

Research Article

Relaxation Kinetic Study of Eudragit® NM30D Film Based on Complex Modulus Formalism

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Abstract. This study is aimed at resolving and characterizing the primary (α) and secondary relaxations (β) in Eudragit® NM30D film based on apparent activation energies derived from complex modulus formalism using dielectric analysis (DEA). The glass transition (T_g) of the film was determined using differential scanning calorimetry (DSC). The α relaxation corresponding to T_g and the β relaxations occurring below T_g were probed using DEA. The occurrence of α and β relaxations in Eudragit® NM30D film was elucidated using the complex modulus of the dielectric response employing loss modulus and permittivity data. Activation energies of these relaxations and the fundamental frequency so determined support the assignment of the relaxation pattern in the Eudragit® NM30D film. DEA methodology of the complex modulus formalism is a useful tool for differentiating the α and β relaxation kinetics in Eudragits® not easily studied using traditional thermal methods such as DSC. The kinetics associated with α and β relaxations so determined will provide formulation design support for solid orals that incorporate Eudragit® polymers. As mobility changes can affect stability and diffusion, the dipolar α and β relaxations revealed through DEA analysis may enable a better correlation to functionality of Eudragit® based pharmaceutical dosage forms.

KEY WORDS: activation energy; loss modulus; permittivity; primary relaxation; secondary relaxation.

INTRODUCTION

Molecular motions typically occurring in polymers in the glassy state can be classified as primary (α) and higher order, secondary (β, γ) relaxations. The α relaxation processes relate to long-range translational motion of the polymer occurring at and above the glass transition (T_g) of the polymer. The secondary relaxation processes correspond to short-range motion arising from the rotation of side chains within the polymer at temperatures below the T_g . Polymethacrylates exhibit α relaxation related to motion of the polymer backbone and β relaxation corresponding to rotation of the acetyl side groups. Internal motion within the side group arising from rotation of methyl groups and oxy carbonyl groups gives rise to the γ relaxation process. Secondary relaxation (β) in glassy polymers may also be induced by the presence of a diluent in the polymer system (1,2).

Glassy state relaxations can be studied using DSC, which detects the energy of the transitions; however, the

method suffers from the fact that these are low energy transitions and therefore often very challenging to detect (3). Dielectric analysis (DEA), which is a structural complement to the energetically based thermal analysis method, detects the motion of permanent dipoles. DEA is often a more sensitive method in ascertaining individual relaxations, as it sees very small changes (molecular relaxation of the order of nanometers) under an applied electric field at varying frequencies and has the additional advantage of requiring minimal sample preparation/manipulation relative to that required by DSC (4,5).

Dielectric relaxation behavior in acrylate polymer films such as poly(methyl methacrylate) (PMMA) has been studied extensively by polymer scientists; however, DEA has not been commonly used to describe dielectric relaxations (particularly β relaxations) of Eudragits®, which are acrylate-based polymers, widely used in pharmaceuticals. The molecular level changes in these Eudragit® films have the potential to manifest as macroscopic changes in the film structure and also alter the functionality of film-coated dosage forms (6).

This report is focused on elucidating the occurrence and the kinetics of α and β relaxations of Eudragit® NM30D film, a polymer widely used for sustained release formulations (7). Studying the relaxation processes and assessing their kinetics will help to correlate molecular relaxation contributions to stability and diffusion mechanisms, which could affect the product performance of dosage forms using Eudragit® polymers.

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Dielectric Relaxation Theory

Dielectric analysis of a polymer sample involves measuring the current in response to the energy dissipated from reorientation of dipoles within a material subjected to an oscillating electric field (1,4). In the DEA of amorphous polymers, the relatively lower frequency α “peaks” correspond to the cooperative motion of the polymer backbone, while the higher frequency peaks β and γ are manifestations of noncooperative or “local” mechanisms. The noncooperative side chain relaxations also occur above T_g , but it is in the glassy state that these relaxations may become uncoupled from the α relaxations and hence are better observed (1,8,9).

In DEA, the magnitude of the response and the phase relationship between the voltage and the current for the sample studied is expressed by complex permittivity (ϵ^*). It consists of a real (ϵ') out of phase component and an imaginary (ϵ'') in phase component expressed as (1,4,6):

$$\epsilon^* = \epsilon' - i\epsilon''$$

Both ϵ' and ϵ'' are functions of the measurement frequency, and the ratio of ϵ''/ϵ' is called the dissipation or loss tangent:

$$\tan \delta = \epsilon''/\epsilon'$$

where δ is the phase angle between the applied voltage and the current response.

The orientation model proposed by Debye assumes an ideal behavior of a monodisperse population of spherical dipoles and expresses the relative permittivity (ϵ') representing the amount of alignment of dipoles and loss factor (ϵ''), which is the energy required for the alignment of the dipoles as:

$$\epsilon'' = (\epsilon_0 - \epsilon_\infty)\omega\tau / [1 + (\omega\tau)^2]$$

$$\epsilon' = \epsilon_\infty + (\epsilon_0 - \epsilon_\infty) / [1 + (\omega\tau)^2]$$

where ϵ_0 is the permittivity at low frequency, ϵ_∞ is the permittivity at high frequency, and τ is the dipole relaxation time inversely related to the angular frequency of relaxation ω , which is a function of frequency ν ($\nu = \omega/2\pi$).

For relaxations that follow Debye's model (for dipoles in a viscous fluid), which are noncooperative rotational motions such as β and γ , an Arrhenius dependence with temperature (T) is observed (10).

$$\nu = \nu_0 \exp(-E_a/kT)$$

where ν_0 and ν are low and high frequency, respectively, E_a is activation energy, and k is the Boltzmann constant.

Cooperative motions arising from α relaxations as well as motion of molecules or ions in dissimilar environments show

non-Arrhenius behavior described by the Vogel–Fulcher–Tammann equation (VFT) (10,11).

$$\nu = \nu_0 \exp(-dT_0/T - T_0)$$

where d is a dimensionless quantity called strength parameter.

