



Investigating the effect of humidity on the α -relaxations of low-density polyethylene using dielectric spectroscopy

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ABSTRACT

A previous work from our lab reported the higher sorption of lipophilic preservatives in LDPE form-fill-seal packs that were stored at 75% relative humidity (RH) as against 25% RH. The aim of the present work was to investigate structural changes taking place in LDPE on exposure to higher humidity. The crystallinity of LDPE, determined by differential scanning calorimetry, was found to be similar for the packs charged at both humidity conditions. Dielectric spectroscopy (1.0E–02 Hz to 1.0E02 Hz in the temperature range of 75–87 °C), however, showed faster α relaxation of LDPE films exposed to higher humidity. The activation energy of α relaxations was lower at 75% RH (99.735 kJ/mol) than at 25% RH (113.112 kJ/mol) after two weeks of storage. This work presents previously unreported evidence of the plasticization effect of water on LDPE, using dielectric spectroscopy. Furthermore, changes in α relaxation on exposure to humidity support the latest theory of its origin to be from the constrained amorphous regions. The authors suggest the employment of extreme humidity conditions (low and high), during accelerated stability studies of aqueous products in plastic packs to track the sorption loss of formulation components.

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1. Introduction

Plastic containers are economical, light-weight, shatter-proof, and can be molded into custom-designs having desired rigidity. The past few decades have seen a shift from glass to plastic packaging materials, even for sterile multi-dose products, where traditionally glass had been the preferred choice of packaging material. This shift has been further encouraged by the blow-fill-seal (BFS) or form-fill-seal (FFS) technology. The main polymers utilized in the BFS/FFS technology for extrusion blow molding are polyolefins – polyethylene like low density polyethylene (LDPE) and polypropylene – usually used in the virgin state without any additives. High sorption potential of plastics is responsible for loss of lipophilic components of the formulation by way of sorption (Bergquist et al., 2006; Croce et al., 1991; Holdsworth et al., 1984; Illum and Bungaard, 1982; Kenley and Jenke, 1990; Richardson et al., 1977; Roberts et al., 1980, 1983; Wong et al., 2006). Previous reports (Delassus, 1997; Giacin and Hernandez, 1997) have compiled permeability and diffusion coefficients of different lipophilic compounds in a variety of plastics. They have discussed the effect of different treatments

to plastics, solute concentration/vapor pressure, temperature and humidity on the rate and extent of mass transport of various solutes.

It is generally assumed that, for aqueous-based products packed in semi-permeable containers, the environmental humidity affects the rate of water loss from the formulation, with lower humidity conditions accelerating the water loss. Indeed, ICH Q1A (R2) stability guideline (Feb., 2003) has incorporated 40 °C/75% RH as the accelerated stability condition for liquid products packed in semi-permeable containers.

Another effect, the prevailing humidity of the storage conditions could have, is on the barrier properties of the packaging material. A previous work from our lab investigated the effect relative humidity on the sorption of methyl paraben and propyl paraben from their aqueous solutions (0.015%, w/v) when stored in LDPE FFS packs for three months at 40 °C. Methyl paraben (MPB) and propyl paraben (PPB) gave significantly higher losses in LDPE packs when stored at 75% RH, as against those stored at 25% RH (Amin et al., 2010). Although, polyolefins are considered to be too hydrophobic to be affected by environmental humidity (Delassus, 1997), our results from the above-mentioned study indicate the plasticization effect of humidity on LDPE. This is a surprising observation, especially in the light of a study by Borek and Osoba (2001), which reports the anti-plasticization effect of water on polyethylene based on the decrease in free volume of the polymer, aged in high humidity conditions.

Mass transport of penetrants through semicrystalline polymers (like LDPE), is widely accepted to occur through the continuous

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amorphous phase existing between the crystallites since the penetrant is insoluble in the crystalline phase (Lützow et al., 1999; Neway, 2003). Segmental mobility in the amorphous regions above the T_g is known to facilitate the transport of penetrants (Hedenqvist et al., 1996; Schott, 2001). Hence, it is reasonable to assume that reduction in the crystalline component or enhancement in polymer chain mobility in amorphous regions (plasticization), can affect the transport properties. Crystallinity of a polymer is usually determined using differential scanning calorimetry or X-ray diffraction (Charmette et al., 2009; Friess et al., 2009; O'Leary and Paul, 2006). Dielectric relaxation spectroscopy is widely used for polymers to map the molecular mobility of the polymeric chains (Craig, 1995).

Many literature reports have correlated the transport of small molecules through polymers focussing on the influence of crystallinity, (Charmette et al., 2009; Friess et al., 2009; Huang and Paul, 2004; Komatsuka et al., 2008; O'Leary and Paul, 2006; Pino et al., 2005). The latter, however, may not provide the complete picture and a better understanding of the transport process can be achieved by mapping the overall molecular environment. Reports correlating the barrier properties of polymers with the latter's dielectric relaxations, are scarce in the literature (Lee et al., 2003; Richards et al., 2009), and are mostly restricted to gas transport.

The aim of the present work was to investigate the structural changes taking place in LDPE on exposure to different humidity conditions that could affect its barrier properties. Dielectric spectroscopy (DES) was used to investigate the water-induced changes in the mobility of polymeric chains of LDPE.

2. Materials and methods

2.1. Materials

LDPE film of approximately 0.1 mm thickness was procured from Ansa Printpack Pvt. Ltd., India. Water purified by reverse osmosis (Ultra pure water system, USF Elga, UK) was used for all the experiments.

2.2. Determination of crystallinity

Differential scanning calorimeter (DSC 821^e Mettler Toledo, GmbH, Switzerland), equipped with an intra-cooler and calibrated for temperature and heat flow using high purity indium and zinc standards, was used to determine the degree of crystallinity in FFS packs exposed at different humidity conditions for three months. The calorimetric response of different samples was measured. The samples (3–8 mg) were analyzed under dry nitrogen purge (80 ml/min) in sealed and pin-holed aluminum (Al) pans. They were heated from 40 °C to 170 °C at a rate of 10 °C/min. Degree of crystallinity of the LDPE was calculated from the heat of fusion as per Eq. (1):

$$X\% = \frac{\Delta H_f}{\Delta H_f^c} \times 100 \quad (1)$$

ΔH_f is the heat of fusion of the sample and ΔH_f^c is the heat of fusion of 100% crystalline sample. The ΔH_f^c of LDPE is 285 J/g (Chabira et al., 2006).

