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Effect of plasticizers on properties of pregelatinised starch acetate (Amprac 01) free films

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Abstract

Film coating is a technique widely used in the pharmaceutical field to improve and modify technological and release characteristics of capsules, tablets and granules.

In this paper physical and mechanical properties of free films of Amprac 01, obtained by the solvent cast method, were studied in order to investigate the film forming ability of this modified starch and the effects of the addition of different plasticizers.

A morphological microscopical analysis (SEM) was performed to study surface properties of the films, while thermal analysis (DSC) was carried out to investigate the influence of different types of plasticizers on the glass transition temperature of the polymer.

Then a mechanical characterization permitted to evaluate important parameters such as film crack resistance and deformation at break. Extensional creep/relaxation tests were also performed to investigate the viscoelastic characteristics.

As clearly demonstrated by the T_g values, the residual water present in the films acted as plasticizers, making possible the formation of free films characterised by good macroscopical and mechanical properties.

Except glycerol, the kind and amount of the other tested plasticizers did not markedly improve the mechanical and crack resistance of the films.

Keywords: Amprac 01; Free films; Plasticizer

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1. Introduction

Film coating is a technique widely used to improve aesthetic of dosage forms, to mask unpleasant taste and smell, to prolong the drug release, to obtain gastro-resistant forms and to provide physical protection to the tablet core increasing its resistance to rupture. Thus, the evaluation of the mechanical and intrinsic properties of coating films is very important. For practical reasons such as the difficulty on taking away the applied film without damage, in this paper, they are tested using free-film, i.e., film "free" from the core of tablets and capsules.

The choice of the free film preparation technique, which is determinant for the characteristics of the film itself, is quite difficult (Aulton, 1982; Bodmeier and Paeratakul, 1994; Tarvainen et al., 2002; Gibson et al., 1988). Some authors studied different methods to obtain free films simulating the coating process as spraying polymer solutions from nozzle or casting them onto a flat surface (Aulton, 1982; Zaro and Smith, 1972; Narisawa et al., 1994). Furthermore, in the pharmaceutical coating even the choice of polymers is fundamental and usually they are primarily based on cellulosic or acrylic polymers and are often formulated in aqueous dispersion to avoid problems associated with the use of organic solvents (Lehamann, 1982). Anyway, the possibility of using new coating material with good film forming properties can help to overlap many problems which still arise from the coating procedure as cracking during the drying process (Gibson et al., 1988) and shelf life of the product or interactions between drug and coating polymers (Schmid et al., 2000). In this paper the attention was pointed out on a pregelatinized maize starch, the Amprac 01, chemically modified by substituting a portion of the hydroxyl groups at the D-glucose monomers by acetyl groups in an esterification reaction. Recently, different studies

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showed the possibility of using modified starch as a film-forming polymer. The mechanical properties of starch acetate films were compared with those obtained using ethyl cellulose as coating polymer (Tarvainen et al., 2002, 2004). Good mechanical properties and low drug permeabilities were obtained, making starch acetate a promising novel aqueous coating material (Tarvainen et al., 2002) even for controlled release products (Tarvainen et al., 2004). The aim of this work was the study of the film forming ability of Amprac 01 aqueous dispersions and then the investigation of the influence of the addition of different plasticizers on the properties of the free films obtained by the solvent cast method.

2. Materials and methods

2.1. Materials

Amprac 01 (Rofarma Italia, Milan, Italy) was used as film forming material. Glycerol F.U. (A.C.E.F., Piacenza, Italy), Triacetin (Carlo Erba Reagenti, Milano, Italia), trietyl citrate (Merck-Schuchardt Hohenbrunn, Germany), dibutyl sebacate (Acros Organics, New Jersey, USA), propylene glycol (J.T. Baker B.V., Deventer, Holland) were the selected plasticizers.

