. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

macromolecules in solution, which leads to an increase of hydrodynamic volume. Hence, Ch/PEGF blends are found to be miscible only when Ch content is more than 80% (w/w) in the blend compositions. Below this critical concentration, little or no slope was observed in the Huggin's plot, due to phase separation. Some criteria for miscibility of polymer blends are proposed according to the solution deviation from ideal behavior. Chee suggested that non-ideal behavior of polymer blends can be reflected by the difference observed between the experimental b_{12} and the ideal b_{12}^i values.¹⁷ Namely, ΔB :

$$\Delta B = b_{12} - b_{12}^i = b_{12} - (b_{11} + b_{22})/2 \quad (5)$$

where b_{11} , b_{22} , and b_{12} are slopes of reduced viscosity versus concentration curves for polymer (1) i.e. pure Ch and polymer (2); PEGF, and their blends, respectively. $\Delta B \geq 0$ signifies miscibility, whereas $\Delta B < 0$ indicates phase separation. Chee also proposed a more effective criterion i.e., μ using the same data to predict polymer-polymer miscibility which was expressed as:

$$\mu = \left(\frac{\Delta B}{([\eta]_2 - [\eta]_1)^2} \right) \quad (6)$$

where $[\eta]_1$ and $[\eta]_2$ are intrinsic viscosities for the pure components solutions.¹⁷ Accordingly, $\mu \geq 0$ shows miscibility whereas $\mu < 0$ indicates phase separation.^{17,24} The values of μ calculated with the preceding expression at 30, 40, and 50°C, are presented in Table II and shown in Figure 4(a).

The computed values of μ were found to be negative when Ch content was lower than 80% (w/w) and positive beyond.

Sun et al. suggested another criterion for polymer blends miscibility, based on the classical Huggins equation and Huggins coefficient K_m in the blends in terms of a thermodynamic

Table II. The Values of Interaction Parameters and C^* of Ch/PEGF Blends at 30, 40, and 50°C

Composition of Ch/PEGF	Interaction parameters						C^* (g dL ⁻¹)		
	30°C		40°C		50°C		30°C	40°C	50°C
	μ	α	μ	α	μ	α			
100/0	-	-	-	-	-	-	0.2627	0.3083	0.3759
90/10	0.2081	0.2278	0.0155	0.1014	0.0175	0.2742	0.3257	0.3448	0.4222
80/20	0.1624	0.1131	0.2902	0.0238	0.0333	0.2576	0.3438	0.4310	0.4774
70/30	-0.4129	-0.2565	0.0001	-0.2135	-0.1357	-0.0248	0.3665	0.4367	0.4870
60/40	-0.1435	-0.1043	-0.0272	-0.2232	-0.1715	-0.0509	0.4103	0.5000	0.5584
50/50	-0.2824	-0.1506	-0.1593	-0.2619	-0.2906	-0.0764	0.4732	0.5556	0.6249
40/60	-0.3107	-0.271	-0.2332	-0.268	-0.291	-0.194	0.5443	0.6667	0.7519
30/70	-0.3032	-0.6635	-0.4538	-0.3351	-0.4421	-0.1994	0.5515	0.7407	0.9087
20/80	-0.3861	-0.2057	-0.5577	-0.3724	-0.7536	-0.2185	1.0637	0.9615	1.0511
10/90	-0.3935	-0.2212	-0.7279	-0.3929	-0.7086	-0.2708	1.9736	1.6667	1.9850
0/100	-	-	-	-	-	-	11.4942	14.9925	28.1690

parameter.¹⁸ According to their approach for a ternary system, three types of interaction may contribute to K_m value including long-range hydrodynamic interaction of pairs of single molecules given by K_{m1} ; the formation of double molecules given by K_{m2} ; and intermolecular attraction or repulsion given by K_{m3} .³⁶ Thus, the overall K_m turns out to be:

$$K_m = K_{m1} + K_{m2} + K_{m3} \quad (7)$$

In the absence of strong interactions that would encourage aggregation, and at sufficiently low concentrations, the second term K_{m2} can be neglected. Reabbreviating K_{m3} as α which is indicative of the nature and strength of the molecular interactions and rearranging the final equation yields:

$$\alpha = K_m - K_{m1} \quad (8)$$

$$\alpha = K_m - \frac{K_1[\eta]_1^2 w_1^2 + K_2[\eta]_2^2 w_2^2 + 2\sqrt{K_1 K_2}[\eta]_1[\eta]_2 w_1 w_2}{\{[\eta]_1 w_1 + [\eta]_2 w_2\}^2} \quad (9)$$

where K_1 , K_2 , and K_m are the Huggin's constants for individual components (1 and 2) and the blend, respectively. K_m is the

experimentally obtained Huggins constant. The terms w_1 , w_2 indicate the weight fraction of the polymer 1 and polymer 2.¹⁸

Sun et al. proposed that a blend will be miscible when $\alpha \geq 0$ and immiscible when $\alpha < 0$. In this research, the long-range interaction, α , are taken into account for confirmation the results.^{18,39} The values of α calculated with the preceding expression at 30, 40, and 50°C, are shown in Figure 4(b). α is found to be negative when the Ch content is below 80% (w/w) and then positive beyond 70% (w/w) at 30, 40, and 50°C. For the sake of simplicity and to make comparisons on the miscibility behavior of different blends of the polymers, Figure 2(a,b) depict together the miscibility parameter values presented in Table II as a function of the weight fraction of Ch in the blends at tree temperatures studied.

The positive values of μ and α , originating from experimental viscosity data for these polyblends, indicate attractive intermolecular interactions between Ch and PEGF in solution. Table II and Figure 4(a,b) shows the miscibility window for Ch/PEGF blends in the buffer solution. Also the content of critical concentration ($C^* \approx 1/[\eta]$)⁴⁰ of each blends are summarized in

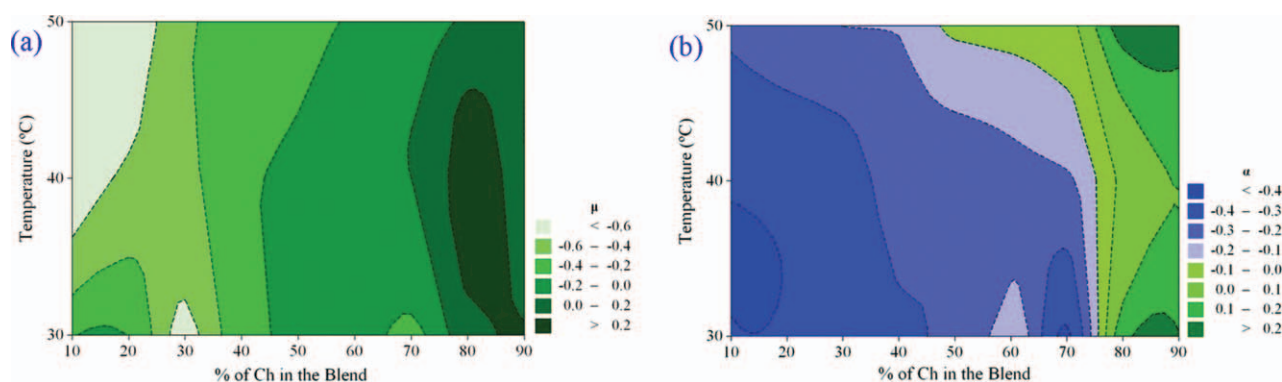


Figure 4. Contour Plots of μ (a) and α (b) versus temperature; Ch content. [Color figure can be viewed in the online issue, which is available at www.onlinelibrary.com.]

