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Der Pharmacia Lettre, 2011, 3(2): 257-263
(http://scholarsresearchlibrary.com/archive.html)

ISSN 0975-5071
USA CODEN: DPLEB4

Effect of Different Plasticizers on Eudragit RS100 and RL100 Free Film

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ABSTRACT

The physical properties of polymers used for modified-release coating of pharmaceutical dosage forms are governed by several variables such as plasticization, temperature and humidity. For plasticization, special plasticizers are used that weaken the intermolecular attractions between polymer chains. The addition of plasticizers to a coating formulation generally increases the elongation and flexibility of the coating while reducing the tensile strength and elastic modulus. EUDRAGIT® RS100 and EUDRAGIT® RL 100 polymer films would become brittle without the addition of plasticizers. The present study compares the influence of the plasticizers polyethylene glycol 6000 (PEG) and dibutyl phthalate (DBP) on the flexibility of these coatings. The prepared films were evaluated for clarity, thickness, moisture absorption and mechanical properties and the optimum amount of these plasticizers for coating formulations was determined. Eudragit RS: RL (2:1) and RS: RL (3:1) polymers in coating solution are suitable for controlled release coating of drug loaded pellets with DBP as plasticizer in the range of 1.0% - 2.0% w/v in coating solution.

Key words: Eudragit, Polyethylene glycol 6000, dibutyl phthalate.

INTRODUCTION

Polymeric film coating has been applied to pharmaceutical dosage forms for a variety of reasons, e.g., taste masking, as a moisture-resistant barrier, and as a method of controlling the release of drugs. The physicochemical properties of film depend upon its composition under specified environmental conditions. A typical film coating formulation includes a film-forming polymer, insoluble filler such as pigments and opacifiers, soluble fillers such as salts, sugars, plasticizers and solvents. The polymers are most often cellulose derivatives or methacrylic acid derivative and may or may not be water soluble. Insoluble fillers add color and protect from light. Pigments are usually aluminum lakes and titanium dioxide. Soluble fillers are used to alter the permeability characteristics of the film like plasticizers[1]. The film forming polymer can be evaluated by studying properties of free film of polymer alone or with other additives. Films are cast and subjected to evaluation for a wide range of

properties like water vapor transmission, oxygen permeability, moisture absorption, permeability, mechanical, thermal and photo-oxidation effect. In this study, the effects of the plasticizers like dibutyl phthalate and polyethylene glycol 6000, on the viscoelastic properties of EUDRAGIT® RS100 and EUDRAGIT® RL 100 a copolymer consisting of polymethacrylate and polymethacrylic acid, were measured by evaluating tensile strength, yield point, % elongation, breaking strength, plastic deformation, relative surface energy and toughness index . The selection of the components of film coatings formulation like suitable plasticizers and its concentration and concentration of different polymers in the sustained release coating solution and their interaction was essential for reproducibility of end product, saving time and money.

MATERIALS AND METHODS

Materials

RS100 and RL100, polyethylene glycol 6000, dibutyl phthalate, cetyl alcohol were procured from Zim Laboratories ltd. Mercury, isopropyl alcohol, acetone were purchased from LOBA Chemicals and potassium acetate, potassium carbonate, sodium chloride , potassium nitrate were purchased from Merck ltd.

Film preparation

Drug free film of RS100 and RL100 were prepared on a mercury substrate[2] by solvent evaporation technique using isopropyl alcohol and acetone as the solvents and dibutyl phthalate and polyethylene glycol-6000 as plasticizers. Solutions of 5% RS100 and RL100 were prepared in combination by taking different ratios (1:2 and 1:3,) in isopropyl alcohol (IPA): acetone (1:1). Composition of free films prepared using RS100 and RL100 is given in Table **1**. These polymers solutions were poured into petri-dish containing mercury, allowing the solvent to evaporate for 24hr, the films were taken outside and dried at room temperature for 48 hr and stored in desiccators at ambient temperature for 24hr. These films were evaluated for thickness uniformity, tensile strength, and percentage of elongation, moisture absorption, water vapor transmission and scanning electron microscopy (SEM).

