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# Influence of water soluble and insoluble plasticizers on the physical and mechanical properties of acrylic resin copolymers

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## Summary

The effect of different types and levels of plasticizers on the thermal and physical-mechanical properties of equilibrated methacrylic acid copolymers was studied. The efficiency of this plasticization was studied by determining the dependence of the copolymer's thermal and physical-mechanical properties on plasticizer concentration and molecular structure. Gas chromatography (GC) and headspace-gas chromatography techniques were used to specifically determine the levels of plasticizer and residual solvent, respectively, in the polymeric film, and to exclude any solvent-induced plasticization. The effect of plasticizer on the thermal properties showed a strong correlation with the mechanical behavior of the methacrylic acid copolymer. Results indicated that the ability to interact with the methacrylic acid copolymer may not solely be dependent on the aqueous solubility of the plasticizer, but also on the chemical structure of the plasticizers. Of the plasticizers investigated, triacetin (TRI) had the greatest effect on reducing the brittleness of the polymer, followed by triethyl citrate (TEC). This effect was related to their differences in molecular size and subsequent greater ability to interact with the polymer chains as compared to the other plasticizers investigated including acetyl triethyl citrate (ATEC), tributyl citrate (TBC), and acetyl tributyl citrate (ATBC).

## Introduction

Many polymers used for film coating tablets and beads display brittle properties under normal ambient temperatures and humidity conditions. The incorporation of a plasticizer is necessary to obtain an effective coating without defects such as cracks, edging or splitting. Plasticizers are also added to polymeric solutions and dispersions to increase the flexibility or distensibility of the polymeric material. The addition of plasticizer may lower the melt viscosity, the glass transition temperature ($T_g$), or the elastic modulus of the polymeric material (Nielsen, 1974). These effects are the result of the plasticizer weakening the polymer intermolecular attractions and increasing the polymer's free volume, thus allowing the polymer molecules to move more freely to cause an increase in their flexibility.

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The degree of plasticization of a polymer is dependent to a large extent on the amount of plasticizer in the film and the interactions between the plasticizer and the polymer. For a plasticizer to be effective, the plasticizer must be able to diffuse and interact between the polymer chains and have minimal or no tendency for migration, exudation, or volatility (Sears and Darby, 1982). The stability requirement of the plasticizers is very important since any changes in the composition of the original formulation will influence the final properties of the polymeric film. Several researchers have addressed the importance of the $T_g$ of a polymer used for film coating, since knowledge of the $T_g$ has been demonstrated to be a good indicator of the polymer's behavior under ambient and coating conditions (Rowe and Forse, 1981; Porter and Ridway, 1983).

Lowering of the glass transition temperature alone, however, cannot be used as a sole predictor of the final coating performance or response to changes in the applied stress or strain (Sinko and Amidon, 1989). Physical-mechanical testing can be a useful guide in predicting not only the film coating performance (Goodhart et al., 1984), but also in comparing the effect of plasticizers in film samples as a function of formulation compatibility, type, and level (Bindschaedler, 1987; Arwidsson et al., 1991; Lin et al., 1991). In addition, the incidence of cracking or edge splitting (Rowe, 1981) and the effect of solid inclusions (Aulton and Abdul-Razzak, 1984; Okhamafe and York, 1984; Gibson et al., 1988), as well as the effect of aging and storage conditions (Guo et al., 1991; Gutiérrez-Rocca and McGinity, 1992) can be predicted from physical-mechanical testing.