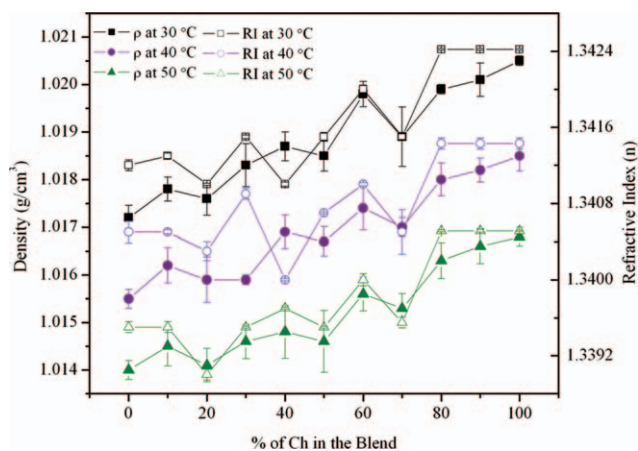


Figure 5. Effect of temperature on the variation of density and refractive index with composition of 1% (w/v) of Ch/PEGF blend in solution. [Color figure can be viewed in the online issue, which is available at [wileyonlinelibrary.com](http://www.wileyonlinelibrary.com).]

Table II. As can be followed in Table II, the C^* value of both homopolymers and blends increases with increasing temperature and the C^* values of the polymer blends vary between those of neat polymers, indicating the existence of intermolecular interactions between the unlike polymer segments when blended together. The long-range hydrodynamic interactions are considered in the equation for α [eq. (9)] ends to more accurate interpretations than μ .³⁴ Our results attest these equations can be used to describe the interaction of unlike molecules and predict the miscibility of polymer blend in this specific system.

Computed value of α is found to be negative when the chitosan content is at or below 70% and positive beyond this value, however; μ is found to be negative when chitosan content is at or below 60% and then positive beyond this value at 45°C. Some discrepancy is observed in some instances where one of the interaction parameters is positive; however, the other one is negative for a specific blend composition as reported by Jayaraju et al., for Ch and polyvinyl alcohol blends hence, miscibility conclusions based on the viscosity results should be confirmed by another method.¹ To this end, density (ρ) and refractive index (n) of the blended compositions are shown in Figure 5, and the values are given in Table III.

Figure 5 shows both linear and nonlinear regions. It was already established that the variation is linear for miscible and nonlinear for immiscible blends.⁴¹ In the present study, the variation is found to be linear when Ch content is more than 80% (w/w) at all temperatures studied. This may be due to the Ch, which is a rigid polymer with coil conformation and PEGF is a flexible polymer and as the molecular weight of Ch is higher than PEGF it may act as a pseudo solvent for the unsaturated polyester by entangling around the short flexible PEGF chains. As the fraction of PEGF in the mixture increases and the fraction of Ch decreases, the possibility of chain entanglement, which may lead to miscibility, decreases. Hence, miscibility is observed for the blend Ch/PEGF when the Ch fraction is more than 80% in the blend. This observation is in confirmation with μ and α values. Therefore the present study indicates the existence of

Table III. The Values of Refractive Index and Density of Ch/PEGF Blends at 30, 40, and 50°C