2.2. Preparation of the free films

Films were prepared by the casting method using water as solvent. Amprac 01 was gently added to hot water (65 °C) and stirred (Eurostar digital, Ika Labortecnik, Staufen, Germany) for 30 min. Then, the plasticizer (glycerol, tryacetine, trietyl citrate, dibutyl sebacate or propylene glycol) was added dropwise under stirring for a period of 5 min in three different concentrations (10%, 20% and 30% w/w). Afterwards, dispersions were cast in a metallic circular mould (inner diameter 13 cm, deepness 200 μm) and the solvent was allowed to evaporate at room temperature for 48 h, under an extractor hood. Thickness of the films was determined three times by a screw micrometer (Mitutoyo, Japan, 0–25 mm). The resulting film thickness was 50 ± 1.0 μm.

2.3. Film appearance

Homogeneity and appearance of the film surface were examined by visual observation and scanning electron microscopy (Cambridge Stereoscan 360, Cambridge, UK). Films were mounted on a metal stub with a double-sided adhesive tape and then recovered under vacuum with a gold layer of 200 Å thickness using a metallizator (Balzer MED 010, Linchestein). A 300× magnification was used for all films.

2.4. Differential scanning calorimetry studies

The thermal analysis was performed to determine the glass transition temperature (T_g) both of Amprac 01 powder and free films. Samples (10–12 mG) were analysed by a differential scanning calorimeter (DSC, Pyris 1, Perkin-Elmer, Norwalk, USA) equipped with a cooling devise (Intracooler 2P, Cooling Accessory, Perkin-Elmer, Norwalk, USA). DSC was calibrated for temperature and heat flow using a pure sample of indium and zinc standards. Runs were performed in triplicate under nitrogen purge gas (20 mL/min). Free films were cut into small pieces and placed in 50 μL pierced aluminium pans, where they were heated at a rate of 100 K/min from 233.16 to 523.16 K. Amprac 01 powder was firstly heated from 233.16 to 473.16 K, at a heating rate of 10 K/min to allow water evaporation and then a second heating was performed at 100 K/min to determine the extrapolated onset glass transition temperature (T_g) of the anhydrous material.

2.5. Mechanical properties of the free films

2.5.1. Stress–strain test

Films were cut into 3.0 cm × 1.4 cm strips and their mechanical properties were examined by a Tensil Tester Instron 5543 (High Wycombe, England) at the extension speed of 5 mm/min. Tests were performed in five replicates and average and standard deviations were calculated.

The calculated parameters were tensile strength (σ_T) and deformation at break ΔL. The tensile strength (MPa) was cal-

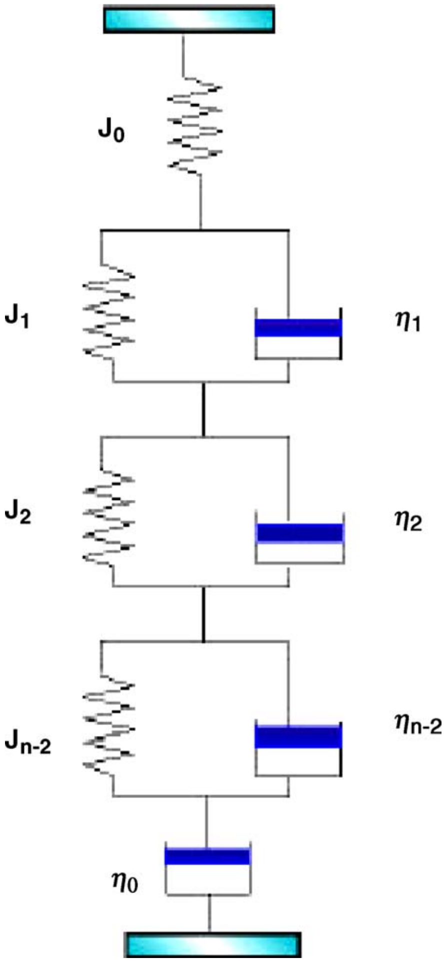

Fig. 1. Kelvin–Voigt's generalized model (Couarraze and Grossiord, 2000).

culated according to the following equation:

$$\sigma = \left[\frac{F}{hb}\right] \times \left(1 + \frac{\Delta L}{L}\right) \tag{1}$$

where F is the force at break, h the film thickness, b the film width, ΔL the samples elongation at break and L is the initial samples length (Tarvainen et al., 2002).