The strength parameter d is quantified as the fragility index m , given by the expression (11):

$$m = \left[\frac{d \log(\tau)}{d(T_g/T)} \right]_{T=T_g}$$

The extent of the deviation from Arrhenius behavior is described by m , which classifies the polymers as strong or fragile glass formers. Strong glass formers have small m values that follow closely an Arrhenius behavior ($m=16$), while a fragile polymer shows large deviations from the Arrhenius kinetics (11).

The dielectric relaxation spectra of many heterogeneous low and high molar mass supercooled systems, which exhibit dipolar relaxations (α, β, γ), may be masked by interfacial polarization or Maxwell–Wagner–Stellar (MWS) effects, electrode polarization, and conductivity relaxation arising from charge migration in the polymer system (1,8,9). The MWS effect occurs from the accumulation of free charges between different phases or domains within the bulk of a polymer. Separate phases of a polymer film may be formed in a non-homogeneous film due to presence of moisture, monomers, and additives (12). Electrode polarization occurs due to charge build-up at the interface of the sample and the electrode. Complexities that may arise from incomplete contact of the film with the sensor and also discontinuity of film from cracks or voids can form spurious boundary layers that give rise to discharged ions (9,12). All the above are characteristic of the structural variation in a polymer film and occur at low frequencies since the dipoles have sufficient time to align with the electric field. Thus, at the low frequency region of the dielectric relaxation spectrum, the level of homogeneity of the polymer may be inferred and transitions relating to either dipolar viscoelastic relaxations or conductivity relaxation can be resolved by examination of ϵ^* .

In complex modulus formalism, the viscoelastic behavior and conductivity relaxations are better expressed by the complex electric modulus, M^* the inverse of ϵ^* given by (1,13):

$$M^* = 1/\epsilon^* = M' + iM'' = \epsilon' / (\epsilon'^2 + \epsilon''^2) + i\epsilon'' / (\epsilon'^2 + \epsilon''^2)$$

where M' and M'' are permittivity modulus and loss modulus, respectively.

The model for M^* corrects for the affects from nonhomogeneity in the polymer and allows elucidation of the MWS and electrode polarization affects, thus separating the conductivity behavior due to mobility of free charges from dipolar relaxations. A distribution of relaxation times occurs for dipolar relaxations; these can be distinguished from conductivity relaxations that follow a Debye model assuming a single relaxation time (13). The frequency dependence of M'' vs. M'

given by an Argand plot shows a semicircle for a Debye model; however, dipolar relaxations deviate from the Debye model and do not show a semicircle in an Argand plot (1,12,13). Thus, based on the analysis of the M^* dielectric data, the relaxation behavior of a polymer film and their kinetics can be assessed.

MATERIALS AND METHODS

Eudragit® NM30D Film

Aqueous dispersion (30%) of Eudragit® NM30D, a poly(ethylacrylate-co-methyl methacrylate) copolymer, was donated by Röhm America Inc (Piscataway, NJ, USA) and used as received (Fig. 1). The average molar mass of Eudragit® NM30D is 600,000 g/mol. Eudragit® NM30D films were prepared by casting the dispersion onto rectangular silicone cookie dies and allowed to dry at room temperature (RT) for 48 h. After film formation the films were cured at 60°C for 1 h in a constant temperature oven. Films stored at RT were cut to appropriate dimensions for parallel plate sensor DEA studies after measuring the thickness of the film samples using a micrometer (Mitutoyo).

Differential Scanning Calorimetry

Measurements were made using a DSC Q10 (TA instruments) at a heating rate of 10°C/min. Eudragit® NM30D film sample was analyzed in hermetic sealed aluminum pans for the T_g after taking a baseline and performing temperature calibration using indium.

Thermal Gravimetric Analysis

Eudragit® NM30D film sample was analyzed in a TGA 2050 (TA instruments) at a heating rate of 10°C/min.

Dielectric Analysis

Dielectric measurements were made using a DEA 2970 (TA instruments). The Eudragit® NM30D film sample was placed on gold plated parallel plate sensor after calibrating the sensor on the furnace. A ram force of 250 N was applied, and

the distance between the ram and the sensor was maintained (and recorded) based on the film thickness. The DEA was run in the isothermal frequency scan mode keeping the temperature constant while applying a frequency sweep between 1 Hz and 100 kHz under a continuous nitrogen gas purge. The temperature was stepped up at constant increments of 5°C and frequency sweep performed isothermally at each temperature.

RESULTS AND DISCUSSION

Differential Scanning Calorimetry

DSC shows a broad T_g or α relaxation event from approximately -10°C to 30°C (Fig. 2) and does not resolve β transitions. The breadth in T_g is likely due to the presence of a distribution of molecular weights of the co-polymer, which has a relatively high average molar mass of 600,000 g/mol. This may include contributions of different domains within the polymer that slowly relax and/or heterogeneity due to uneven curing. The T_g of the Eudragit® NM30D film in DSC analysis is broad and begins below RT; therefore, it was assumed that the β relaxation corresponding to the rotation of the acetyl groups are decoupled from α relaxations at subzero temperatures below T_g and are visible by DEA analysis.

Thermal Gravimetric Analysis

Eudragit® NM30D films prepared from the aqueous latex dispersion show very little residual moisture, of approximately 0.5% of the film weight (Fig. 3).

Dielectric Analysis

Using DEA, it was possible to differentiate the α and β relaxations in Eudragit® NM30D film and also assign probable causes for the occurrence of these transitions. One can think of the ϵ' as detecting the degree of dipolar motion and the ϵ'' as the energy associated with the motion; hence, they should be correlated when detecting molecular motion. Although DEA data were acquired through all frequencies, for the ϵ' , ϵ'' , and M^* plots, only 1 Hz, 10 Hz, 100 Hz, 1 kHz, 10 kHz, and 100 kHz are presented.