Composition of Ch/PEGF	Density (g/cm ³) (mean \pm SD)					
	30°C		40°C		50°C	
	30°C	40°C	30°C	40°C	30°C	40°C
100/0	1.34242 \pm 1.0E -5	1.34143 \pm 5.7E -5	1.34051 \pm 1.5E -5	1.34051 \pm 1.3E -4	1.0185 \pm 3.0E -4	1.0168 \pm 2.0E -4
90/10	1.34242 \pm 1.0E -5	1.34143 \pm 5.7E -5	1.34051 \pm 1.5E -5	1.0201 \pm 3.5E -4	1.0182 \pm 2.5E -4	1.0166 \pm 3.6E -4
80/20	1.34242 \pm 1.0E -5	1.34143 \pm 5.7E -5	1.34051 \pm 1E -5	1.0199 \pm 1.0E -4	1.0180 \pm 3.5E -4	1.0163 \pm 3.7E -4
70/30	1.34150 \pm 3.0E -5	1.34050 \pm 2.3E -4	1.33955 \pm 5.7E -5	1.0189 \pm 4.2E -4	1.0170 \pm 2.0E -4	1.0153 \pm 3.1E -4
60/40	1.34200 \pm 4.2E -5	1.34100 \pm 1.7E -5	1.34000 \pm 6.3E -5	1.0198 \pm 2.6E -4	1.0174 \pm 4.5E -4	1.0156 \pm 3.5E -4
50/50	1.34150 \pm 4.6E -5	1.34070 \pm 1.0E -5	1.33950 \pm 1.0E -5	1.0185 \pm 3.2E -4	1.0167 \pm 3.1E -4	1.0146 \pm 3.5E -4
40/60	1.34100 \pm 2.3E -5	1.34000 \pm 1.1E -5	1.33970 \pm 1.0E -5	1.0187 \pm 3.1E -4	1.0169 \pm 3.5E -4	1.0148 \pm 5.5E -4
30/70	1.34150 \pm 2.0E -5	1.34090 \pm 5.7E -5	1.33950 \pm 1.0E -5	1.0183 \pm 4.5E -4	1.0159 \pm 1.0E -4	1.0146 \pm 3.6E -4
20/80	1.34100 \pm 1.0E -5	1.34030 \pm 1.0E -4	1.33900 \pm 5.7E -5	1.0176 \pm 3.5E -4	1.0159 \pm 4.7E -4	1.0141 \pm 3.5E -4
10/90	1.34130 \pm 3.0E -5	1.34050 \pm 2.1E -5	1.33950 \pm 5.7E -5	1.0178 \pm 2.5E -4	1.0162 \pm 3.7E -4	1.0145 \pm 2.3E -4
0/100	1.34120 \pm 5.7E -5	1.34050 \pm 1.1E -5	1.33950 \pm 5.7E -5	1.0172 \pm 1.2E -4	1.0155 \pm 2.0E -4	1.0140 \pm 2.0E -4

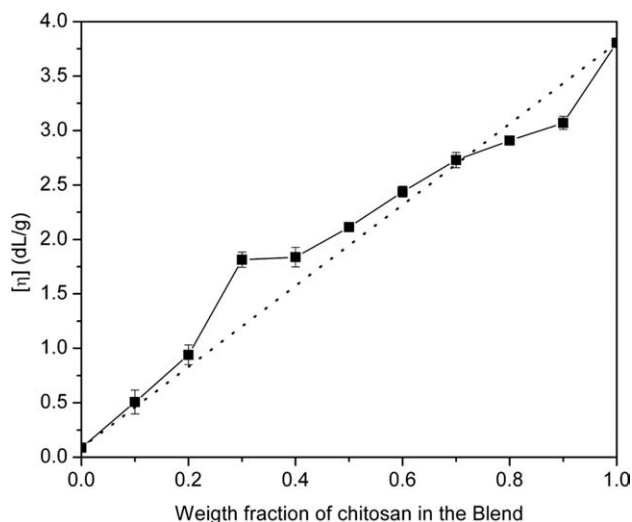


Figure 6. Intrinsic viscosity ($[\eta]$) dependence on weight fraction of Ch in the blends. Dotted line indicates the ideal values of ideal intrinsic viscosity $[\eta]_m^i$ which follows the weighted additive rule.

miscibility windows when the Ch content is more than 80% (w/w) in the blend. This may be due to the more pronounced interactions between the polymer segments in the polyblends when Ch content is more than 80% (w/w), thereby, leading to miscibility of the blend. Here, the miscibility of the blends may be due to some specific interactions like H-bonding between Ch/PEGF. Furthermore, the interaction parameter μ and the revised thermodynamic parameter α provided reliable and convenient united criteria for determination of intermolecular interaction of these two macromolecules.