2.5.2. *Creep test*

The extensional test was carried out by the same Tensil Tester Instron 5543. Sample Compliance is calculated when system is submitted to a constant and instantaneous stress for a known period of time. In fact, in a creep test a stress is suddenly applied to the sample at $t = 0$ and held constant while the strain is recorded in function of time. In our case the stress applied, for a chosen time of 3 min, was one third of the maximum stress at break measured in the stress/strain test.

The creep compliance J_c at any time is defined as the ratio between the strain (ε) at time t and the applied stress (σ_0).

$$J_c(t) = \frac{\varepsilon(t)}{\sigma_0} \tag{2}$$

A typical mechanical model used to represent the viscoelastic properties of the material as a combination of spring (elastic component) and dashpot (viscous component) are shown in Fig. 1. The parameters J_0 (the initial elastic compliance which represents the elastic stretching or compression of primary bonds), J_R (the retarded elastic compliance which represents the contribution of the retarded elastic region to the total compliance) and the viscosity (obtained from the reciprocal of the slope of the linear portion of the curve) were calculated by fitting the creep curves with the help of the Origin Pro 7.0 software applying a one Maxwell and three Kelvin–Voigt units model. These elements were enough to obtain a very good fitting of the experimental data. At the same time by applying the generalised Kelvin–Voigt model (Fig. 1) (Couarraze and Grossiord, 2000) a spectrum of the retardation times was obtained. Retardation times are the times necessary for the breakage and the reformation processes of secondary bonds which characterised the structure of the studied material and, since bonds break and reform at different rates, a spectrum of retardation times exists (Çelik and Aulton, 1996).

This continuous distribution of retardation processes for a Kelvin model termed *retardation spectrum H* is represented by