2.3. Dielectric spectroscopy

The real permittivity (ϵ'), imaginary permittivity (ϵ'') and $\tan \delta$, of various LDPE film samples in the form of discs were measured with a Broadband Dielectric Spectrometer (Concept 40, Novocontrol, Germany) as a function of frequency (10^{-2} Hz to 10^6 Hz) in the temperature range of 40–95 °C. For detailed analysis, a range from 10^{-2} Hz to 10^2 Hz is shown, since the plots were devoid of

any prominent peaks at higher frequency. Temperature was controlled by purging compressed dry air connected to Quadro system initialized for dry gas option. The temperature during isothermal measurement was controlled within ± 0.05 K. The dried samples were sandwiched between gold-coated electrodes (30 mm diameter) and mounted on the sample holder. The diameter and thickness of LDPE film samples were 30 mm and 0.10 ± 0.02 mm, respectively.

The dielectric loss spectra (imaginary permittivity ϵ'') at different temperatures were fitted to the Havriliak Negami (HN) equation using WinFIT software (version 3.2, Germany) to obtain the characteristic relaxation time, τ_{HN} . A conductivity term $[(\sigma_0/\epsilon_0\omega)^N]$ was included in all HN-fittings to account for d.c. conductivity.

2.4. Sample treatment protocols

An experiment, involving extreme conditions, was conducted to understand and capture the changes in the dielectric relaxations of LDPE film on exposure to humidity. LDPE films, one in dry condition and other immersed in water, were exposed to 70 °C for 12 h. Such extreme conditions were used to enable identification of the range of temperature and frequency of dielectric relaxations which could capture the changes between the water-treated and untreated samples.

The next experiment simulated the ICH prescribed accelerated stability conditions for aqueous products stored in semi permeable containers (40 °C/25% RH) and for general case (40 °C/75% RH) (Feb., 2003). Heat sealed triangular pouches (made from 15 cm × 15 cm LDPE film square pieces) filled with ~50 ml water, were made ensuring minimum air entrapment inside the pouches. These pouches were inspected for absence of leakage and charged at 40 °C/25% RH (sample code: P4025) and 40 °C/75% RH (sample code: P4075). These pouches ($n=3$) were subjected to DES analysis after 2 weeks, to capture the differences in mobility of polymeric chains.

3. Results and discussion

3.1. Crystallinity of FFS packs

DSC was used to quantify the crystalline fraction of LDPE of FFS packs. Table 1 shows the experimentally obtained enthalpy of fusion and the calculated degree of crystallinity of LDPE packs exposed at 25% RH and 75% RH. Student's *t*-test indicated no statistically significant difference between crystallinity of LDPE packs stored at the two humidity conditions.

3.2. Dielectric spectroscopy

With no changes in crystallinity of LDPE packs with changing humidity, it was hypothesized that the structural relaxations, especially in the amorphous regions of the polymer, might be altered due to humidity thus affecting sorption of the preservatives. DES is frequently used to characterize the molecular mobility of semi-crystalline polymers.

Initial experiments were performed with plastic discs cut out from FFS packs. However, noise/artifacts in the relaxation peaks, made the quantification of relaxation times (τ_{HN}) from HN-fitting difficult. Therefore, in absence of any quantitative parameter for statistical comparison, a reliable conclusion could not be made.

The reasons for the noise/artifacts can be ascribed to poor electrode contact, caused by the uneven film thickness of LDPE FFS pack walls. In order to gain a systematic and reliable understanding of the effect of humidity on the relaxations of LDPE, virgin LDPE film of uniform thickness of 0.1 mm was used for further DES studies.

Table 1

Enthalpy and crystallinity of LDPE packs containing MPB (methylparaben) and PPB (propylparaben) solutions (buffered at pH 5) at different relative humidities (RH) as obtained using DSC. The reported values of enthalpy of fusion are an average of three observations with their standard deviations. Degree of crystallinity has been calculated from the enthalpy values.

Sample	Enthalpy of fusion (J/g)	Degree of crystallinity (%)
90-day LDPE pack with MPB (25% RH)	86.06 ± 9.97	30.20 ± 3.50
90-day LDPE pack with MPB (75% RH)	89.94 ± 1.87	31.56 ± 0.66
90-day LDPE pack with PPB (25% RH)	76.73 ± 3.70	32.23 ± 0.81
90-day LDPE pack with PPB (75% RH)	77.84 ± 5.24	32.79 ± 0.48

3.2.1. Dielectric relaxations of untreated LDPE film

The complex permittivity, $\varepsilon^*(\omega)$, defines the dielectric properties of a material in the frequency domain. Mathematically it can be represented as a combination of the real part, $\varepsilon'(\omega)$, and the imaginary part, $\varepsilon''(\omega)$ [equation: $\varepsilon^*(\omega) = \varepsilon'(\omega) - i\varepsilon''(\omega)$]. The peak in imaginary permittivity and step change in real permittivity, which represents the relaxation, can be described mathematically by the Havriliak–Negami (HN) equation:

$$\varepsilon^*(\omega) = \frac{\Delta\varepsilon}{\{1 + (i\omega\tau)^{1-\alpha}\}^\beta} + \varepsilon_\infty \quad (2)$$

where $\Delta\varepsilon$ (the dielectric increment) and τ (the relaxation time constant) describe the strength and time dependence of the relaxation process respectively and the quantity ε_∞ is the real permittivity at frequencies much higher than the relaxation process (i.e. the instantaneous behaviour). α and β in Eq. (2) represent the HN-shape parameters.

α is the width parameter and describes the slope of the low frequency side of the imaginary permittivity peak. β is the asymmetry factor. $-\alpha\beta$ gives the slope of the high frequency side of the imaginary permittivity peak. A large value of $(1 - \beta)$ implies a broad distribution of relaxation times (Pearson and Smith, 1998).