Table 1: Composition of free films using RS100 & RL100

Formula no.	RS100	RL100	Polyethylene glycol 6000	DBP
1	3.35 %	1.65%	0.5%	-
2	3.35 %	1.65%	1.0%	-
3	3.35 %	1.65%	1.5%	-
4	3.35 %	1.65%	2.0%	-
5	3.75%	1.25%	0.5%	-
6	3.75%	1.25%	1.0%	-
7	3.75%	1.25%	1.5%	-
8	3.75%	1.25%	2.0%	-
9	3.35 %	1.65%	-	0.5%
10	3.35 %	1.65%	-	1.0%
11	3.35 %	1.65%	-	1.5%
12	3.35 %	1.65%	-	2.0%
13	3.75%	1.25%	-	0.5%
14	3.75%	1.25%	-	1.0%
15	3.75%	1.25%	-	1.5%
16	3.75%	1.25%	-	2.0%

Evaluations of free polymeric films

Clarity: The films were evaluated for clarity and were graded as transparent, translucent, or opaque.

Thickness: A micrometer screw gauge was used to measure the thickness at different points throughout the free film and recorded as the mean of five measurements.

Moisture absorption: The dried films were cut into 25 x 10mm, weighed and transferred to a tarred petri-dish. Glass desiccators were maintained at controlled relative humidity conditions by using following saturated salt solutions with excess amount of salts[3].

Saturated salt solution	% Relative humidity
Potassium acetate	23
Potassium carbonate	43
Sodium chloride	75
Potassium nitrate	93

After equilibrating the desiccators with appropriate concentration of saturated salt solution for three days, accurately weighed previously dried films placed in petri-dishes were kept in the desiccators undisturbed for 14 days. The difference in the weight gave the amount of moisture absorbed at various relative humidity. Percentage moisture absorption was then determined. The values reported in Table **2.** are mean of three readings for each film.

Mechanical properties of films: The films were cut into size of 12 x 130 mm and the thickness of the film was measured at five places by micrometer screw gauge[4,5]. Plastic tensile test was performed as American Society for testing material (ASTM) using an instrument Model-4467 of Instron Corp., Canton, MA. The gauge length was kept 50 mm and cross head speed was 25 mm/min and the test was performed at 50% RH at 25^{o}C. The tensile strength, percentage elongation and modulus of elasticity were automatically computed by the instrument. Each experiment was repeated at least three times.

Permeability Study: The permeability studies[6,7].of polymeric films were carried out on 'Keshary Chien skin permeation cell' having a diffusion cell with receptor compartment without jacket and a donor compartment. Both the compartments were fabricated using borosilicate glass. The area of the mouth of the receptor compartment was 4.449cm^2.

The rate of WVT (water vapor transmission)[8,9].across the film was determined with 23%, 43%, 75% and 93% RH inside and 0% RH outside the cell. A film of appropriate dimension was mounted on the permeation cell containing saturated salt solution. The charged cells were weighed and placed in pre equilibrated desiccators maintained at 0% RH. The cells were again weighed at 24, 48,72hr. The amount of water vapor transmitted through the film was found by the loss in weight of the assembled cell. Three samples were used for transmission of each film of different polymers. The rate of WVT was calculated using Utsumi's equation[10]. The results in terms of gcm/cm^2 per 24hr, 48hr and 72hr respectively are given in Table **4**.

$$Q = \frac{WL}{S}$$

Where,

W = water transmitted, L = film thickness (cm), S = surface area (sq. cm), Q = Water vapor transmission (g.cm / cm^2 / 24 hours)

Scanning Electron Microscopy

Surface topographical analysis of selected polymeric film was carried out by Scanning Electron Microscopy and results are shown in figure **1**.

RESULTS AND DISCUSSION

Eudragit RS100 and RL100 have shown good film forming property. As the thickness of film was increased, WVT rate decreased irrespective of plasticizers concentration. Therefore, 5% polymeric solutions were used for the sustained release coating.

Table 2: Mechanical properties of free films of RS100 & RL 100

Formula no.	Thickness (mm)	Tensile strength (kg F/mm^2)	Percentage elongation	Modulus of elasticity
1	0.183	0.382	17.5	100.42
2	0.179	0.345	25.9	91.82
3	0.185	0.314	35.6	88.58
4	0.193	0.289	45.3	65.83
5	0.196	0.418	16.2	95.26
6	0.182	0.368	22.1	86.31
7	0.175	0.325	28.9	80.22
8	0.186	0.296	38.2	60.53
9	0.158	0.461	11.2	68.92
10	0.145	0.383	18.7	53.82
11	0.156	0.320	24.1	38.42
12	0.153	0.300	26.8	34.62
13	0.182	0.482	12.8	69.42
14	0.182	0.415	20.5	54.5
15	0.181	0.345	26.9	37.3
16	0.179	0.301	33.8	25.1