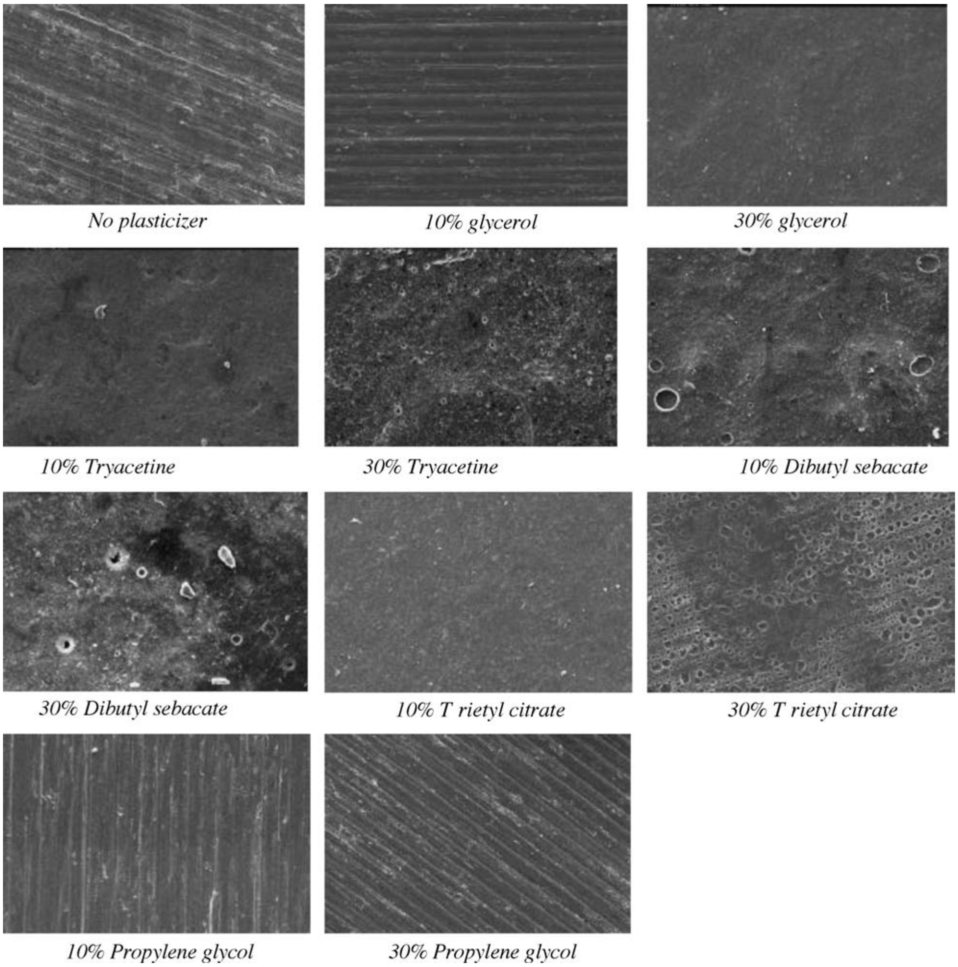

Fig. 2. Scanning electron microscopy images of Amprac 01 films (300×) obtained by adding either 10% or 30% of the different plasticizers in comparison with the film casted without plasticizer.

the following equation (Goodwin and Hughes, 2000):

$$J(t) = \int_{-\infty}^{+\infty} H \left[1 - \exp\left(-\frac{t}{\tau}\right)\right] \mathrm{d}\ln\tau \qquad (3)$$

where τ is the retardation time.

3. Results and discussion

3.1. Characterization of the free films

First of all, films were macroscopically homogeneous and sufficiently transparent. Also their thickness was uniform being about 0.050 ± 0.001 mm. SEM microphotographs are given in Fig. 2. SEM analysis showed no micropores and a good homogeneity for films obtained without a plasticizer. The presence of streaking may be due to a quite high consistency of the dispersion and to a certain difficulty encountered in the casting procedure. Films containing glycerol were quite compact and lacking in micropores particularly when the percentage of added plasticizer was 30%. The presence of streaking was observed only in films containing a low amount of plasticizer. Surface appeared quite smooth when the 30% of glycerol was added. The appearance of the films obtained by adding tryacetine was strongly dependent on the percentage of plasticizer. Low percentage (10%) gave compact films without micropores even if the surface was slightly irregular. At increasing tryacetine content, film surface was less compact, rough and characterised by the presence of micropores. The addition of dibutyl sebacate gave quite smooth and homogeneous films. Unfortunately, micropores are visible particularly at high plasticizer concentrations. The same dependence on plasticizer percentage was observed with triethyl citrate. In fact, when the 30% of triethyl citrate was added, the film appeared striped and micropores covered completely the surface, while film containing only the 10% of plasticizer appeared more homogeneous, despite the surface was formed by irregular particles forming a layer of uniform thickness. Propylene glycol films showed numerous streaking at any plasticizer concentration probably originating in the casting phase but no pores are visible.

Table 1 shows the values of the T_g onset of the different films. DSC thermal analysis was firstly performed on Amprac 01 powder. The thermogram showed a large and main endotherm between 20 and 180 °C (Fig. 3). This endotherm corresponds to the loss of residual water in the starch amorphous structure that hides the glass transition. The powder water content was of about 9.40%, as it was calculated by a thermobalance (Scaltec SMO 01, Goettinger, Germany). A new heating, after the first scan that promotes the water removal, permits to distinguish the glass transition that corresponds to that typical of the anhydrous powder (260.0 ± 2.71 °C). Amprac 01 film prepared without plasticizer (Table 1) showed a definitely lower T_g (97.47 ± 4.56) compared to that observed for the Amprac 01 powder. This result was obviously dependent on the presence of residual humidity in the film. In fact, 11% (Table 2) water content was calculated weighting the film before and after the heating cycle. Therefore, this important residual humidity can act as plasticizer lowering the T_g.