Properties of polymeric films used for many drug delivery systems are generally determined within a short period of time after manufacturing. However, the time required to form a stable film without aging effects is variable and will depend on the relaxation of the copolymer chains towards a state of equilibrium. In our previous report (Gutiérrez-Rocca and McGinity, 1993) it was demonstrated that the extent of these changes was influenced by the amount of plasticizer added, the length of drying time, the solvent residuals, and the temperature and humidity conditions of storage. Determination of the properties of recently manufactured films may present completely different results to those of equilibrated films because of the non-equilibrium nature of the polymeric system. The objective of the present investigation was therefore to study the effects of different levels of water soluble and insoluble plasticizer on the thermal and physical-mechanical properties of equilibrated polymeric films. Furthermore, the thermal properties of a series of equilibrated plasticized polymeric films were correlated with the mechanical properties based on the chemical structure of the plasticizer and the methacrylic acid copolymer.

## Experimental

### *Materials*

The enteric copolymer used in this investigation was poly(methacrylic acid, ethyl acrylate), commonly known as the aqueous dispersion Eudragit® L 30D and the spray-dried form Eudragit® L 100-55. These commercially available enteric copolymers were donated by Röhm Pharma, Weiterstadt, Germany. The plasticizers, triethyl citrate, acetyl triethyl citrate, tributyl citrate, and acetyl tributyl citrate, were donated by Morflex, Inc., Greensboro, NC. Triacetin was purchased from Aldrich Chemical Co., Milwaukee, WI. Isopropyl alcohol certified A.C.S. was purchased from J.T. Baker, Inc., Phillipsburg, NJ.

### *Film preparation*

Aqueous and organic cast films containing different amounts of water soluble and insoluble plasticizers were prepared based on methods described previously (Gutiérrez-Rocca, and McGinity, 1992). Films were equilibrated at 23°C and 50% relative humidity for approx. 60 days to ensure the removal of isopropyl alcohol from the polymeric matrix. Films were then exposed to a 0% relative humidity in vacuum desiccators for a further 30 days to minimize any moisture effect. Aqueous cast films were prepared using the same technique. The thickness of the films was determined in five places along the testing area using a micrometer (P.N. Gardner Co., Pompano Beach, FL). The thickness of the films investigated was approx. 150 μm with less than 8% variation over the film's length.

### *Mechanical properties*

The method used for evaluating the mechanical properties was based on the guidelines of the American Society for Testing Materials method D 882-75b. The three strain rates that were used included, 0.1, 10, and 100 mm/min. The initial grip separation was 100 mm. The tensile strength, elongation at break, and elastic modulus of each film were calculated from the resulting stress-strain curves obtained. A minimum of five samples of each formulation was tested using an Instron® model 4201 (Instron Corp., Canton, MA) universal testing apparatus.

### *Plasticizer determination*

Dried polymeric films containing various amounts of plasticizer were quantitated for plasticizer content prior to testing. Film samples (3–5 mg) were accurately weighed on a micro-balance before being dissolved in 10 ml of methyl alcohol. The sample solutions were directly injected into a gas chromatogram (Tracor® 540) with a flame ionization detector (FID). The chromatographic conditions consisted of a megabore column DB-17, protected with an easy to remove Cap Saver Pre-Filter (Craven Labs, Austin, TX) to prevent the non-volatile residue from damaging the column. No derivatization, extraction or complicated separation steps were necessary to analyze for plasticizer content.

### *Residual solvent determination*

A known weight of the film was placed in special tube vials and crimped for perfect sealing. These sample vials were then tested for organic solvent residues (isopropyl alcohol) in a Tekmar® 7000 headspace sampler connected to the Tracor® 540 and the FID detector.

### *Differential scanning calorimetry*

The glass transition temperature of the copolymers (8–12 mg sample) was measured using a differential scanning calorimeter (Perkin Elmer DSC-2C/TADS system) with a thermal analysis data station. Thermal analyses were performed at temperatures ranging from 270 to 420 K at a scan rate of 10 K per min. No previous heating or quenching was performed in the film samples.