Table 3: Moisture absorption studies of free films

Formula no	Percentage moisture absorption at			
	23% RH	43% RH	75% RH	93% RH
1	0.689	1.718	2.352	3.328
2	0.542	1.532	2.832	3.512
3	0.629	1.932	2.568	3.628
4	0.481	1.468	2.801	3.928
5	0.680	1.623	2.236	3.235
6	0.538	1.532	2.893	3.562
7	0.520	1.496	2.942	3.895
8	0.482	1.410	3.123	4.212
9	0.483	1.342	1.986	2.892
10	0.485	0.942	1.496	1.942
11	0.412	1.052	1.568	2.032
12	0.385	0.985	1.601	2.289
13	0.410	0.823	1.125	1.568
14	0.385	0.735	1.081	1.432
15	0.375	0.715	1.095	1.442
16	0.370	0.720	1.080	1.411

Table 4: WVT rate studies of free films

Formula no	%RH	Thickness (cm)	Area (cm^3)	WVTR x 10^4 (g cm/cm^2)		
				24h	48h	72h
1	23	0.0189	4.310	0.75	1.86	2.54
	43			0.98	2.42	3.15
	75			1.15	2.61	3.86
	93			2.01	3.18	4.15
2	23	0.0183	4.562	0.82	1.94	2.83
	43			1.10	2.11	3.80
	75			1.98	2.84	4.23
	93			2.56	3.62	4.86
3	23	0.0178	4.440	0.86	1.96	2.95
	43			1.56	2.86	3.99
	75			2.83	4.52	6.32
	93			3.36	5.62	7.78
4	23	0.0188	4.015	0.95	2.01	2.98
	43			1.68	2.88	4.12
	75			2.90	4.62	6.53
	93			3.86	5.89	7.89
5	23	0.0192	4.150	0.68	1.23	2.58
	43			0.88	1.59	3.28
	75			1.10	2.82	4.52
	93			1.58	3.55	5.69
6	23	0.0190	4.150	0.72	1.53	2.56
	43			1.20	2.11	3.45
	75			1.89	3.01	4.01
	93			2.52	3.58	4.88
7	23	0.0186	4.028	0.85	1.99	2.86
	43			1.35	3.12	3.64
	75			2.52	4.56	5.22
	93			3.12	5.34	6.15
8	23	0.0180	4.028	0.99	2.11	2.88
	43			1.52	2.72	3.87
	75			2.65	4.15	5.65
	93			3.33	5.38	6.82
9	23	0.0186	4.330	0.95	1.12	2.45
	43			1.32	1.86	2.96
	75			3.26	4.42	5.62
	93			4.15	5.92	7.32
10	23	0.0178	4.159	0.88	0.98	1.92
	43			1.15	1.52	2.62
	75			2.60	3.45	4.11
	93			3.15	4.10	5.38
11	23	0.0188	4.260	0.78	0.92	1.15
	43			0.89	1.32	2.15
	75			1.15	1.98	2.98
	93			1.85	2.38	3.42
12	23	0.0176	4.252	0.65	0.82	1.08
	43			0.75	0.92	1.15
	75			0.92	1.32	1.98
	93			1.08	1.82	2.56
13	23	0.0178	4.158	0.75	0.95	1.32
	43			1.32	1.58	2.18
	75			1.95	2.69	3.25
	93			3.03	4.82	5.89
14	23	0.0182	4.205	0.68	0.82	0.98
	43			1.05	1.39	2.52
	75			1.90	2.58	3.10

	93			2.95	4.08	5.12
15	23 43 75 93	0.0182	4.082	0.52 0.80 1.11 1.78	0.80 1.25 1.46 2.19	0.93 2.10 1.83 3.15
16	23 43 75 93	0.0181	4.132	0.48 0.65 0.86 0.95	0.59 0.85 0.98 1.52	0.86 1.08 1.24 2.09

The uniformity in thickness was maintained with all the prepared films. The films plasticized with DBP possessed high tensile strength and low percentage of elongation compare to the film prepared using PEG. The tensile strength of the film decreased in the order of 0.5%DBP > 1.0%DBP >1.5%DBP > 2.0%DBP and 0.5%PEG > 1.0% PEG >1.5% PEG > 2.0% PEG. Whereas the order of percentage of elongation was 2.0%DBP > 1.5%DBP >1.0%DBP > 0.5%DBP and 2.0%PEG >1.5% PEG >1.0% PEG > 0.5% PEG. These results indicate that the films of DBP were more tough as compared to PEG films, and also showed that as the concentration of plasticizer was increased the tensile strength decreased and percentage elongation increased.