Fig. 1A and B shows the imaginary permittivity of a LDPE film as a function of frequency. Fig. 1A shows the spectrum in the high frequency range of 10^2 Hz to 10^6 Hz. Because of the strong increase in the ε'' values (at higher temperatures) on lowering the frequency, the response of the higher frequency of the spectrum has flattened out. A closer view can be obtained from the inset of Fig. 1A, which shows the spectra of LDPE film at 40°C , 50°C , 60°C , 70°C and 80°C , in the high frequency range. At 40°C and 50°C , the spectrum shows a curved response, indicating the presence of some weak relaxations. However, at higher temperatures, the curve starts merging with an emerging peak of high intensity seen towards the low frequency area. This emerging peak is seen in its entirety in Fig. 1B (low frequency region: 10^{-2} Hz to 10^2 Hz) at 80°C . At lower temperatures, the mobility of chains, contributing to a relaxation, is less and therefore peak-max of the relaxation was at a frequency lower than the experimental range of frequency employed. As the temperature increased, the mobility of polymeric chains increases and the relaxation peaks have shifted towards higher frequency. As mentioned above, at 80°C the relaxation had shifted sufficiently to higher frequency to emerge as a peak.

Works of Suljovrujic (2002, 2005) with LDPE indicate the presence of noticeable β relaxations in the high frequency range between temperatures of -50°C and 50°C . However, it can be seen from his works that β relaxations show maximum intensity near 0°C , and on either side of the temperature scale there is a decrease in intensity. Based on these reports, we can infer that the low intensity curve in the high frequency range of the present work visible at 40°C (see inset Fig. 1A) can be attributed to the β relaxations in LDPE. The β relaxations are associated with the glass–rubber transition region and are thought to arise from the amorphous domains, since the decrease in the amorphous fraction leads to the decrease in the intensity of this relaxation. The molecular origin of the β

relaxation process is the motion of side branches, as well as of the chain-end motion (Suljovrujic, 2002).

The relaxation peaks of LDPE in Fig. 1B (low frequency region: 10^{-2} Hz to 10^2 Hz) are similar to those reported by Fu et al. (2007). They observed a fully resolved Debye-type loss peak in the low frequency range at temperatures 60°C and above, for LDPE films which were gamma-irradiated. These peaks shifted to higher frequency with increasing temperature. They attributed these peaks to the Maxwell–Wagner relaxation, which is a form of dielectric polarization typically observed when local regions of conduction are in series with blocking capacitive interfaces. These relaxations represent the presence of charge carriers and/or their mobility in the sample (Fu et al., 2007). However, for the following reasons, caution is exercised in attributing the low frequency peaks of the present work to Maxwell–Wagner relaxations. Fu et al. (2007) had observed the Maxwell–Wagner peaks only for LDPE samples gamma-irradiated in oxidative atmosphere. They did not observe this phenomenon for control (untreated samples) LDPE films. Considering that the LDPE films of the present work are not irradiated, the presence of Maxwell–Wagner relaxation and subsequently the presence and mobility of charge carriers (polar groups) within the sample is implausible.

Polyethylene demonstrates three principal relaxations: α , β and γ in order of decreasing temperature. α processes of polyethylene range from 30°C to 120°C with activation energies ranging between 80 and 210 kJ/mol (Fried, 2007). β relaxations mostly occur at temperatures -53°C to 7°C . γ relaxations occur in the range of -150°C to -120°C . The activation energies of β and γ processes range from 150 kJ/mol to 200 kJ/mol (Fried, 2007). Since the resolved dielectric relaxation peaks in Fig. 1B (low frequency region: 10^{-2} Hz to 10^2 Hz) start appearing around the temperature of 80°C with Arrhenius activation energy of 130 kJ/mol (see later sections), we can infer that these are α relaxations. The origin of dielectric α relaxation of LDPE is still under debate; however, traditionally it has been thought to arise from the chain movements in the intracrystalline regions of LDPE (Vaisman et al., 2003).

At frequencies lower to the α peak (Fig. 1B), an increase in ε'' is observed, which can be attributed to the d.c. conductivity of LDPE. The d.c. conductivity at 40°C was found to be $3.15 \times 10^{-16} \text{ S/cm}$. This increased with increasing temperature.

3.2.2. Dielectric relaxations of LDPE film subjected to stress conditions

Subsequent to the exposure at 70°C for 12 h, dielectric loss spectra were recorded for both the films (dry and water-treated) in high and low frequency range at selected temperatures. In the previous experiment, a complete α relaxation peak appeared at high instrument temperature (80°C). Therefore, for this experiment the spectra were recorded at 80°C , 85°C , 90°C and 95°C (Fig. 2). Loss spectra in the high frequency range (10^2 Hz to 10^6 Hz) did not show any peaks and therefore were not analyzed further. Loss spectra at low frequencies (10^{-2} Hz to 10^2 Hz) (Fig. 2A–D) revealed α relaxation peak at all studied temperatures. However, this relaxation peak merged with the d.c. conductivity (identified by a straight line with negative slope in $\log/\log \varepsilon''$ vs. frequency plot) at higher temperature of 95°C .