## Results and Discussion

The effect of different types and levels of plasticizers on the thermal and physical-mechanical properties of the methacrylic acid copolymer films was studied. An equilibration period of 60 days at 23°C and 50% relative humidity was employed in order to facilitate the removal of isopropyl alcohol from the Eudragit® L 100–55 cast films, to levels below 0.1% solvent. Furthermore, films were exposed to a 0% relative humidity vacuum dessicator chamber for another 30 days in order to minimize any moisture effect. In a previous report (Gutiérrez-Rocca and McGinity, 1993), it was demonstrated that exposure to a vacuum or low humidity conditions did not effectively remove the residual solvent; instead, higher humidity conditions accelerated the rate of solvent evaporation. It was also demonstrated that after approx. 90 days at room temperature, the films approached a stable state of equilibrium where the mechanical behavior of the free films containing the different plasticizers remained constant. Determination of the thermal and physico-mechanical properties prior to a stabilization period could result in an erroneous interpretation of polymer behavior, since amorphous polymers have been demonstrated to be in an unstable state of equilibrium at room temperature (Struik et al., 1986). At room temperature, triacetin and triethyl citrate were soluble in water at concentrations of 7 g per 100 ml and 6.5 g per 100 ml, respectively. The acetyl triethyl citrate showed some degree of solubility in water, (approx. 0.7 g per 100 ml) and was also considered to be in the water soluble group. The other plasticizers studied in the present investigation included, tributyl citrate and acetyl tributyl citrate. They were soluble at levels less than 0.01 g per 100 ml at room temperature and were therefore categorized into the water insoluble group.

Prior to the evaluation of the thermal and physico-mechanical properties, the Eudragit® L100-55 and L 30D film samples were completely dissolved in methyl alcohol and analyzed for plasticizer content. The plasticizer content in the films after an equilibration time of 90 days is summarized in Table 1. Films containing the water soluble and insoluble citrate ester plasticizers demonstrated a minimal loss after equilibration, i.e., less than 5% from initial amount added was lost after 90 days. On the other hand, all films containing the triacetin demonstrated a loss of approx. 10% calculated on a percent basis from the amount added to the initial polymer solution. This triacetin loss indicated a tendency for triacetin either to evaporate or to degrade under normal ambient temperatures. Statistical analysis of the data using a one-way analysis of variance (ANOVA) demonstrated no significant difference between the film formulations containing the different types and amounts of plasticizers, with the exception of the films containing triacetin.

It has been reported that repeated differential scanning calorimetry (DSC) runs are recommended to minimize erratic results caused by the appearance of broad endotherms, usually due to water (Sakellariou et al., 1985) or typically seen with polymethacrylates (Kusy et al., 1978). In this investigation, the glass transition temperature of the polymeric samples was determined from the onset values of the first DSC run. Our studies demonstrated that heating and quenching the plasticized film samples resulted in over 6% weight loss from the initial weight. This initial loss could have been due in part to the loss of plasticizer during the initial heating of the films prior to quenching. Thermal analysis of films containing the plasticizers did not show broad endotherms for the range of plasticizer concentration studied. In addition, the onset of the transition temperature was reproducible within a few degrees for the same specimens being tested.

TABLE 1

*Amount of plasticizer content remaining in methacrylic acid copolymer films (Eudragit® L100-55) after 90 days* [a]

| Plasticizer type | Plasticizer remaining (%) [b] | | |
|---|---|---|---|
| | 10% | 20% | 30% |
| Triethyl citrate | 94.60 ± 3.51 | 99.30 ± 3.20 | 96.54 ± 2.01 |
| Acetyl triethyl citrate | 98.14 ± 1.45 | 97.14 ± 1.52 | 96.20 ± 1.91 |
| Tributyl citrate | 97.30 ± 1.97 | 97.04 ± 1.26 | 96.46 ± 2.47 |
| Acetyl tributyl citrate | 99.11 ± 0.52 | 96.14 ± 0.40 | – |
| Triacetin | 90.80 ± 2.25 | 91.62 ± 4.68 | 90.26 ± 2.77 |

[a] 60 days 23°C and 50% R.H. followed by 30 days at 23°C and 0% R.H.