Table 1
Extrapolated onset glass transition temperature (mean and standard deviations $n = 3$) of the different polymeric films

Film	Plasticizer (%)	T_g onset (°C)
Amprac 01 powder	–	260.0 ± 2.71
Amprac 01[a]	–	92.47 ± 4.56
Glycerol	10	79.36 ± 7.38
	20	78.92 ± 4.74
	30	76.61 ± 9.20
Tryacetine	10	69.68 ± 4.30
	20	70.48 ± 10.3
	30	72.54 ± 9.42
Dibutyl sebacate	10	81.57 ± 18.8
	20	78.56 ± 13.2
	30	90.10 ± 8.67
Triethyl citrate	10	94.38 ± 3.40
	20	79.51 ± 8.00
	30	80.80 ± 6.02
Propylene glycol	10	73.61 ± 5.09
	20	73.75 ± 3.43
	30	73.21 ± 12.8

[a] No plasticizer.

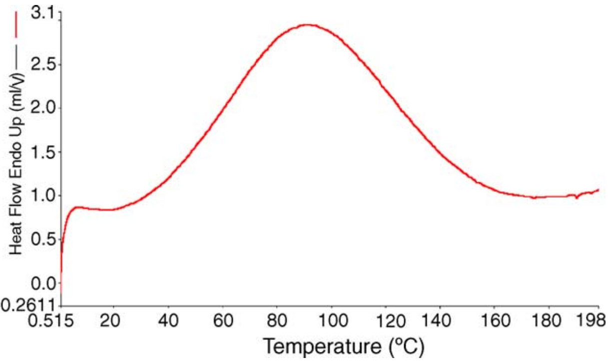

Fig. 3. DSC thermogram for the first heating of the Amprac powder. The large endotherm corresponds to the desolvation of the residual water associated with the polymer.

Furthermore, films obtained by adding the different types and amounts of plasticizers showed T_g values only a little lower than those observed for the Amprac 01 film. In Fig. 4, the thermogram for the 10% glycerol Amprac film is given as en example. All other films exhibit the same typical layout, and they are used to calculate the T_g values. It must be considered that a considerable

Table 2
Weight loss of the different polymeric films containing the 30% of plasticizer compared with the Amprac 01 film

	Weight loss (%)
Amprac 01[a]	11.0
Glycerol	12.2
Tryacetine	8.54
Dybutil sebacate	10.1
Triethyl citrate	11.8
Propylene glicol	9.33

[a] No plasticizer.

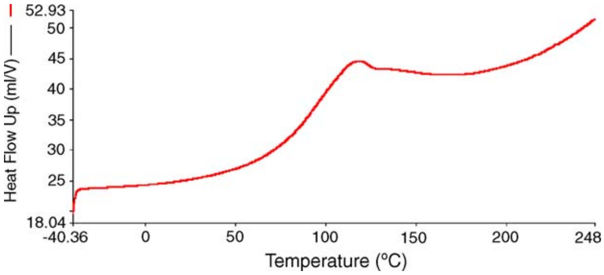

Fig. 4. DSC thermogram of the 10% glycerol Amprac film. The change in C_p is associated with the T_g.

amount of residual water (8–13%) is always retained by the film even when the 30% of plasticizer was added (Table 2). So, plasticizer role did not seem determinant.

Moreover T_g values were independent of the percentage of the added plasticizer (Table 1), but more likely they depended on the percentage of residual water. For this reason only a bland polymer/plasticizer interaction can be detected by DSC analysis.

3.2. *Mechanical properties of the free films*

The unplasticized Amprac 01 film showed a remarkable crack resistance and consequently a high tensile strength ($\sigma_T = 56.3 \pm 7.59$ MPa). The quite low film deformation at break ($\Delta L/L = 1.97\%$) demonstrated that Amprac 01 film was only moderately flexible (Table 3). Samples obtained by adding glycerol as plasticizer showed tensile strength values strongly dependent on the amount of plasticizer itself. As expected, the film containing the 10% of glycerol did not show remarkable differences in the texture properties compare to the Amprac 01 sample, while higher percentages of plasticizer (20% and 30%) drastically reduced film resistance at break. On the contrary, the deformation at break is particularly high for the sample containing the 30% of glycerol ($\Delta L/L = 9\%$).

When the considered plasticizers are dibutyl sebacate and tryacetine, a lowering in texture parameters, as tensile strength did not correspond to an increase of deformability. Films obtained by adding propylene glycol showed an interesting crack resistance that is independent on the amount of propylene glycol itself but also in this case deformability is rather low (Table 3).