Permittivity

In dielectric analysis, ϵ' relates to molecular mobility in the sample studied, so when a polymer undergoes a structural transition, high ϵ' values should appear in the dielectric relaxation spectrum at low frequencies relative to the characteristic time of the molecular motion. With an increase in temperature, segmental motion of a polymer chain increases, and therefore, ϵ' values also increase (1,14). Increase in ϵ' values can also arise from mobility associated with ions as well as from interfacial polarization occurring in a multiphase/heterogeneous system due to charge accumulation at the interfaces.

In the isochronal ϵ' plot (i.e., ϵ' at each ν vs. T) of Eudragit® NM30D film (Fig. 4), ϵ' values increase gradually from subzero temperatures. The ϵ' values also show an inflection at approximately -10°C at 1 Hz, which is frequency dependent as it shifts with temperature. The temperatures at

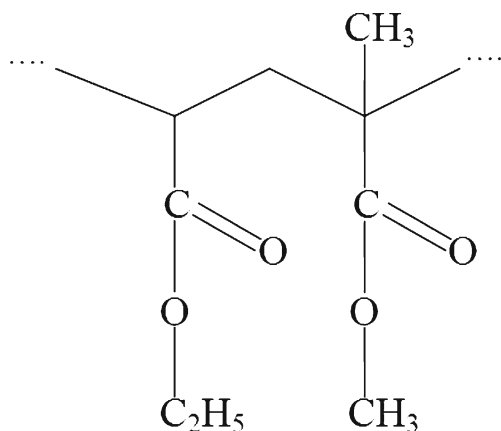


Fig. 1. Eudragit® NM30D chemical structure

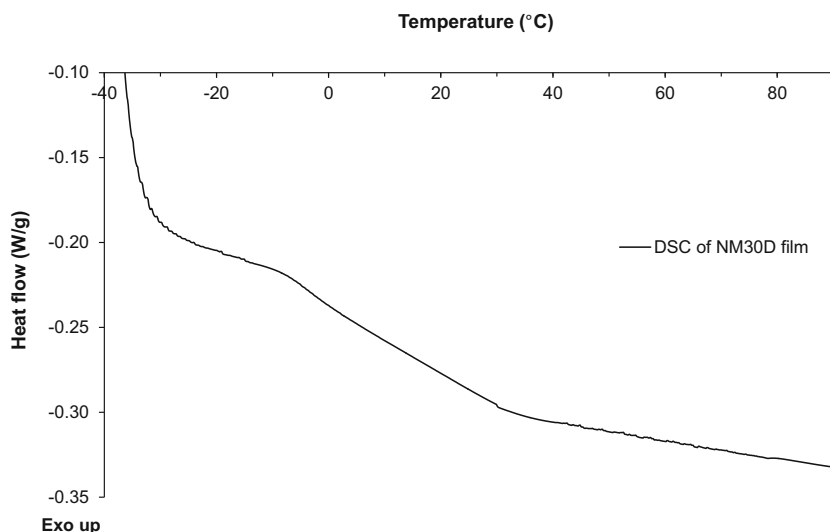


Fig. 2. DSC analysis of Eudragit® NM30D film

which ϵ' values rise significantly at 1 Hz (-10°C and 30°C) correspond well to the onset and offset T_g values observed in DSC analysis of the Eudragit® NM30D film (Fig. 2). In order to ascertain the relaxation mechanisms observed in the ϵ' plot, ϵ'' plots of the dielectric data were further analyzed.

Loss

From analysis of the isochronal ϵ'' plot (Fig. 5), a broad dielectric spectrum with peak maxima at approximately -10°C at 1 Hz occurs, which shifts towards higher temperatures with increasing frequencies. From the isochronal plots of ϵ' and ϵ'' , a good correlation between rise of ϵ' values and occurrence of ϵ'' peak maxima indicate that the relaxations occurring at the temperature range from approximately -10°C to 30°C is dipolar. These ϵ'' peaks beginning at subzero temperatures corresponding to dipolar relaxation are associated with T_g or α relaxation and is consistent with the DSC analysis (Fig. 2).

In the ϵ'' plot (Fig. 5) below -20°C , shoulder peaks are observed at higher frequencies from 1 kHz through 100 kHz from approximately -80°C to -30°C that shift towards higher temperatures. These peak maxima may correspond to β relaxation associated with rotation of the acetyl side groups, as such small-scale motion are usually observed as shoulder peaks near α relaxation (2).

Sharp rise in ϵ'' values are observed at 1 Hz from 50°C (Fig. 5, inset) that shift with temperature but do not show any ϵ'' maxima peaks when the complete ϵ'' vs. T data is plotted. These high ϵ'' values at lower frequencies, which decrease from 1 Hz to 10 Hz seem to completely mask the occurrence of ϵ'' peak maxima occurring at lower temperatures (Fig. 5) and are most likely associated with free charge motion due to conductivity. In a heterogeneous polymer system, there is often a charge build-up within the polymer (interfacial polarization) and between the electrode and the polymer (electrode polarization) causing conduction. This is supported by the isothermal log ϵ'' plot (Fig. 6), which does not show ϵ'' peak