[b] Data reported as the mean ± SD of nine film samples.

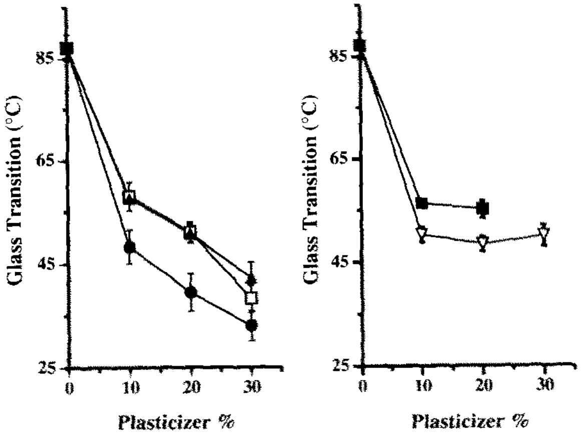

Fig. 1. Effect of different levels of water soluble plasticizers on the thermal properties of Eudragit® L 100–55 films. (60 days at 23°C, 50% R.H. followed by 30 days at 23°C, 0% R.H.) Bars represent S.D. ($n = 5$). (●) TRI, (□) TEC, (▲) ATEC, (▽) TBC, (■) ATBC.

The effect of water soluble and insoluble plasticizers on the thermal properties of Eudragit® L 100-55 is shown in Fig. 1. The water soluble plasticizer had a direct relationship between increasing amounts of plasticizer concentration and $T_g$ depression with all film formulations. However, the increased concentration of the water insoluble plasticizers did not result in a continuous decrease in the glass transition temperature of the polymer. Dechesne and co-workers (1984) indicated that the addition of plasticizers to acrylic resin copolymers lowers the glass transition and the degree of lowering was dependent on the quantity and type of plasticizer used. It is also well documented in the literature that the more efficient the plasticizer, the greater the lowering of the glass transition temperature. Based on these criteria, all the plasticizers used effectively decreased the glass transition temperature of the

Eudragit® L 100-55 at the 10% level. The profiles in Fig. 1 show triacetin to be the most effective plasticizer for the methacrylic acid copolymers. Films containing the triethyl and acetyl triethyl citrate have somewhat higher $T_g$ values compared to those containing the triacetin. Interestingly, tributyl citrate was demonstrated to be the second most effective plasticizer in reducing the $T_g$, indicating that the ability to interact with the methacrylic acid copolymer was not solely dependent on the aqueous solubility of the plasticizer. The addition of 20–30% of all three water soluble plasticizers used in this investigation resulted in an almost linear decrease in the glass transition temperature of the films, as demonstrated in the $T_g$ profiles of Fig. 1. No further reduction in the $T_g$ of the polymers was seen at 10% or higher concentrations of the water insoluble plasticizers, due in part to the poor miscibility of the hydrophobic plasticizer with the polymer at these levels.

Uniaxial stress-strain analysis, at a constant rate of grip separation, was used to investigate the physical-mechanical properties of each film formulation. Although all polymer-plasticizer formulations demonstrated a significant increase in the flexibility of the free films with increases in plasticizer content, the elongation of films containing the various levels of plasticizer was less than 4%, when tested at the highest strain rate used in this investigation (100 mm/min). This low elongation could be attributed to the speed of testing or strain rate. Higher strain rates can result in a higher tensile strength and a lower elongation at break (Hsiao et al., 1951; Hall et al., 1968). This may be related to the existence of cracks, notches, voids or crazing in the polymeric film being tested (McCrum et al., 1989). Flaws represent weak spots where failure or rupture will occur. In the methacrylic acid copolymer tested under standard temperature conditions, methacrylic acid copolymers were quite brittle, and even when the strain rates were varied over wide ranges, there was still almost no plastic flow. At even the lowest strain rate of 0.1 mm/min, the elongation was in the range of 2–6%. Differences were observed when films containing 30% plasticizer showed some necking-down when less than 10 mm/min strain rates were used. Films containing 20% plasticizer or less showed little plastic flow when tested at all three strain rates. The profiles in Fig. 2 show various stress-strain curves for films containing 20 and 30% triethyl citrate when tested at different strain rates. Lower strain rates facilitated the determination of the elastic modulus and decreased the incidence of failure; however, longer testing times were required. Therefore, 10 mm/min. was determined to be the optimal speed of testing for the mechanical properties.