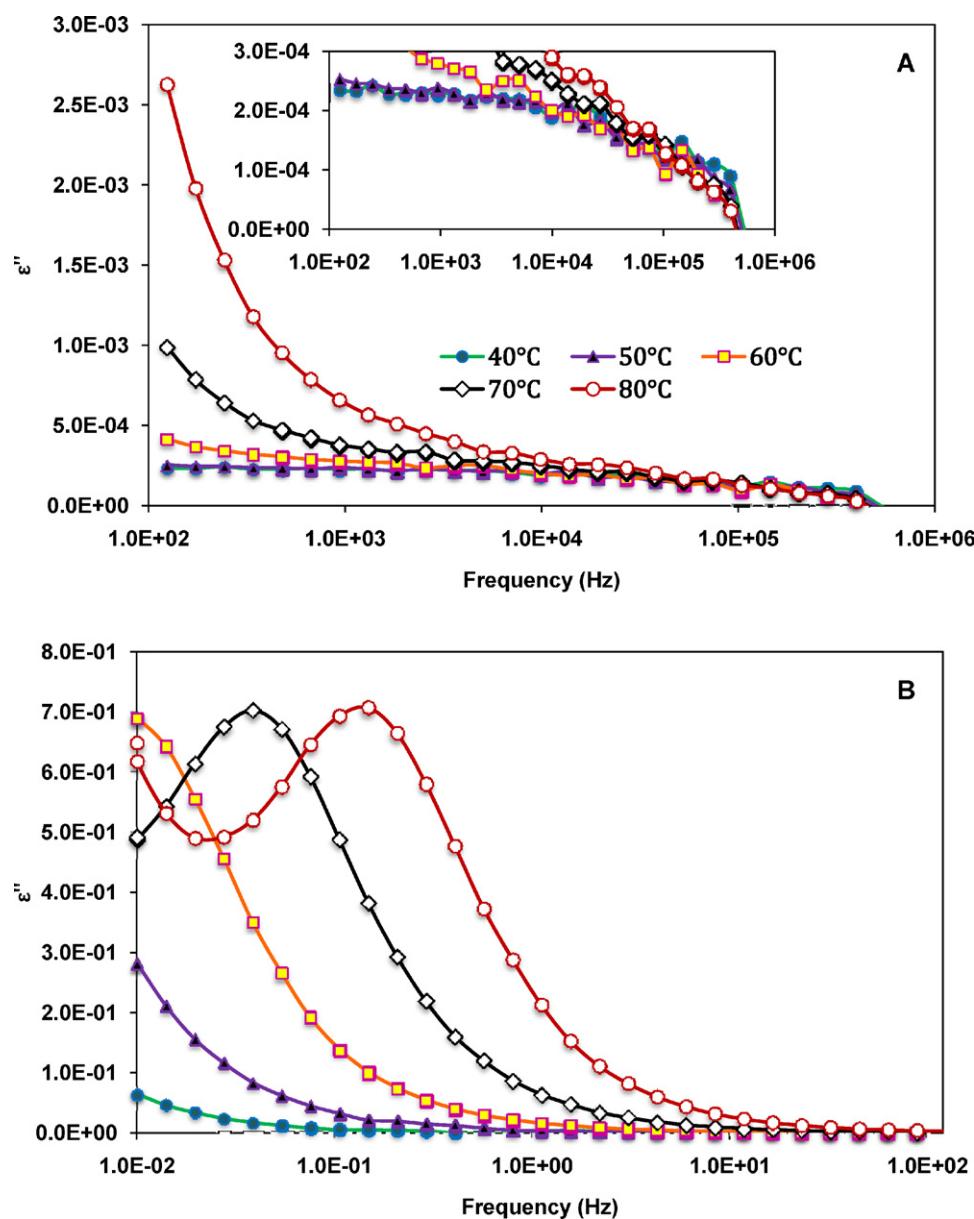


Fig. 1. Imaginary permittivity (dielectric loss) spectra of virgin LDPE film in the high frequency range (A) and low frequency range (B) at various instrument temperatures ranging from 40 °C to 80 °C. Inset in (A), which shows the zoomed in plot of permittivity curves, indicates the presence of a weak peak at lower temperatures.

The intensity of α relaxation peak was almost same for both, the dry and water-exposed films. However, the peak shifted to higher frequency for the water-exposed film. This difference in peak-max frequencies was most prominent at temperatures of 80 °C and 85 °C. Relaxation at higher frequency (Hz) indicates a lower relaxation time (τ_α in seconds) i.e. faster chain relaxations as compared to the dry film. The resolved ε'' peaks at 80 °C, 85 °C and 90 °C were fitted to the HN-equation and the resulting τ values (τ_α or τ_{HN}) are reported in Table 2.

3.2.3. Dielectric relaxations of LDPE film pouches stored at 25% RH and 75% RH

Although the above experiment indicated the effect of water on LDPE relaxations, caution needs to be exercised in extrapolating these results to the actual stability studies which employed comparatively milder conditions (40 °C with 25% or 75% RH). Also, an obvious argument arises, regarding the presence of water (100% RH) inside FFS packs at 25% RH or 75% RH. So, with 100% RH inside

the packs, could the polymeric chain relaxations differ due to external humidity? To address this doubt, and to make the DES results relevant to the actual stability conditions, the stability conditions (with 100% RH inside) were simulated with LDPE films. LDPE films

Table 2

Fit parameters of dielectric response of (i) dry LDPE film stored at 70 °C and (ii) LDPE film immersed in water at 70 °C. Relaxation times of α loss peak (τ_{HN}), at various temperatures, were obtained by fitting the frequency dependent imaginary permittivity peaks to the HN-equation.

Instrument temperatures (°C)	Relaxation times (τ_{HN}) for α relaxation (s)	
	Dry LDPE film stored at 70 °C	LDPE film immersed in water stored at 70 °C
80	1.222	0.710
85	0.704	0.594
90	0.394	0.372