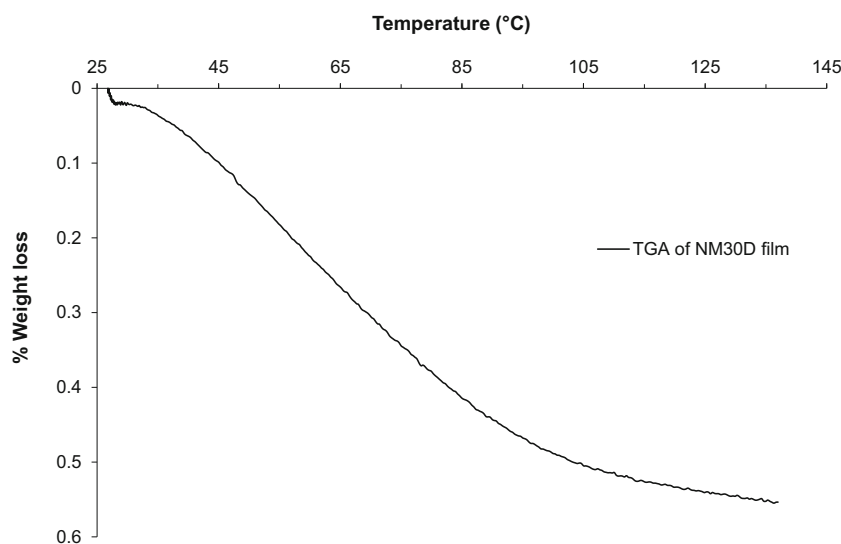


Fig. 3. TGA analysis of Eudragit® NM30D film

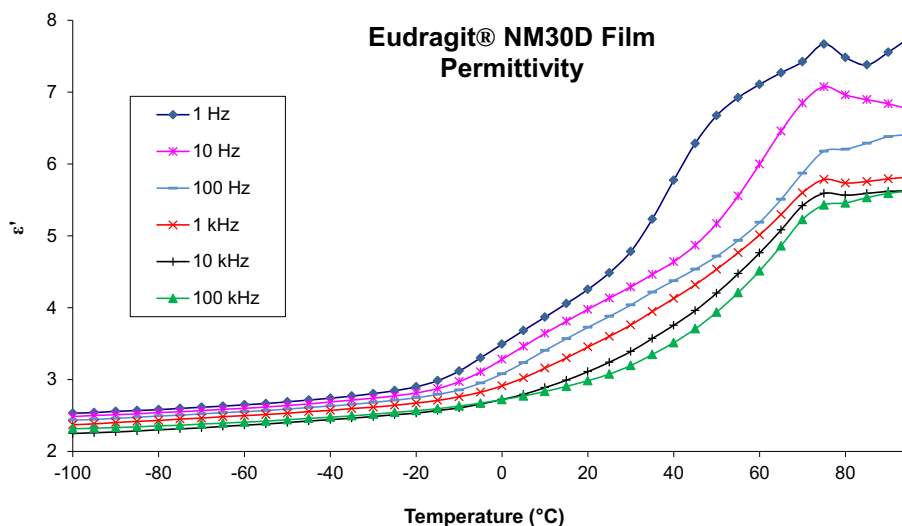


Fig. 4. Permittivity plot of Eudragit® NM30D film

maxima at corresponding lower frequencies, but does exhibit slopes close to -1 (Fig. 6, inset) at higher temperatures from 50°C that is what is predicted for conductivity relaxation (10).

Eudragit® NM30D aqueous dispersion contains 0.7% of macrogol stearyl ether as an emulsifier (15). The presence of the emulsifier, which is an additive and the residual 0.5% moisture as seen from thermal gravimetric analysis (TGA) analysis (Fig. 3), will likely contribute to interfacial polarization as well as conductivity affects when the film exhibits sufficient mobility at the T_g (12). Above T_g , a polymer will enter a liquid state exhibiting greater mobility of the polymer backbone (14). Although liquid-liquid transition, α' in DEA are being reported for glassy poly(*n*-alkyl methacrylate) polymers (16,17), the quantification of the slope in $\log \epsilon''$ plot (Fig. 6, inset) reveals the sharp rise at low frequencies for higher temperatures in the Eudragit® NM30D film is likely from conductivity relaxation masked by MWS and electrode polarization affects in a heterogeneous co-polymer system. Thus, at the T_g offset (approximately 30°C) of the Eudragit®

NM30D film, the polymer is in a liquid state, and the mobility of the molecules of the emulsifier and moisture is greater causing long-range migration of charges in the bulk polymer contributing to conductivity relaxation. The dielectric relaxation spectra of the Eudragit® NM30D film therefore need to be analyzed using the M^* formalism to separate the charge migration affects from dipolar relaxation.

Complex Modulus

With M^* formalism, the isochronal M'' plot (Fig. 7) shows three distinct regions of M'' maxima corresponding to different relaxations.

Primary Relaxation. From approximately -10°C at 1 Hz to approximately 35°C at 100 kHz (Fig. 7), the α relaxation from mobility of polymer backbone occurs, which is also supported by the transition occurring in the ϵ'' plot (Fig. 5) at similar temperatures. In the isothermal $\log M''$ vs. $\log \nu$ plot