Even triethyl citrate gave films of reduced resistance without an increase in samples deformability. Therefore tensile strength is a parameter not strictly dependent on deformability values. The addition of plasticizers led in general to a reduction in the mechanical resistance of the films without increasing their flexibility except for glycerol if added in considerable amount. It is evident that all the plasticizers, with the exception of glycerol present only a negligible interaction with Amprac 01. In fact glycerol is the only plasticizer able to improve films deformability even if a greater flexibility corresponds to a quite low samples resistance at break. Creep tests (Table 4) confirmed the results obtained with the stress/strain experiments showing that a viscoelastic characterisation may be a useful support for the definition of the mechanical aspects of the analysed films. In fact, Amprac 01 film without plasticizers presented the lowest values of compliance, immediate (J_0) and retarded (J_R) (Table 4). It means that it possesses the lowest deformability, the highest resistance to stress and a remarkable elastic character. Regarding viscosity, also in this case, the Amprac 01 sample presented the greatest value confirming that this polymer is characterized by good film forming properties being able to give rise to dense and strong films. Since J_0, J_R and viscosity data presented in Table 4 are not discriminant within the different plasticizers, the investigation of the retardation spectra was performed outlining behaviour quite different for glycerol 30% film. In fact, the retardation time spectrum of this sample presented various

Table 3
Mechanical properties of Amprac 01 film and Amprac 01/plasticizers films (mean and standard deviation, $n = 3$)

	Plasticizer (%)	F (N)	$\Delta L/L$ (%)	S_T (MPa)
Amprac 01[a]	–	38.64 ± 2.94	1.97	56.30 ± 7.59
Glycerol	10	13.98 ± 4.01	1.63	20.45 ± 5.38
	20	7.030 ± 1.00	2.37	10.22 ± 1.32
	30	3.198 ± 0.58	9.00	4.98 ± 0.65
Tryacetine	10	8.480 ± 1.59	0.70	12.27 ± 2.28
	20	7.260 ± 0.50	0.92	10.47 ± 0.73
	30	6.050 ± 1.17	1.30	8.720 ± 1.69
Dibutyl sebacate	10	19.84 ± 1.94	1.30	28.71 ± 2.26
	20	15.45 ± 1.70	1.40	22.39 ± 4.14
	30	13.20 ± 0.59	1.63	19.17 ± 1.01
Propylene glycol	10	25.99 ± 1.62	1.61	37.88 ± 3.90
	20	23.73 ± 1.37	2.00	36.82 ± 8.13
	30	25.44 ± 2.22	2.20	34.66 ± 3.58
Triethyl citrate	10	13.16 ± 1.20	1.31	19.06 ± 2.15
	20	13.74 ± 1.97	1.38	19.92 ± 3.15
	30	17.74 ± 1.35	1.48	20.35 ± 3.27

[a] No plasticizer.

Table 4
Creep parameters of Amprac 01 films with and without plasticizer

	Plasticizer (%)	J_o (1/Pa)	J_R (1/Pa)	Viscosity (Pa s)
Amprac 01[a]	–	1×10^{-9}	0.0004	2903445
Glycerol	10	0.0015	0.7900	1669.490
	20	0.0016	0.8100	1258.480
	30	0.0017	0.8300	1057.460
Tryacetine	10	0.0017	0.7700	5347.170
	20	0.0074	0.8400	2412.200
	30	0.0090	0.9000	1347.830
Dibutyl sebacate	10	0.0012	0.8100	455392.1
	20	0.0016	0.9600	36902.48
	30	0.0025	0.9900	12330.44
Propylene glycol	10	0.0013	0.8100	1293.310
	20	0.0015	0.7800	1446.770
	30	0.0016	0.7200	1143.050
Triethyl citrate	10	0.0014	0.8000	1270.290
	20	0.0017	0.7800	1335.620
	30	0.0077	0.7700	1267.430

[a] No plasticizer.