Considering the weighted additive rule applicable to the viscosity results as shown in eq. (10) and experimental results on intrinsic viscosity of Ch and PEGF polyblends, it is obvious that the experimental values for intrinsic viscosity of polymer solutions do not follow the weighted additive rule quite well (Figure 6).

$$[\eta]_m^i = [\eta]_1 w_1 + [\eta]_2 w_2 \quad (10)$$

Garcia et al. have proposed other miscibility criterion as $\Delta[\eta]$ which is based on the difference between the experimental and ideal values of $[\eta]_m$ (Eq. 11). If $\Delta[\eta] < 0$, the system is miscible, and if $\Delta[\eta] > 0$, the system is immiscible.⁴²

$$\Delta[\eta] = [\eta]_m^{\text{exp}} - [\eta]_m^i \quad (11)$$

where $[\eta]_m^{\text{exp}}$ and $[\eta]_m^i$ are experimental and ideal values of intrinsic viscosity of the blends.

Up to 70% (w/w) Ch in the blends, the experimental intrinsic viscosity results are somewhat smaller than the expected ideal values, exhibiting negative deviation. Positive deviation was also observed for the rest compositions of the blends hence; Ch/PEGF blends are only miscible when Ch content is more than 80% (w/w) in the blend at 30°C. The values of $[\eta]_m^{\text{exp}}$ and $[\eta]_m^i$ and sign of $\Delta[\eta]$ of Ch, PEGF, and their blends in solution at different temperatures are summarized in Table IV. The similar

Table IV. The Values of Experimental and Theoretical Viscosities Data and Signs of $\Delta[\eta]$ of Ch, PEGF, and Their Blends in Solution at 30, 40, and 50°C

Ch/PEGF blend composition	30°C			40°C			50°C		
	Mean $[\eta] \pm \text{error}$	$[\eta]_m^i$	$\Delta[\eta]$ Sign	Mean $[\eta] \pm \text{error}$	$[\eta]_m^i$	$\Delta[\eta]$ sign	Mean $[\eta] \pm \text{error}$	$[\eta]_m^i$	$\Delta[\eta]$ sign
Ch	2.6603 ± 0.0130	2.6603		3.2436 ± 0.0335	3.2436		3.8066 ± 0.0045	3.8056	
90/10	2.3685 ± 0.0208	2.3978	-	2.9002 ± 0.0044	2.9259	-	3.0703 ± 0.0054	3.43374	-
80/20	2.0947 ± 0.0049	2.1353	-	2.3202 ± 0.0078	2.6082	-	2.9087 ± 0.0065	3.06188	-
70/30	2.0534 ± 0.0102	1.8728	+	2.2899 ± 0.0602	2.2905	-	2.7285 ± 0.0086	2.69002	+
60/40	1.7908 ± 0.1196	1.6104	+	2.0000 ± 0.0209	1.9728	+	2.4372 ± 0.0111	2.31816	+
50/50	1.6003 ± 0.0588	1.3479	+	1.7999 ± 0.0212	1.6551	+	2.1133 ± 0.0102	1.9463	+
40/60	1.3300 ± 0.0825	1.0854	+	1.4999 ± 0.0206	1.3375	+	1.8372 ± 0.0071	1.57444	+
30/70	1.1005 ± 0.0344	0.8229	+	1.3501 ± 0.0124	1.0198	+	1.8132 ± 0.0058	1.20258	+
20/80	0.9514 ± 0.1324	0.5605	+	1.0400 ± 0.0206	0.7021	+	0.9401 ± 0.0071	0.83072	+
10/90	0.5038 ± 0.0221	0.2980	+	0.6000 ± 0.0088	0.3844	+	0.5067 ± 0.0088	0.45886	+
PEGF	0.0355 ± 0.0516	0.0355		0.0667 ± 0.0078	0.0667		0.0870 ± 0.0096	0.087	

behaviors are found from Table IV. The results confirm the results of interaction parameters of α and μ .