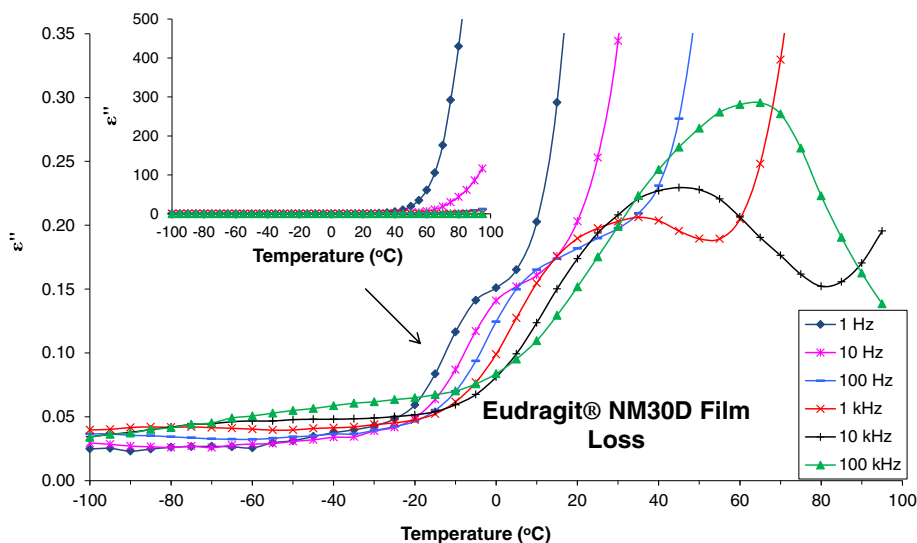


Fig. 5. Loss plot of Eudragit® NM30D film

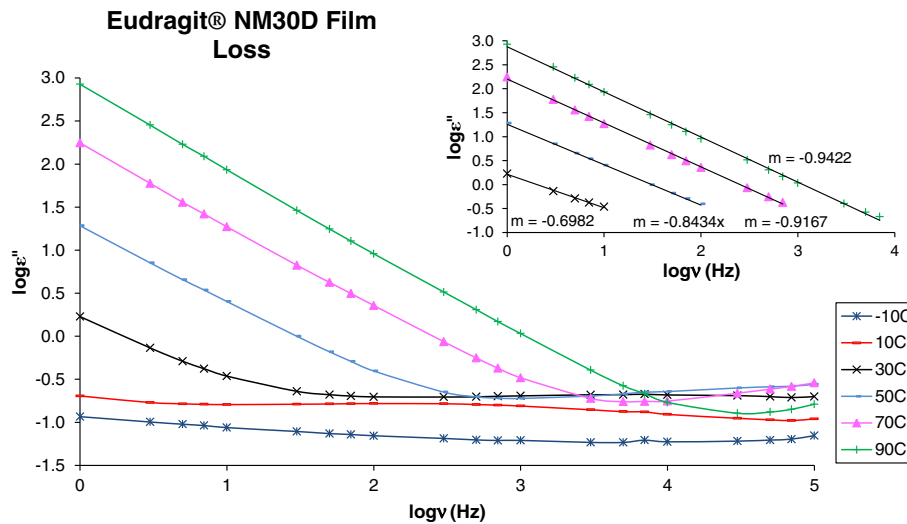


Fig. 6. Log loss plot of Eudragit® NM30D film

(Fig. 8), broad peaks are clearly seen that shift towards higher frequencies around approximately 10°C that indicates a broad distribution of relaxation time associated with α relaxation.

Secondary Relaxation. M'' peaks that are decoupled from α relaxation occur at subzero temperatures between -80°C and -20°C at higher frequencies from 1 kHz to 100 kHz (Fig. 7, inset). These maxima likely correspond to β relaxations as they occur at temperatures below the α relaxation event.

In poly(*n*-alkyl methacrylates) having different ester side chain groups such as methyl ester, -COOCH₃ in PMMA and ethyl ester, -COOC₂H₅ in poly(ethyl methacrylate) (PEMA), β relaxations have been reported at similar temperatures between approximately -80°C to -30°C by DEA (2,18). These maxima occurring below T_g in the dielectric spectrum for the

Eudragit® NM30D film are therefore believed to correspond to β relaxation associated with ester side chain mobility. This is consistent with what is known about the likely order for the molecular source of possible transitions in DEA.

As the polymer film is formed from an aqueous suspension and has an emulsifier, the higher order relaxations at the subzero temperatures below T_g may also arise due to diluent induced β relaxation (1,2). Trapped water molecules in the polymer film as seen in the TGA analysis as well as the emulsifier present in the film may both be set into motion either independently of the side chain or cooperatively with the side chains. The water molecules present are also likely linked through hydrogen bonding to the side chains (2). Diluent-induced β relaxations have been reported for PMMA in the subzero temperature range between -110°C and -73°C