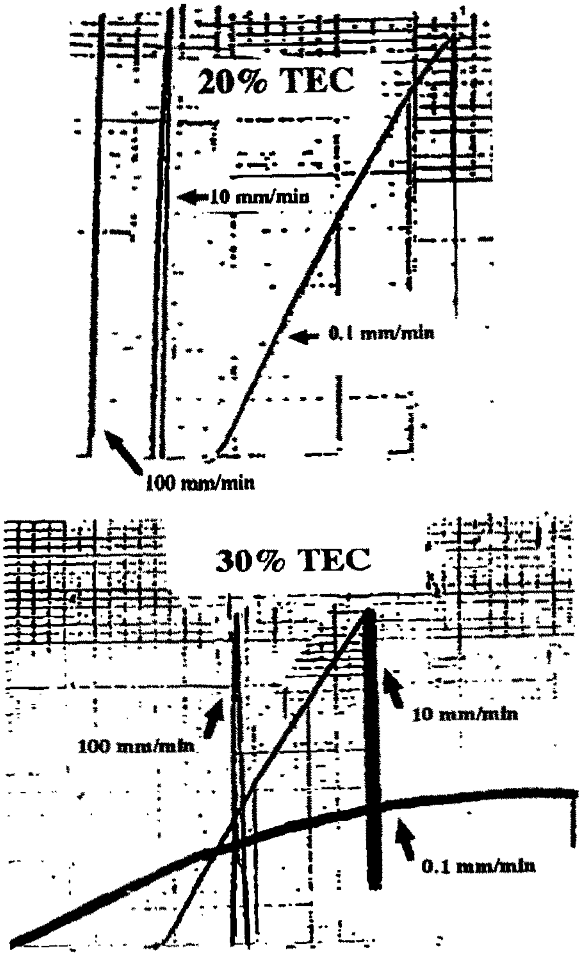

Fig. 2. Actual illustration of stress-strain curves for films containing 20 and 30% triethyl citrate tested at different strain rates.

TABLE 2

*Effect of plsticizer type and amount on the tensile strength of Eudragit® L100-55*

| | Tensile strength (MPa) [b] | | |
|---|---|---|---|
| Eudragit® L 100-55 | | | |
| No plasticizer | 40.82 ± 5.86 | | |
| Plasticizer type | 10% | 20% | 30% |
| Triethyl citrate | 37.19 ± 6.75 | 30.89 ± 1.69 | 25.86 ± 1.76 |
| Acetyl triethyl citrate | 34.88 ± 6.14 | 30.19 ± 2.57 | 26.35 ± 4.90 |
| Tributyl citrate | 34.19 ± 4.24 | 28.96 ± 6.74 | 28.64 ± 3.68 |
| Acetyl tributyl citrate | 34.03 ± 3.28 | 27.70 ± 2.29 | – |
| Triacetin | 31.26 ± 3.82 | 30.62 ± 4.13 | 24.76 ± 2.06 |

[a] 60 days 23°C and 50% R.H. followed by 30 days at 23°C and 0% R.H.

[b] Data reported as the mean ± SD of six film samples.