Blend composed of Ch/PEGF in 90/10 (w/w) showed the highest deviation which may be attributed to the more strong interactions between Ch and polyethylene glycol fumarate segments than the rest compositions.

CONCLUSIONS

Miscibility of Ch and polyethylene glycol fumarate blends was studied in this work. Based on the viscosity, density, and refractive index measurements, it is concluded that polymer blends of Ch/PEGF is miscible when the Ch content is more than 80% (w/w) in the blend at all the temperatures studied. Below this critical Ch concentration, the blends were found to be immiscible. It may be due to some specific interactions e.g., repulsive interactions between the carbonyl groups of Ch and hydroxyl groups in PEGF backbone, which may lead to miscibility of the blend. Further, the miscibility of these blends is independent with respect to the changes in temperature. These findings might be useful to prepare homogenous solution blend of Ch and PEGF for biomedical application as wound healing.

ACKNOWLEDGMENTS

The authors would like to express their sincere gratitude to Iran National Science Foundation (Grant No. 89001749) and also Iran Polymer and Petrochemical Institute for supporting this research.

REFERENCES

- Jayaraju, J.; Keshavayya, J.; Rai, S. K.; Basavaraju, K. C. *J. Macromol. Sci. Pure* **2008**, *45*, 271.
- Bagheri-Khoulenjani, S.; Mirzadeh, H.; Etrati-Khosroshahi, M. *Iran. J. Polym. Sci. Technol.* **2011**, *23*, 487.
- Kabiri, K.; Mirzadeh, H.; Zohuriaan-Mehr, M. J. *J. Appl. Polym. Sci.* **2010**, *116*, 2548.
- Prasad, P.; Guru, G. S.; Shivakumar, H. R.; Rai, K. S. *J. Appl. Polym. Sci.* **2008**, *110*, 444.
- Kabiri, K.; Mirzadeh, H.; Zohuriaan-Mehr, M. J.; Daliri, M. *Polym. Int.* **2009**, *58*, 1252.
- Jayaraju, J.; Basavaraju, K. C.; Keshavayya, J.; Rai, S. K. *J. Macromol. Sci. B* **2006**, *45*, 741.
- Sakurai, K.; Maegawa, T.; Takahashi, T. *Polymer* **2000**, *41*, 7051.
- Wanchoo, R.; Thakur, A.; Sweta, A. *Chem. Biochem. Eng. Q.* **2008**, *22*, 15.
- Lewandowska, K. *Thermochim. Acta* **2009**, *493*, 42.
- Minfeng, Z.; Xudong, S.; Yun, W.; Xiandong, Y.; Huiquan, X.; Baoyi, W.; Chenze, Q. *Radiat. Phys. Chem.* **2008**, *77*, 1062.
- Jayaraju, J.; Keshavayya, J.; Rai, S. K.; Rama, S. R. *J. Macromol. Sci. Phys.* **2008**, *47*, 296.
- Ye, Y.; Dan, W.; Zeng, R.; Lin, H.; Dan, N.; Guan, L.; Mi, Z. *Eur. Polym. J.* **2007**, *43*, 2066.
- Tıgılı, R.; Gümüşderelioğlu, M. *J. Mater. Sci.: Mater. Med.* **2009**, *20*, 699.
- Jayaraju, J.; Raviprakash, S. D.; Keshavayya, J.; Rai, S. K. *J. Appl. Polym. Sci.* **2006**, *102*, 2738.