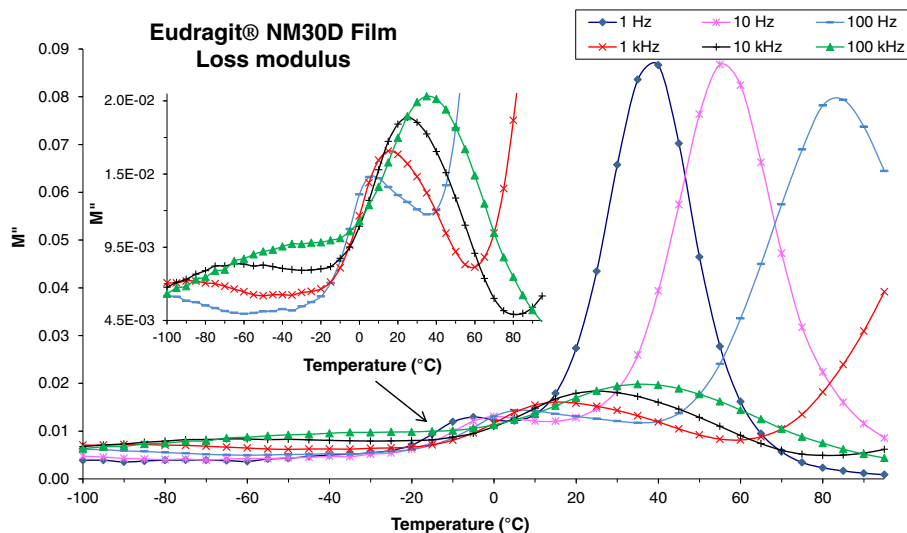


Fig. 7. Loss modulus plot of Eudragit® NM30D film

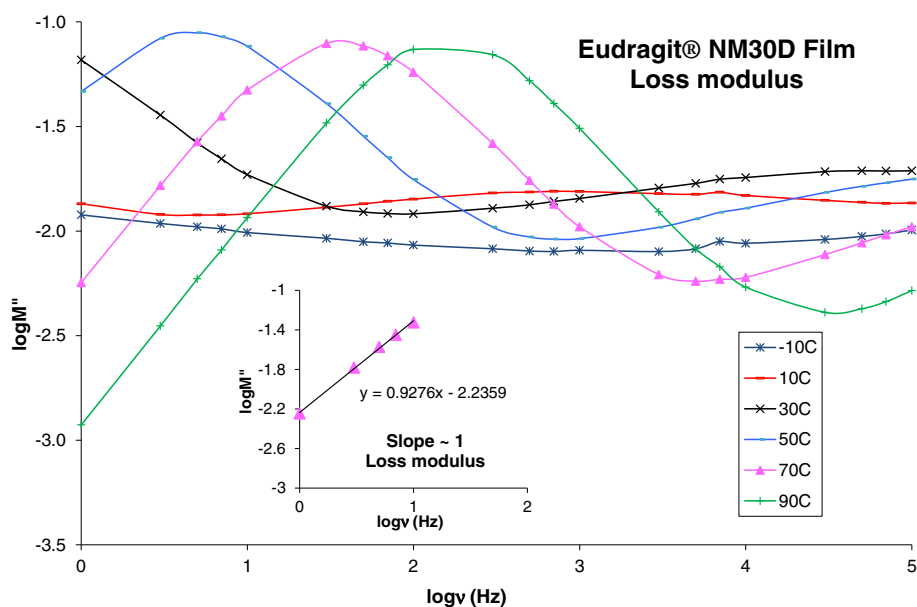


Fig. 8. Log loss modulus plot of Eudragit® NM30D film

but are absent in the dry state of the polymer (2). As Eudragit® NM30D is a derivative of the PMMA chemical structure, similar observation may be made in the subzero temperature range below the T_g . However, it is likely that β relaxation from side-chain mobility is coupled with β induced relaxation at the subzero temperatures; therefore, it is difficult to isolate the two relaxation mechanisms as they occur at similar temperatures.

Conductivity Relaxation. At higher temperatures from 40°C (Fig. 7), relaxation peaks with significantly higher magnitudes occur that shift with temperature. As these occur at temperatures above T_g , they are attributed to free charge motion occurring in the liquid state of the polymer. This is further supported by isothermal $\log M''$ plot (Fig. 8), which

shows new peaks in the low frequency region that shift to higher frequencies with temperature and correspond to conductivity at similar frequencies in the $\log \epsilon''$ plot (Fig. 6).

In M^* formalism at lower frequencies, when isothermal M'' plots show new peaks with a slope of +1 and M' plots show a sharp rise in M' values with a slope of +2, these phenomenon in DEA correlate to presence of conductivity relaxation (13,19). A similar observation was evident in the isothermal $\log M''$ plot (Fig. 8, inset), which exhibits a slope of ~ 1 at higher temperatures. Likewise, the isothermal $\log M'$ plot (Fig. 9, inset) shows sharp rise in values above T_g offset temperatures with a slope value of ~ 2 .

Further analysis with an Argand plot (Fig. 10) reveals an arc at lower frequencies for higher temperatures from 50°C, which is indicative of conductivity relaxation. At lower