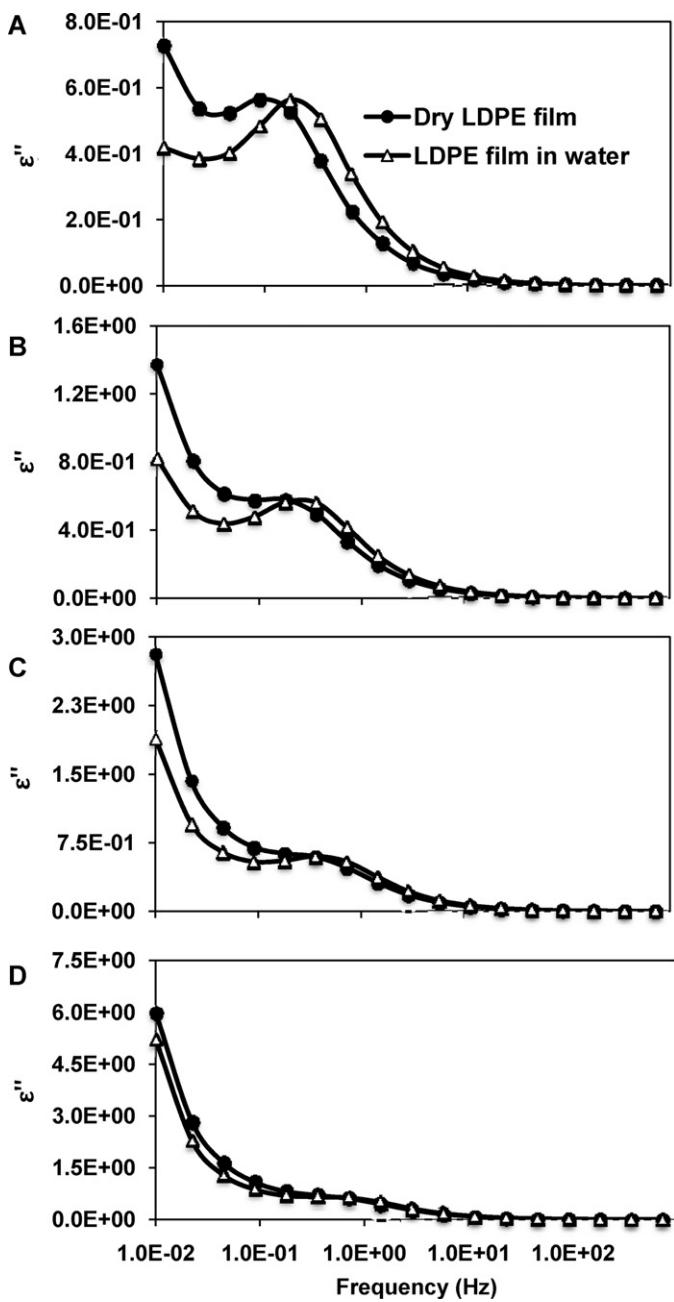


Fig. 2. Comparison of imaginary permittivity of dry LDPE film and film immersed in water, both stored at 70 °C for 12 h. Spectra were taken as a function of frequency in the low frequency range at instrument temperatures of 80 °C (A), 85 °C (B), 90 °C (C) and 95 °C (D).

were made into pouches and filled with water. They were charged (in triplicate) at 40 °C/25% RH and 40 °C/75% RH for two weeks.

At the end of 2 weeks, pouches ($n=3$) were subjected to a detailed DES analysis. In the previous experiment, it was observed that 80 °C instrumental temperature presented the optimum temperature to record a resolved dielectric relaxation peak. Therefore, for determining the activation energies of α relaxation, a temperature range of 75 °C to 87 °C, with 3 °C increments, was chosen for the study.

Fig. 3 compares the dielectric loss spectra of LDPE film from pouches stored at 25% RH and 75% RH at the five selected temperatures. The error bars indicate good reproducibility at the peak values. The spectra were fitted to HN-equation to get the relaxation times (τ_{HN}), HN-shape parameters, α and β , which are presented in

Table 3. At all temperatures studied, significantly lower relaxation times were observed for LDPE pouches stored at higher humidity (75% RH), indicating faster relaxations induced in LDPE by higher humidity. The HN-shape parameter, α , gradually decreased, for LDPE pouches stored at 25% RH, from 0.942 to 0.913 with increasing instrument temperature. However, it decreased for LDPE pouches stored at 75% RH, only slightly, from 0.947 to 0.932. At 87 °C instrument temperature, the α parameter is statistically different indicating differences in the slope of the low frequency side of the relaxation peak. The β parameter remained constant throughout the temperature range of study and among different humidity conditions.

In this case (Fig. 3), unlike the previous one, visually, the intensity of the loss peak is not the same. As observed from Fig. 3, LDPE treated to higher humidity gave a lower d.c. conductivity. It might be the higher contribution of d.c. conductivity in the 25% RH samples, which raised the intensity (visually) of the loss peak. This was confirmed by similar $\Delta\epsilon$ (dielectric increment or intensity) values obtained by the HN-fitting, for both samples.

Temperature dependence of the dielectric relaxations ($\log(\tau) \rightarrow f(1/T)$) of α relaxations can be described either by the Vogel–Fulcher–Tammann (VFT) relationship (Eq. (3)) or, by the Arrhenius plot (Eq. (4)) (Sengers et al., 2005).

$$\tau(T) = \tau_{\infty} \exp \left[\frac{E_V}{R(T - T_V)} \right] \quad (3)$$

Here τ_{∞} is the pre-exponential factor, E_V is the 'Vogel' energy in kJ/mol, R is the gas constant and T_V is the reference temperature.

The Arrhenius type behaviour can be characterized by the following equation:

$$\tau(T) = \tau_{\infty} \exp \left(\frac{E_a}{RT} \right) \quad (4)$$

where E_a denotes a 'true' Arrhenius activation energy.

The latter (Arrhenius relationship) is always typical for the thermally activated process and is observed in a temperature range far from the glass transition zone of polymer. The former usually describes the relaxation which can be related to a step-like transition in the DSC curve (Danch et al., 2003).

Calculated relaxation times (τ_{HN}) from the respective spectra were used to construct Arrhenius plots for LDPE at 0-day, P4025 and P4075 (Fig. 4). The Arrhenius fit parameters for the same are presented in Table 4. The activation energy is maximum for the dry 0-day LDPE film, followed by P4025 and P4075. This indicates that the chain mobility is most restricted for 0-day LDPE film. The chain mobility increases for P4025, followed by P4075. This again implicates the role of water in plasticization of LDPE. The pre-exponential factor (τ_{∞} , entropy effect) with the highest value, indicating least cooperativity in relaxation, was observed for P4075, followed by P4025, and untreated LDPE film.

Giacin and Hernandez (1997) have presented numerous examples of effect of humidity on transport properties of polymers. These examples show that humidity increased the mass transport properties of numerous polymers, thus indicating its plasticization effects. However, Delassus was of the opinion that polyolefins, being hydrophobic, do not have tendency to absorb water in concentrations which are high enough to alter their barrier/permeability properties (Delassus, 1997). Nevertheless, in the present work, statistically significant differences in the sorption of parabens stored at two humidity conditions were observed.

The effect of plasticization on the relaxation times and activation energy of polymer relaxations has been previously studied using dielectric spectroscopy. The activation energy indicates the energy barrier that must be overcome for molecular relaxation. Plasticized poly(vinyl chloride) showed lower relaxation times and activation