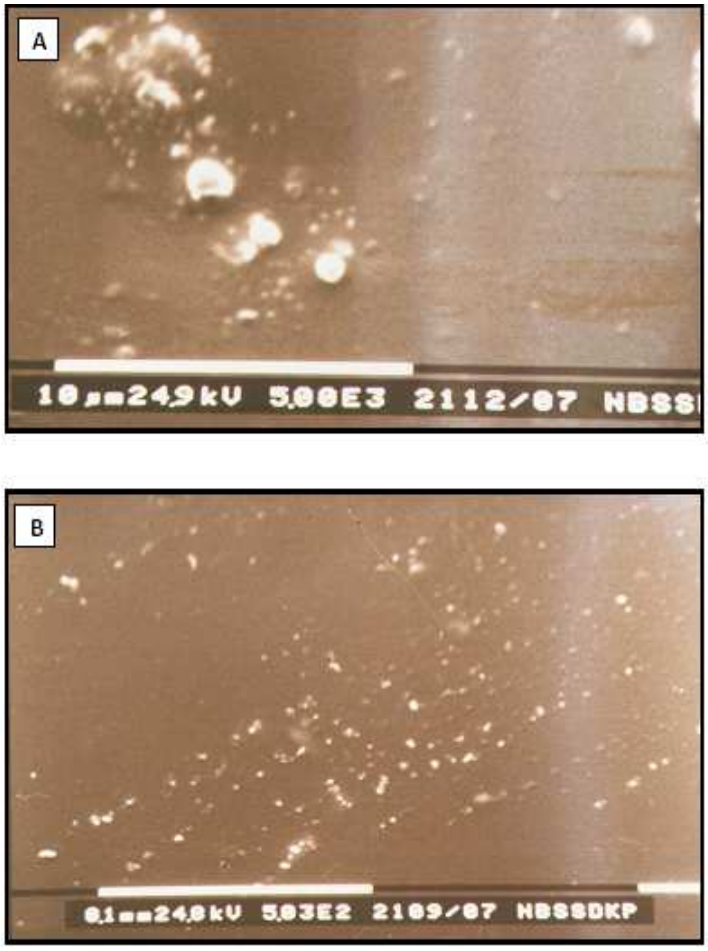

Figure 1: Stereomicrograph of free films (A) eudragit RS: RL (2:1) F-12 and (B) eudragit RS: RL (3:1) F-16

The WVT rate was higher in case of PEG films as compared to DBP films. The diffusion rate was decreased as the concentration of DBP was increased and increased as the concentration of PEG was increased. RS100 and RL100 were used in the ratio 2:1 and 3:1 for the sustained release coating to get desirable release of drug because RL100 was more permeable as compare to RS100. From the above results, it was found that DBP was suitable plasticizer in the range of 1.0% - 2.0% w/v in coating solution used for sustained release of drug.

Scanning electron microscopy (SEM) of the films of ethyl cellulose F-15, eudragit RS: RL (2:1) F-26, and eudragit RS: RL (3:1) F-30 showed smooth surfaces.

CONCLUSION

Eudragit RS100 and eudragit RL100 have good film forming property. DBP and PEG were found to be optimum as plasticizer in the range of 1.0% - 1.5%, and give smooth, flexible and transparent films. The films of DBP were tougher as compared to PEG. The 2:1 and 3:1 eudragit RS100 and eudragit RL100 was selected to get desirable release of drug because eudragit RL100 is more permeable as compare to eudragit RS100.The results show that 5% RS: RL (2:1) and RS: RL (3:1) polymers in coating solution were suitable for controlled release coating of drug loaded pellets with DBP as plasticizer in the range of 1.0% - 2.0% w/v in coating solution. Scanning electron microscopy (SEM) of the free films of eudragit RS: RL (2:1) F-12 and eudragit RS: RL (3:1) F-16 show smooth surface.

Acknowledgement
We are thankful to Head of Department, Department of Pharmaceutical Sciences, R.T.M. Nagpur University, Nagpur for providing Laboratory facilities, equipments & their valuable guidance time to time.

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