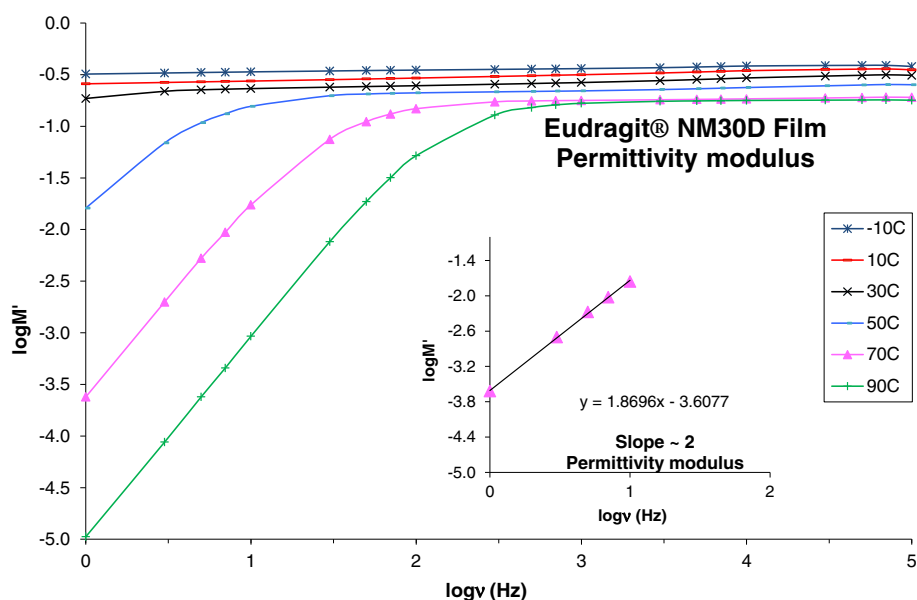


Fig. 9. Log permittivity modulus plot of Eudragit® NM30D film

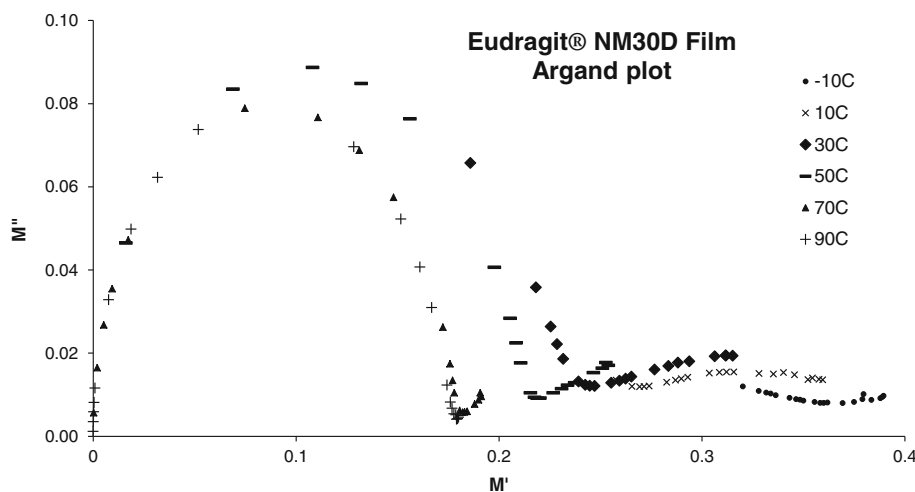


Fig. 10. Argand plot of Eudragit® NM30D film

temperatures around T_g , the Argand plot shows a deviation from the semicircular Debye model, indicating these are associated with viscoelastic dipolar relaxations (13,19). A normalized plot of $M''/M''_{(max)}$ vs. $\log v/v_{(max)}$ (Fig. 11) at higher temperatures from 50°C shows a single master curve. This is indicative that the distribution of the conductivity relaxation process at these temperatures in the heterogeneous polymer system is independent of temperature and thereby has same E_a and follows an Arrhenius behavior (20).

Thus, the M^* formalism of the DEA data of Eudragit® NM30D film clearly isolates the α , β , and conductivity relaxations, which are not clearly observed in the ϵ'' plot. Using the M'' and M' plots, the probable mechanisms for the relaxation events were also proposed. Further analysis based on Arrhenius kinetics was investigated to support the assignment of these relaxation events.

Relaxation Kinetics

The logical assumption for the system studied is that the magnitude of the activation energy, E_a for α and β relaxations

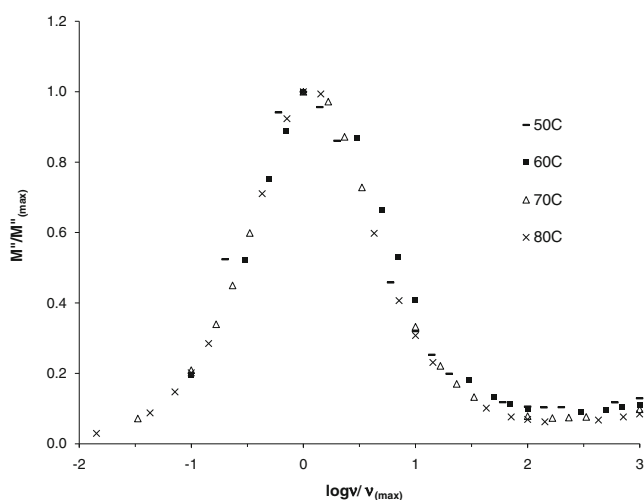


Fig. 11. Normalized plot of loss modulus vs normalized frequency at different temperatures

should be consistent with the structural explanation and correlate to the literature. It is a sub-hypothesis that the relaxation kinetics determined should also agree with the fundamental relaxation frequency (ν_0), which supports the interpretation of α and β relaxations. This was found to be the case in the current polymer study as is discussed. The relaxation kinetics of the transitions observed in the Eudragit® NM30D film was determined based on Arrhenius dependence of the M'' peak maxima with temperature. Although α relaxations do not have to adhere to Arrhenius kinetics, based on the wide relaxation time distribution of α and β relaxations with temperature an Arrhenius behavior can be assumed for simplicity in quantifying the relaxations (16). The conductivity relaxation also follows Arrhenius behavior and is a thermally activated process (19). The focus of the relaxation kinetics analysis is in differentiating the α and β relaxations as well as the conductivity relaxation based on their E_a and to assess their consistency with the proposed molecular origins of the observed transitions.

The E_a for dielectric relaxations are expected to decrease in order from α , β , and γ processes for a particular polymer. Compared to the cooperative α processes, the noncooperative β and γ relaxation processes have significantly lower E_a but are the major relaxation mechanism for glassy materials below their T_g (1,9,14). The ν_0 of the β relaxation in amorphous polymers is approximately $10^{13\pm 2}$ Hz and is common among amorphous polymers (2,21). Thus, based on the E_a and ν_0 , one may be able to differentiate the dynamics of the α and β processes.

The E_a for the α relaxation of the Eudragit® NM30D film based on M'' peak maxima with temperature is 179 kJ mol^{-1} (Fig. 12). This value is within range of α relaxation of polymers of similar chemical composition [e.g., poly(ethyl acrylate) (PEA) and PEMA] (12,14,18). The E_a for the conductivity relaxation was 93 kJ mol^{-1} , significantly lower than the E_a for α relaxation. At higher temperature above T_g offset, the polymer chains have greater mobility thereby lowering the energy associated with mobility of charges. The E_a of higher order secondary relaxation in Eudragit® NM30D at subzero temperatures is 30 kJ mol^{-1} . The ν_0 value of this relaxation is approximately 10^{11} , which agrees with the ν_0 values reported for β relaxations of a number of related