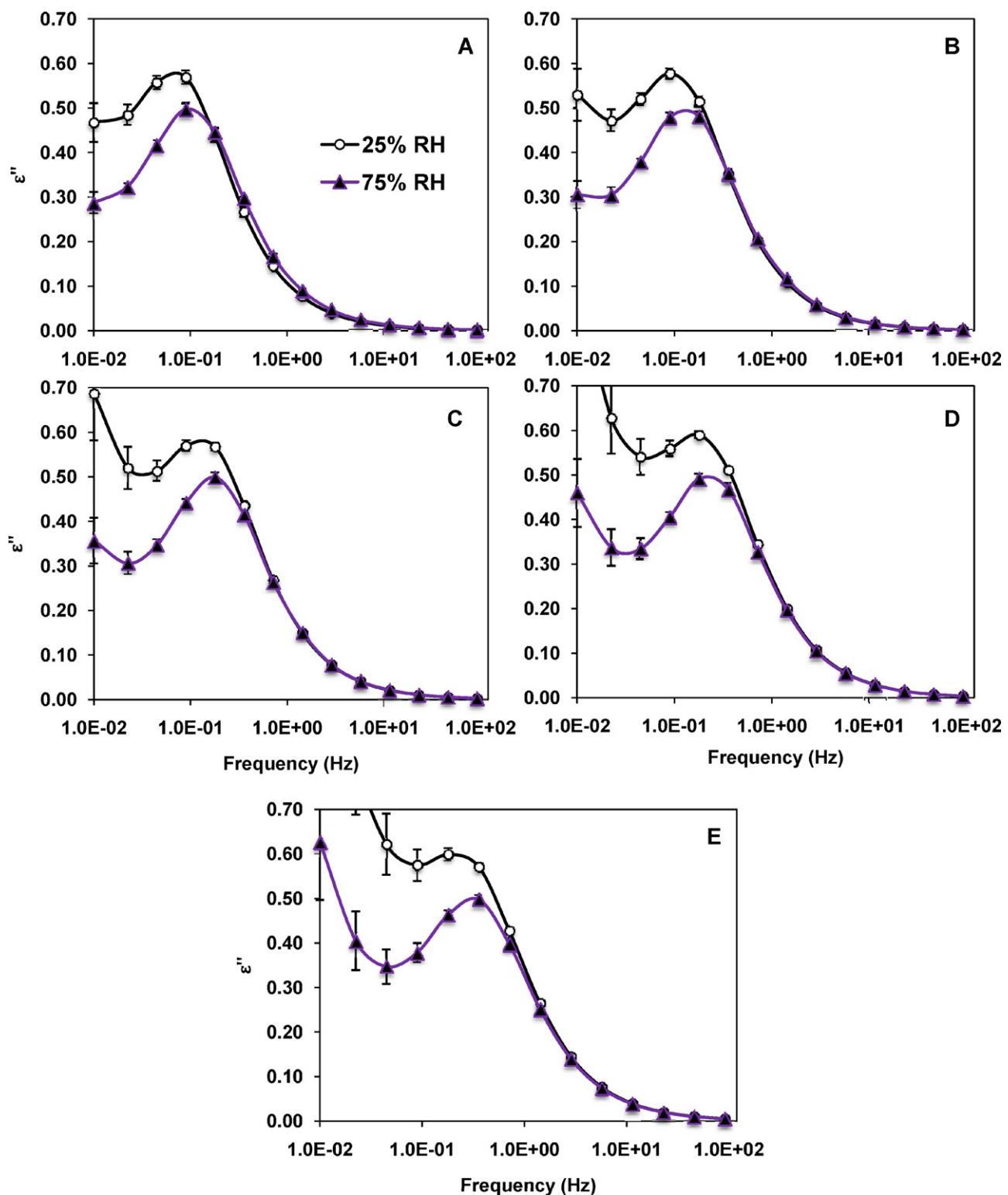


Fig. 3. Comparison of imaginary permittivity of LDPE film pouches exposed to 25% RH and 75% RH. The studies were carried out at 40 °C for a duration of 2 weeks. The spectra are compared at instrument temperatures of 75 °C (A), 78 °C (B), 81 °C (C), 84 °C (D) and 87 °C (E).

energy for the α relaxations, indicating higher molecular mobility (Elicegui et al., 1997). Likewise, maltose, an oligomer, when plasticized by glycerol, showed a decrease in activation energy of α relaxation (Lourdin et al., 1998).

In literature, the plasticization effect of water on polymers has been associated with concomitant changes in the dielectric relaxation. Pissis et al. (1999) observed an overall increase in molecular

mobility of polyacrylamide hydrogel, indicated by a decrease in relaxation times, with increasing hydration. Xian and Karbhari (2007) proved the role of water ingress in facilitating segmental relaxations in epoxy resins by studying the relaxation time and activation energy of wet and rejuvenated (dried) samples. They found wet samples showing lower relaxation times and activation energy than the dried epoxy samples.

Table 3

HN fit parameters of dielectric relaxations of LDPE film pouches stored in 25% RH and 75% RH for two weeks at a temperature of 40 °C. The values indicate average \pm standard deviation (of 3 samples).

Temp. (°C)	LDPE film pouches stored at 25% RH			LDPE film pouches stored at 75% RH		
	τ_{HN} (s)	α parameter	β parameter	τ_{HN} (s)	α parameter	β parameter
75	2.049 \pm 0.084	0.942 \pm 0.006	1.000 \pm 0.000	1.482 \pm 0.049*	0.947 \pm 0.001	1.000 \pm 0.000
78	1.422 \pm 0.044	0.940 \pm 0.006	1.000 \pm 0.000	1.153 \pm 0.014*	0.947 \pm 0.002	1.000 \pm 0.000
81	1.019 \pm 0.018	0.939 \pm 0.006	1.000 \pm 0.000	0.856 \pm 0.014*	0.945 \pm 0.002	1.000 \pm 0.000
84	0.743 \pm 0.012	0.929 \pm 0.009	1.000 \pm 0.000	0.640 \pm 0.014*	0.940 \pm 0.004	1.000 \pm 0.000
87	0.557 \pm 0.002	0.913 \pm 0.009	1.000 \pm 0.000	0.473 \pm 0.018*	0.932 \pm 0.006#	1.000 \pm 0.000

* Significantly different from the corresponding τ value of LDPE stored at 25% RH, using *t*-test at $p < 0.001$.

Significantly different from the corresponding α value of LDPE stored at 25% RH, using *t*-test at $p < 0.05$.

Table 4

Arrhenius fit parameters of dielectric relaxation times of film pouches stored in 25% RH and 75% RH, for 2 weeks. The temperature range of the data is 75–87 °C. The fit parameters for LDPE film at 0-day are given for comparison.

Arrhenius fit parameters	LDPE film at 0-day	LDPE film pouches stored at 25% RH (P4025)	LDPE film pouches stored at 75% RH (P4075)
Activation energy, E_a (kJ/mol)	130.139	113.112	99.735
Pre-exponential factor, τ_{∞} (s)	7.98E–20	2.16E–17	1.65E–15
R^2	0.9944	0.9988	0.9982

On similar lines, in the present work also, the lowering of relaxation times and activation energy of α relaxation of LDPE on exposure to higher humidity reflects the plasticization effect of water on LDPE.