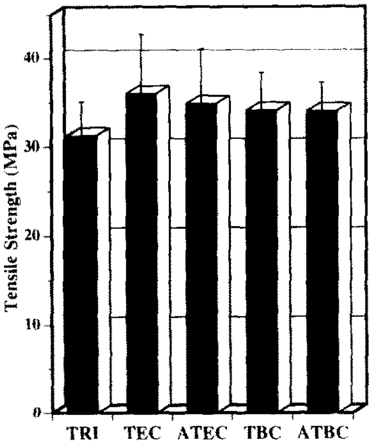

Fig. 3. Comparison of the tensile strength values for Eudragit® L 100-55 films containing 10% plasticizer level. (60 days at 23°C, 50% R.H. followed by 30 days at 23°C, 0% R.H.) Data reported as the mean ± S.D. of six film samples.

In all cases, the addition of the plasticizers had a significant effect on the mechanical properties of Eudragit® L 100-55. These effects on the mechanical properties could be related to a large extent to the chemical structure of the plasticizer molecule and the compatibility of the plasticizer with the methacrylic acid copolymer. The results in Table 2 show the influence of three levels of the different plasticizers on the tensile strength of Eudragit® L 100-55 films stored at 23°C and 0% relative humidity. The acetyl tributyl citrate, which is a water insoluble plasticizer, was not evaluated at the 30% level due to its poor miscibility with the Eudragit® L 100-55 at that concentration. As expected, the addition of plasticizers resulted in a reduction of the tensile strength of the films. A comparison of the tensile strength values for the free films containing 10% plasticizer level is shown in Fig. 3. Although triacetin-containing films resulted in slightly lower tensile strength values when compared to the other types of plasticizers, a statistical analysis of the data showed that there was no significant difference in the tensile strength between the different types of plasticizer at the same concentration level. However, the difference in tensile strength as the level of plasticizer increased from 0 to 30% by dry weight of the polymer was found to be highly significant ($p < 0.01$). Similar results were obtained from the elongation percent of the films, as shown in Table 3, in which the incorporation of 10% plasticizer concentration resulted in no changes or minimal increases in the elongation. This was a very interesting finding, as a plasticizer concentration of 10% by weight of the polymer might be a critical concentration, since below this concentration no significant plasticizing effect could be obtained. Several reports have been published where the addition of less than 10% plasticizer has resulted in an incomplete coalescence of the colloidal polymeric dispersion, re-

TABLE 3

*Effect of plasticizer type and amount on the elongation percent of Eudragit® L100-55 films [a]*

| | Elongation (%) [b] | | |
|---|---|---|---|
| Eudragit® L 100-55 | | | |
| No plasticizer | 1.35 ± 0.56 | | |
| Plasticizer type | 10% | 20% | 30% |
| Triethyl citrate | 1.33 ± 0.43 | 2.37 ± 0.46 | 3.29 ± 0.44 |
| Acetyl triethyl citrate | 1.35 ± 0.25 | 2.01 ± 0.27 | 2.57 ± 0.15 |
| Tributyl citrate | 1.73 ± 0.34 | 1.91 ± 0.36 | 1.96 ± 0.33 |
| Acetyl tributyl citrate | 1.62 ± 0.29 | 1.62 ± 0.34 | – |
| Triacetin | 1.46 ± 0.33 | 1.93 ± 0.35 | 5.43 ± 0.40 |

[a] 60 days 23°C and 50% R.H. followed by 30 days at 23°C and 0% R.H.

[b] Data reported as the mean ± SD of six film samples.

sulting in low fracture strains (Arwidsson et al., 1991) and rapid drug release (Bodmeier and Paeratakul, 1990). With the exception of ATBC, our studies showed that the addition of increasing levels of the plasticizers from 10 to 30% resulted in increases in the elongation percent to varying magnitudes. Substantial elongations were not achieved until plasticizer concentration was 20% or greater. For Eudragit® L 100-55 films containing 30% plasticizer, only the water soluble plasticizers caused a significant increase in the percent elongation compared to the unplasticized films. The addition of TBC, a water-insoluble plasticizer, at the 30% level resulted in less than an 8% increase in the elongation percent of the polymeric films as compared to the films at the 10 and 20% plasticizer content level. The water soluble plasticizers, TEC and ATEC, demonstrated a 4-fold increase in percent elongation, whereas triacetin resulted in a 6-fold increase in the elongation of the films indicating that the water soluble plasticizers used in this investigation have a high affinity to diffuse into and interact with the polymer molecules, thereby increasing the polymer's mobility.