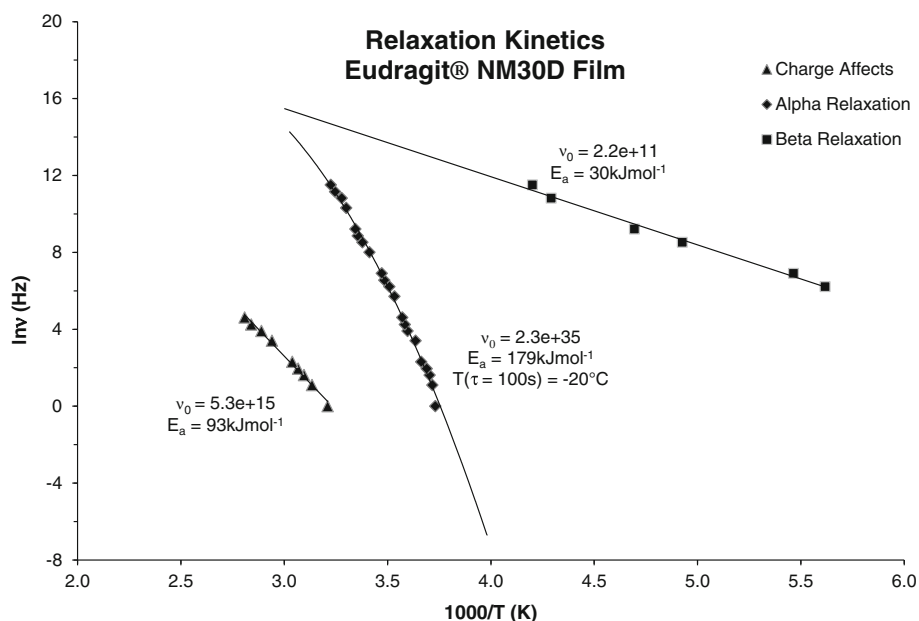


Fig. 12. Primary and secondary relaxation kinetics of Eudragit® NM30D film

PMMA polymers (1,9,17). Based on the ν_0 value and also lower E_a value of this higher order secondary relaxation compared to the E_a of the α relaxation, the transition occurring below -20°C is assumed to reflect β relaxation.

From the relaxation kinetics (Fig. 12), it is clear that the β relaxation and conductivity relaxation follow Arrhenius kinetics; however, α relaxation deviates from Arrhenius behavior and shows a relaxation time, τ , of 100 s at approximately -20°C . The α relaxation typically is a slower process with, $\tau \approx 100$ s at the T_g onset (1,14). The different heating rates as well as the principles of operation of the DSC and DEA will contribute to slightly different T_g values. However, based on extrapolating the β relaxation kinetics in the DEA analysis, it is seen to merge with α relaxation at higher temperatures (Fig. 12), and thus, these are clearly dipolar relaxations based on the relaxation pattern and the τ and ν_0 values.

Deviation from linearity of the T_g may be used to ascertain the $T_{g,\text{mid}}$ of the Eudragit® NM30D film. This is determined from the intersection of the bimodal linear curves displayed over the range of $1/T$ to be 10°C (Fig. 13) and agrees with the reported T_g value (22). The fragility index, m , was 32 for the Eudragit® NM30D film in the temperature range of the α relaxation, thus indicating it is a moderately strong glass former.

Thus, assuming Arrhenius kinetics, the α , β , and conductivity relaxation occurring in Eudragit® NM30D film DEA study were differentiated; these agreed with the reported values lending support to the assignments of the transitions.

CONCLUSIONS

Using the dielectric complex modulus formalism, it was possible to detect and resolve α and β relaxations as well as

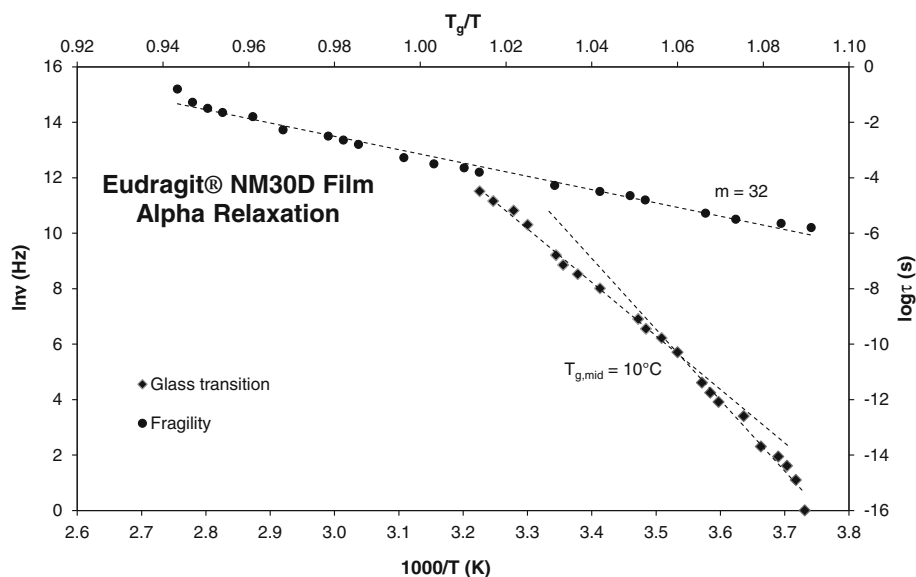


Fig. 13. Fragility index and glass transition temperature of Eudragit® NM30D film

isolate the contribution from conductivity that occurs in a Eudragit® NM30D film unlike traditional thermal methods of analysis such as DSC, which detect only the T_g . DEA is thus a very useful and sensitive technique to probe higher order relaxations not easily followed with traditional DSC methods. DEA measurements of ϵ' and ϵ'' reflect molecular mobility and the energy associated with molecular motion, respectively, in the Eudragit® NM30D film. The M^* formalism helps to elucidate the dipolar relaxations from interfacial polarization and ionic conductivity in the DEA relaxation pattern of the Eudragit® NM30D film, which is further confirmed by the relaxation kinetics both from the magnitude of the E_a as well as the ν_0 value.

Many pharmaceutical dosage forms employ acrylate-based Eudragit® polymers either in tablet coating or as amorphous drug polymer dispersions. As reported here, it is clearly observed that β relaxations at sub- T_g temperatures occur from additives or side chains in the polymer. This could be significant to understanding any intermolecular interactions (e.g., H bonding) between drugs (additive) and a polymer in a polymer matrix that may be affected by the β relaxations, which in turn could influence stability. Knowing the kinetics associated with α relaxations as well as that β transitions have lower E_a can guide formulation design to control the physical stability as well as the macroscopic properties such as diffusion and, consequently, the *in vitro* release of Eudragit®-based dosage forms. The dielectric loss modulus analysis will therefore enable a better correlation of the impact of molecular level mobility changes occurring at and below T_g , on the stability and diffusion properties of Eudragit® formulations.

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