The origin of α relaxation in LDPE is however, not clear. Initially, it was thought to arise from the chain motions in the intra-crystalline regions. Later, an investigation by Danch et al. (2003) using differential scanning calorimetry, dynamic mechanical thermal analysis and positron lifetime measurements, led to the conclusion that the α relaxations of LDPE did not arise from the intra-crystalline regions as originally assumed, but resulted from large-scale motion of the macromolecular segments located within the constrained amorphous regions. These regions are present at the interface of crystalline and amorphous domains.

Permeant molecules traversing across a semi-crystalline polymer do not penetrate the *crystalline region*, and their permeation is facilitated by the segmental motions above T_g in the *amorphous regions only* (Schott, 2001). Plasticization effect of the traversing solute (faster relaxations) should therefore be observed in amorphous regions. The results of the present study, i.e. changes in the α -relaxation of LDPE on exposure to humidity, implied the origin of α -relaxation to be large scale motion of the macromolecular seg-

ments located in the constrained amorphous regions as reported by Danch et al. (2003).

4. Conclusion

Higher sorption of parabens in LDPE packs, when stored at higher humidity, was postulated to be due to the structural changes in LDPE induced by water. The present study indicated that humidity did not affect the degree of crystallinity of the LDPE packs. Dielectric spectroscopy, however, revealed the changes in molecular relaxations of LDPE. The lowering of relaxation times and activation energy, of the α -relaxations, at higher humidity, indicated that water had a plasticization effect on LDPE. This work presents added evidence that the α -relaxations of LDPE originated from the constrained amorphous regions and not the crystalline regions. The differences in molecular relaxations, at different humidity conditions, can lead to changes in the sorptive capacity of the packing material. This study has implications on the selection of humidity conditions during the storage of liquid products packed in semi-permeable containers. Although, a low RH enhances the water loss from the product, it also suppresses the molecular mobility (and hence sorptive capacity) of LDPE. The authors suggest the employment of two stability conditions (one with lower RH and another with higher RH) for accelerated stability studies. This will enable the formulation scientist to envisage the worst-case scenario both in terms of water loss as well as sorption loss of formulation components.

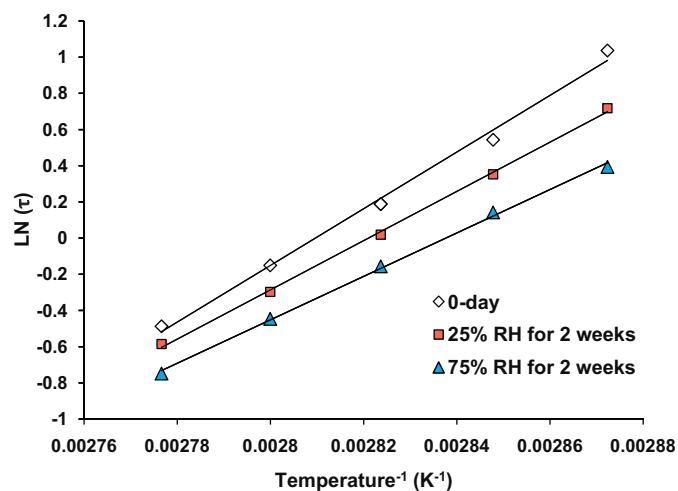
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References

Feb., 2003. International Conference on Harmonization, Q1A(R2): Stability Testing of New Drug Substances and Products, Geneva, Switzerland.
 Amin, A., Chauhan, S., Dare, M., Bansal, A.K., 2010. Sorption of antimicrobial agents in blow-fill-seal packs. *Pharm. Dev. Technol.*, doi:10.3109/10837450.10832010.10516438, Online.

Fig. 4. Arrhenius dependence of relaxation times (τ) of untreated LDPE film and water-filled film pouches stored at 25% RH and 75% RH, for 2 weeks.



Bergquist, P.A., Kemp, E.A., Seburg, R.A., Zhu, L.M., 2006. Acceleration of paraben sorption to polyethylene terephthalate: a freeze-thaw phenomenon. *PDA J. Pharm. Sci. Technol.* 60, 240–247.

Borek, J., Osoba, W., 2001. Free volume changes in physically aged polyethylene by positron annihilation. *Polymer* 42, 2901–2905.

Chabira, S.F., Sebaa, M., Huchon, R., Jeso, B.D., 2006. The changing anisotropy character of weathered low-density polyethylene films recognized by quasi-static and ultrasonic mechanical testing. *Polym. Degrad. Stab.* 91, 1887–1895.

Charmette, C., Sanchez, J., Gramain, P., Masquelez, N., 2009. Structural characterization of poly(ethylene oxide-co-epichlorohydrin) membranes and relation with gas permeation properties. *J. Membr. Sci.* 344, 275–280.

Craig, D.Q.M., 1995. The analysis of polymeric systems. In: Craig, D.Q.M. (Ed.), *Dielectric Analysis of Pharmaceutical Systems*. Taylor & Francis, London, pp. 154–187.

Croce, C.P., Fischer, A., Thomas, R.H., 1991. Packaging material science. In: Lachman, L., Lieberman, H.A., Kanig, J.L. (Eds.), *The Theory and Practice of Industrial Pharmacy*, 3rd ed. Varghese Publishing House, Bombay, pp. 711–732.

Danch, A., Osoba, W., Stelzer, F., 2003. On the α relaxation of the constrained amorphous phase in poly(ethylene). *Eur. Polym. J.* 39, 2051–2058.

Delassus, P., 1997. Barrier polymers. In: Brody, A.L., Marsh, K.S. (Eds.), *The Wiley Encyclopedia of Packaging Technology*, 2nd ed. John Wiley & Sons, Inc., New York, pp. 71–77.

Elicegui, A., Val, J.J.d., Bellenger, V., Verdu, J., 1997. A study of plasticization effects in poly(vinyl chloride). *Polymer* 38, 1647–1657.

Fried, J.R., 2007. Sub- T_g transitions. In: Mark, J.E. (Ed.), *Physical Properties of Polymer Handbook*, 2nd ed. Springer Science + Business Media, New York, pp. 217–232.