- Yilmaz, E.; Erdenizci, N.; Yilmaz, O. *Int. J. Polym.* **2003**, *8*, 327.
- Olabisi, O.; Robeson, L. M.; Shaw, M. T. *Polymer-Polymer Miscibility*; Academic Press: New York, **1979**.
- Chee, K. K. *Eur. Polym. J.* **1990**, *26*, 423.
- Sun, Z.; Wang, W.; Feng, Z. *Eur. Polym. J.* **1992**, *28*, 1259.
- Jiang, W. H.; Han, S. J. *Eur. Polym. J.* **1998**, *34*, 1579.
- Rajulu, A. V.; Sab, P. M. *Eur. Polym. J.* **1996**, *32*, 267.
- Sajal, D.; Singh, R.; Maiti, S. *Polym. Bull.* **1980**, *2*, 403.
- Paladhi, R.; Singh, R. P. *Eur. Polym. J.* **1994**, *30*, 251.
- Paladhi, R.; Singh, R. P. *J. Appl. Polym. Sci.* **1994**, *51*, 1559.
- Parashar, P.; Ramakrishna, K.; Ramaprasad, A. T. *J. Appl. Polym. Sci.* **2011**, *120*, 1729.
- Naveen Kumar, H. M. P.; Prabhakar, M. N.; Venkata Prasad, C.; Madhusudhan Rao, K.; Ashok Kumar Reddy, T. V.; Chowdoji Rao, K.; Subha, M. C. S. *Carbohydr. Polym.* **2010**, *82*, 251.
- Ghazizadeh, Y.; Mirzadeh, H.; Amanpour, S.; Ahmadi, H.; Rabbani, S. *Iran. Polym. J.* **2006**, *15*, 821.
- Bahrami, S. B.; Salahshour Kordestani, S.; Mirzadeh, H.; Mansoori, P. *Iran. Polym. J.* **2003**, *12*, 139.
- Runge, M. B.; Dadsetan, M.; Baltrusaitis, J.; Ruesink, T.; Lu, L.; Windebank, A. J.; Yaszemski, M. J. *Biomacromolecules* **2010**, *11*, 2845.
- Holland, T. A.; Bodde, E. W. H.; Baggett, L. S.; Tabata, Y.; Mikos, A. G.; Jansen, J. A. *J. Biomed. Mater. Res.* **2005**, *75*, 156.
- Park, H.; Temenoff, J. S.; Tabata, Y.; Caplan, A. I.; Mikos, A. G. *Biomaterials* **2007**, *28*, 3217.
- Holland, T. A.; Tabata, Y.; Mikos, A. G. *J. Controlled Release* **2003**, *91*, 299.
- Doulabi, A. S. H.; Mirzadeh, H.; Imani, M.; Sharifi, S.; Atai, M.; Mehdipour-Ataei, S. *Polym. Adv. Technol.* **2008**, *19*, 1199.
- Bohdanecky, M.; Kovar, J. *Viscosity of Polymer Solutions*; Elsevier Scientific Pub. Co.: Amsterdam, **1982**.
- Illiger, S. R.; Fadnis, C.; Demappa, T.; Jayaraju, J.; Keshavayya, J. *Carbohydr. Polym.* **2009**, *75*, 484.
- Aroguz, A. Z.; Kismir, Y. *Eur. Polym. J.* **2007**, *43*, 410.
- Barsbay, M.; Guner, A. *J. Appl. Polym. Sci.* **2006**, *100*, 4578.
- Huggins, M. L. *J. Am. Chem. Soc.* **1942**, *64*, 2716.
- Krigbaum, W. R.; Wall, F. T. *J. Polym. Sci.* **1950**, *5*, 505.
- Pingping, Z. *Eur. Polym. J.* **1997**, *33*, 411.
- Kaneda, I.; Sogabe, A. *Colloids Surf. A* **2005**, *270*, 163.
- Basavaraju, K. C.; Damappa, T.; Rai, S. K. *Carbohydr. Polym.* **2006**, *66*, 357.
- Garcia, R.; Melad, O.; Gomez, C. M.; Figueruelo, J. E.; Campos, A. *Eur. Polym. J.* **1999**, *35*, 47.