An important parameter determined from physical-mechanical testing is the elastic modulus or Young's modulus, which is a measure of the hardness, flexibility or stiffness of a polymer (Schlot, 1983). Results from the physical-mechanical studies with the Eudragit® L polymers demonstrated that the addition of the water soluble plasticizers (TEC, ATEC, and TRI) resulted in a continuous decrease in the elastic modulus as the level of plasticizer added to the Eudragit® L100-55 was increased. However, the reduction of the elastic modulus with the water insoluble plasticizers (TBC and ATBC) resulted in no statistically significant changes when higher than 10% level was added, as shown in Fig. 4. A similar correlation between elastic modulus and glass transition temperature can be seen for the plasticizers, as demonstrated in the profiles in Figs 1 and 4. With water soluble plasticizers, the mechanical properties of the film were directly related to the concentration of the plasticizers. As the concentration of the water soluble plasticizer increased, the brittle character of the polymer was reduced. This effect was demonstrated by a reduction of the elastic modulus and a significant reduction of the $T_g$. Tributyl and acetyl tributyl citrate efficiently decreased the $T_g$ and elastic modulus up to a concentration of 10% w/w. There was no further reduction in the $T_g$ and the elastic modulus at higher concentrations, due to the immiscibility of the hydrophobic plasticizer with the polymer.

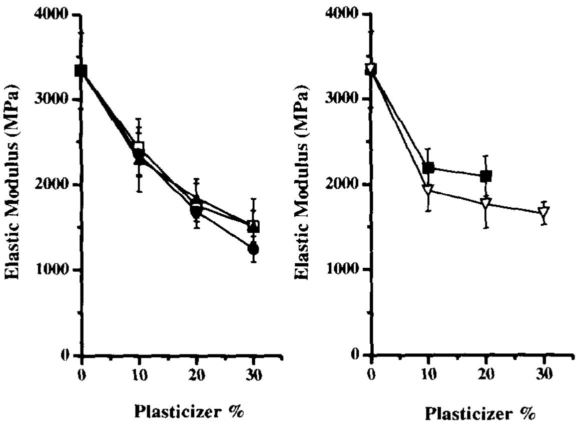

Fig. 4. Effect of different levels of water soluble plasticizers on the elastic modulus of Eudragit® L 100-55 films. (60 days at 23°C, 50% R.H. followed by 30 days at 23°C, 0% R.H.) Bars represent S.D. ($n = 6$). (●) TRI, (□) TEC, (▲) ATEC, (▽) TBC, (■) ATBC.

Of the five plasticizers investigated, triacetin had the greatest effect on reducing the brittleness of the polymer. Lower tensile strength, elastic modulus, and higher elongations were found with this plasticizer when used as the same plasticizer initially added. In addition, the DSC studies correlated very well with the results from the physical-mechanical tests, as the glass transition of the polymer was reduced to the greatest extent by the triacetin. These differences can be explained by considering the chemical structures of the plasticizers, as shown in Fig. 5. Triacetin has a low molecular volume compared to the other plasticizers used in this investigation, thus facilitating its ability to diffuse and interact with the active groups in the polymer. Poly(methacrylic acid, ethylacrylate), which is Eudragit® L 100-55 or L 30D, as shown in Fig. 6, contains carboxylic and ester groups that are capable of interacting with