Friess, K., Jansen, J.C., Vopička, O., Randoval, A., Hynek, V., Šípek, M., Bartovská, L., Izák, P., Dingemans, M., Dewulf, J., Langenhove, H.V., Drioli, E., 2009. Comparative study of sorption and permeation techniques for the determination of heptane and toluene transport in polyethylene membranes. *J. Membr. Sci.* 338, 161–174.

Fu, M., Chen, G., Dissard, L.A., Fothergill, J.C., Zou, C., 2007. The effect of gamma irradiation on space charge behaviour and dielectric spectroscopy of low-density polyethylene. In: Proceedings of the IEEE International Conference on Solid Dielectrics, pp. 442–445, <http://hdl.handle.net/2381/4007>.

Giacin, J.R., Hernandez, R.J., 1997. Permeability of aromas and solvent in polymeric packaging material. In: Brody, A.L., Marsh, K.S. (Eds.), *The Wiley Encyclopedia of Packaging Technology*, 2nd ed. John Wiley & Sons, Inc., New York, pp. 724–733.

Hedenqvist, M., Angelstok, A., Edsberg, L., Larsson, P.T., Gedde, U.W., 1996. Diffusion of small-molecule penetrants in polyethylene: free volume and morphology. *Polymer* 37, 2887–2902.

Holdsworth, D.G., Roberts, M.S., Polak, A.E., 1984. Fate of chlorbutol during storage in polyethylene dropper containers and simulated patient use. *J. Clin. Hosp. Pharm.* 9, 29–39.

Huang, Y., Paul, D.R., 2004. Physical aging of thin glassy polymer films monitored by gas permeability. *Polymer* 45, 8377–8393.

Illum, L., Bungaard, H., 1982. Sorption of drugs by plastic infusion bags. *Int. J. Pharm.* 10, 339–351.

Kenley, R.A., Jenke, D.R., 1990. Determination of solute–polymer interaction properties and their application to parenteral product container compatibility evaluations. *Pharm. Res.* 7, 911–918.

Komatsuka, T., Kusakabe, A., Nagai, K., 2008. Characterization and gas transport properties of poly(lactic acid) blend membranes. *Desalination* 234, 212–220.

Lee, K.J., Jho, J.Y., Kang, Y.S., Dai, Y., Robertson, G.P., Guiver, M.D., Won, J., 2003. Gas transport in modified polysulfones with trimethylsilyl groups: effect of substitution site. *J. Membr. Sci.* 212, 147–155.

Lourdin, D., Ring, S.G., Colonna, P., 1998. Study of plasticizer \pm oligomer and plasticizer–polymer interactions by dielectric analysis: maltose–glycerol and amylose–glycerol–water systems. *Carbohydr. Res.* 306, 551–558.

Lützow, N., Tihminlioglu, A., Danner, R.P., Duda, J.L., Haan, A.D., Warnier, G., Zielinski, J.M., 1999. Diffusion of toluene and *n*-heptane in polyethylenes of different crystallinity. *Polymer* 40, 2797–2803.

Neway, B., 2003. The influence of morphology on the transport and mechanical properties of polyethylene. Royal Institute of Technology, Stockholm.

O'Leary, K.A., Paul, D.R., 2006. Physical properties of poly(*n*-alkyl acrylate) copolymers. Part 1. Crystalline/crystalline combinations. *Polymer* 47, 1226–1244.

Pearson, D.S., Smith, G., 1998. Dielectric analysis as a tool for investigating the lyophilization of proteins. *Pharm. Sci. Technol. Today* 1, 108–117.

Pino, M., Duckett, R.A., Ward, I.M., 2005. Single and mixed gas diffusion through polyethylene films. *Polymer* 46, 4882–4890.

Pissis, P., Kyritsis, A., Konsta, A.A., Daoukaki, D., 1999. Polymer–water interactions in PAA hydrogels. *Colloids Surf. A Physicochem. Eng. Aspects* 149, 253–262.

Richards, J.J., Danquah, M.K., Kalakkunath, S., Kalika, D.S., Kusuma, V.A., Matteucci, S.T., Freeman, B.D., 2009. Relation between structure and gas transport properties of polyethylene oxide networks based on crosslinked bisphenol A ethoxylate diacrylate. *Chem. Eng. Sci.* 64, 4707–4718.

Richardson, N.E., Davies, D.J.G., Meakin, B.J., Norton, D.A., 1977. Loss of antibacterial preservatives from contact lens solutions during storage. *J. Pharm. Pharmacol.* 29, 717–722.

Roberts, M.S., Cossum, P.A., Galbraith, A.J., Boyd, G.W., 1980. The availability of nitroglycerin from parenteral solutions. *J. Pharm. Pharmacol.* 32, 237–244.

Roberts, M.S., Cossum, P.A., Kowaluk, E.A., Polack, A.E., 1983. Factors affecting the availability of organic nitrates from plastic infusion systems: structure of organic nitrate, nature of plastic and effect of temperature. *Int. J. Pharm.* 17, 145–159.

Schott, H., 2001. Polymer science. In: Martin, A. (Ed.), *Physical Pharmacy*, 4th ed. Lippincott Williams & Wilkins, MD, pp. 556–594.

Sengers, W.G.F., Berg, O.v.d., Wübbendorst, M., Gotsis, A.D., Picken, S.J., 2005. Dielectric spectroscopy using dielectric probes: a new approach to study glass transition dynamics in immiscible apolar polymer blends. *Polymer* 46, 6064–6074.

Suljovrujic, E., 2002. Dielectric studies of molecular β -relaxation in low density polyethylene: the influence of drawing and ionizing radiation. *Polymer* 43, 5969–5978.

Suljovrujic, E., 2005. Some aspects of structural electrophysics of irradiated polyethylenes. *Polymer* 46, 6353–6359.

Vaisman, L., González, M.F., Marom, G., 2003. Transcristallinity in brominated UHMWPE fiber reinforced HDPE composites: morphology and dielectric properties. *Polymer* 44, 1229–1235.

Wong, M., Marion, R., Reed, K., Wang, Y., 2006. Sorption of unoprostone isopropyl to packaging materials. *Int. J. Pharm.* 307, 163–167.

Xian, G., Karbhari, V.M., 2007. Segmental relaxation of water-aged ambient cured epoxy. *Polym. Degrad. Stab.* 92, 1650–1659.