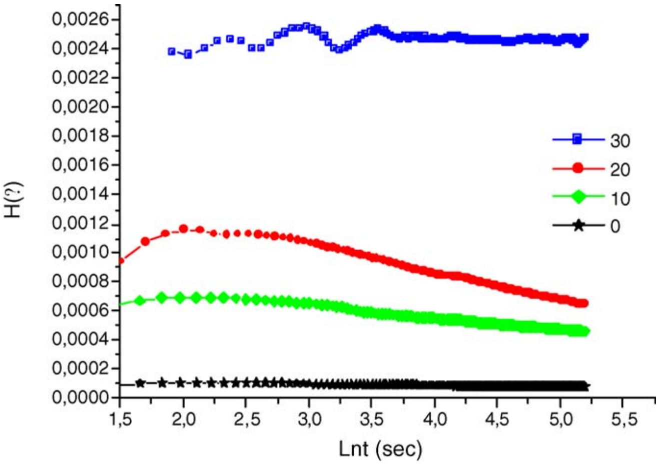

Fig. 5. Retardation spectra of films obtained using different percentages of glycerol as plasticizer compared with the Amprac 01 film.

characteristic peaks (Fig. 5), which could be explained with the presence of a shift in the retardation part of the creep curve. This result is a sign of the presence of a higher retarded than immediate elasticity comparing to the other films. Furthermore, a certain dependence on glycerol amount is present (Fig. 5) as demonstrated by the decrease in the peaks height at lower percentage of plasticizer, which indicates a higher film consistency and the presence of a more consolidate structure. This data could indicate the presence of an effective interaction between Amprac 01, glycerol and water, which give rise to a decrease in films toughness and resistance, and to a far greater deformation at increasing glycerol content. In fact the retarded elasticity region present in the creep curve is more pronounced and the retardations times higher in comparison with the spectra obtained from the films prepared using the other plasticizers. These last films possessed behaviour only partially dependent on the plasticizers percentage and in general a lower breaking resistance. In practice, their behaviour appeared more similar to Amprac 01 sample according to data showed in Table 4 and Fig. 6. In particular, propylene glycol containing films showed retardation spectra and mechanical properties almost superimposed to that of the Amprac 01 film without plasticizer.

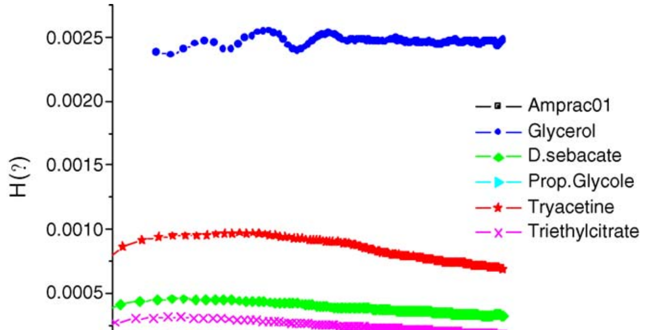

Fig. 6. Retardation spectra of films obtained using the different plasticizers in the percentage of 30% compared with the Amprac 01 film.

4. Conclusions

The aqueous coating processes are a preferable alternative to organic solvent-based film coating for environmental, economic and safety reason and Amprac 01 matches quite well with this need. In fact, Amprac 01 can form films of good mechanical properties because it strongly interacts with residual water, which is present in considerable amount. The addition of a plasticizer, except glycerol when its concentration is at least the 30% (w/w), does not substantially improves the flexibility of the film but only reduces its resistance.

This is due to the chemical structure of glycerol itself, which is, among the used plasticizers, the most similar to the aqueous media. In fact, the obtained results outlined as the characteristics of the plasticizer and its affinity to water play a fundamental role in film appearance, thermal and mechanical properties, particularly in comparison with films containing dibutyl sebacate, the most lipophilic plasticizer.

Since residual water seems to play a fundamental role in films characteristics, future studies will regard the analysis of the stability of the Amprac 01 film in different conditions of relative humidity to investigate the possible changes of the thermal and mechanical behaviour of the sample. Definitely, future works will be focused to the investigation of the Amprac 01 coating performance on model cores.

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