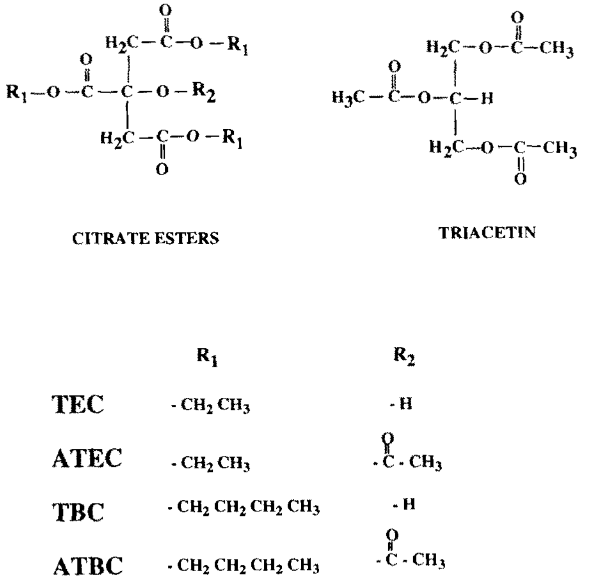

Fig. 5. Molecular structure of triacetin and the citrate ester plasticizers.

other molecules by hydrogen bonding, as well as electrostatic and dispersion forces. All the plasticizers studied have the ability to interact with the copolymer by the above-mentioned forces, but at different strengths of interaction. Triacetin, the smallest molecule, has the greatest ability to break up the polymer-polymer interaction, due to the accessibility of its carbonyl oxygens to interact through hydrogen bonding with the carboxyl hydrogens of the copolymer, as compared to the other plasticizer molecules, which have larger side chains. Thus, there is a decrease in their ability to interact with the active groups in the methacrylic acid copolymer. The triethyl citrate has almost the same ability to interact with the copolymer as triacetin, but to a lower extent, due mainly to the presence of the bulkier ethyl group, which reduces the accessibility of the carbonyl oxygen to interact. This ability to interact with the polymer can explain the similarity of the polymeric film's mechanical behavior observed with triacetin and triethyl citrate. Triethyl and tributyl citrate also have a free hydroxyl group. Although hindered by the presence of the side chains, they still have the ability to hydrogen bond with the copolymer. It is this ability to hydrogen bond that could explain the differences in the lower $T_g$ and elastic modulus values found with tributyl citrate at the 10% level, as compared with acetyl tributyl and acetyl triethyl citrate.

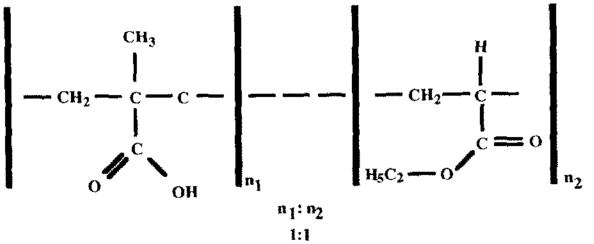

Fig. 6. Structural characteristics of poly(methacrylic acid ethylacrylate), commercially available as Eudragit® L 30D and L 100-55.

In conclusion, the plasticization of equilibrated methacrylic acid copolymers by water soluble and water insoluble plasticizers was demonstrated to be dependent upon the amount of plasticizer and the interaction between the plasticizer and the copolymer. For the water soluble plasticizers, including triacetin, triethyl citrate and acetyl triethyl citrate, there was a decrease in the glass transition temperature and the elastic modulus of the film as the plasticizer concentration increased up to 30%. For the insoluble plasticizers, tributyl citrate and acetyl tributyl citrate, there was a decrease in the $T_g$ and elastic modulus when plasticizer was included in the film at the 10% level. No further decreases were found in the $T_g$ and elastic modulus as the plasticizer increased from 10–30%. The longer elongations seen with the water soluble plasticizers indicated a higher affinity for these compounds to diffuse into and interact with the methacrylic acid copolymer molecules, thereby increasing the mobility of the polymeric chains. Correlations were also found between the chemical structures of the plasticizers and the resulting physical-mechanical and thermal properties of the equilibrated films.

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