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PREPARATION OF ETHYL CELLULOSE PSEUDOLATEX AND STUDIES ON SUITABILITY OF IT AS A BINDER FOR GRANULATION

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ABSTRACT

Ethyl cellulose pseudolatices were prepared by an emulsion-solvent evaporation technique, which consisted of dissolving the polymer in a blend of benzene and ethyl alcohol, followed by the addition of adjuvants. The organic solvents were removed from the emulsion using vacuum distillation. Physical evaluation of the dispersions and the cast films was carried out.

On the basis of characteristics of cast films, selected formulations were used as granulating agents for preparing chlorpheniramine maleate tablets. Good correlation was observed between total solid in the granulating dispersion and the drug release. The possible mechanisms for the drug release from the tablets are suggested.

INTRODUCTION

Aqueous based film coating technique is gaining popularity in recent years due to restrictions imposed by government agencies, possible hazardous effect of organic solvents and/or expensive nature of organic solvents utilised in commercial film coating methods. Commercially pseudolatexes (aqueous colloidal polymeric dispersions) are available containing ethyl cellulose(Surelease; Colorcon; U.K., Aquacoat; FMC; U.S.A), acrylic copolymer dispersions(Eudragit NE 30D; Eudragit RS 30D; Eudragit RL 30D;Rohm Pharma, Germany), or cellulose acetate phthalate (Aquateric; FMC; U.S.A).

Aqueous polymeric dispersions are concentrated products containing extremely small particles with narrow particle size distribution. Solutions, in organic solvent, are more viscous then latex dispersions at an equivalent polymer concentration and are difficult to handle. This study deals with the preparation and evaluation of ethyl cellulose pseudolatex using emulsion - solvent evaporation technique. Studies on latex dispersions was carried out by Savage and Julius[1] and Banker[2]. This report also deals with the use of aqueous ethyl cellulose dispersion as a binder.

EXPERIMENTAL

Method of Preparation Of Ethyl Cellulose Dispersion:

The compositions of different formulation tried by us are shown in Table I. The required quantity of plasticizer (Castor oil and/or n-dibutyl phthalate), Tween 80,Oleic acid were mixed with benzene:ethyl alcohol(80:20) mixture and uniformly mixed. Sodium lauryl sulfate (100 #) and ethyl cellulose(100 #) were then added and the mixture was stirred for 45 minutes. Ammonia solution(33%v/v) was then gradually added and mixed to yield a viscous emulsion. The emulsion was further agitated for 10 minutes at 200 RPM. Fumed silica (Aerosil 200) was first separately dispersed in distilled water and later gradually added to the viscous emulsion while stirring at 150 RPM. The dispersion was then sonicated for ten minutes and benzene was then evaporated from the mixture by vacuum distillation at 65^{o}C. The content of the distillation flask was periodically checked for the absence of traces of benzene. The mixture of ammonia and ethyl alcohol (1:1) was added to maintain fluid state during evaporation. The absence of benzene was determined by smelling the dispersion as well as by adding a few drops of the dispersion to distilled water. The process of vaccum distillation was continued till benzene droplets did not appear on the surface of distilled water.

TABLE 1 : FORMULATIONS FOR THE DISPERSIONS OF ETHYL CELLULOSE

Ingredients		Formulation No.																
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
Ethyl Cellulose	(g)	20	20	20	20	20	20	20	20	20	20	20	20	20	20	20	20	20
Benzene	(mL)	80	80	80	80	80	80	80	80	80	80	80	80	80	80	80	80	80
Ethyl alcohol	(mL)	20	20	20	20	20	20	20	20	20	20	20	20	20	20	20	20	20
Castor oil	(mL)	20	20	20	20	15	12	11	10	08	-	-	-	-	05	05	05	05
n-Dibutyl phthalate	(mL)	-	-	-	-	-	-	-	-	-	15	12.5	12	10	06	07	08	10
Tween-80	(mL)	02	02	02	02	02	02	02	02	02	02	02	02	02	02	02	02	02
SLS	(g)	.3	.5	.6	1.	.6	.6	.6	.6	.6	.6	.6	.6	.6	.6	.6	.6	.6
Ammonia Solution	(mL)	50	50	50	50	50	50	50	50	50	50	50	50	50	50	50	50	50
Fumed silica	(g)	.1	.1	.1	.1	.1	.1	.1	.1	.1	.1	.1	.1	.1	.1	.1	.1	.1
Oleic acid	(mL)	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6
Purified water	(mL)	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100

SLS = Sodium lauryl sulphate

Preparation and Evaluation of cast films:

Ten mL of each formulation was carefully poured on 12 X 12 cm glass plates and the films were detached later on for further evaluation. The dispersions and the films were evaluated for different physical charecteristics. The results are summarised in Table II.

Out of the seventeen formulations, three formulations, namely eighth, twelvth and sixteenth were selected for further studies. Solid content in these formulations was found by evaporating the volatile materials at 60° C.

Preparation and Evaluation of Tablets Using Ethyl Cellulose Dispersions as Binding Agents:

To evaluate the binding property of ethyl cellulose dispersions chlorpheniramine maleate was selected as a model drug. Chlorpheniramine maleate (100#) 200 g, dicalcium phosphate (100#) 500 g and microcrystalline cellulose 300 g were uniformly mixed using Erweka planetary mixer. To 50 g of the powdered mixture were added measured volume of aqueous dispersion of ethyl cellulose and distilled water (wherever necessary) and mixed thoroughly. The compositions of different batches of tablets are shown in Table III.

The wet coherent mass was passed through 10# screen and dried in a tray drier at 55°C for four

TABLE II: PROPERTIES OF DIFFERENT FORMULATIONS (1-17) AND CAST FILMS

Formulation No.	Appearance of dispersion	Transparency	Easily separatable	Cracked on folding	Stickiness
1	Ununiform with clumps	No	No	-	Yes
2	uniform	No	No	-	Yes
3	Straw coloured, uniform	Yes	No	-	Yes
4	Straw, excessive foaming	Yes	No	-	Yes
5	Straw, uniform	Yes	No	-	Yes
6	Straw, uniform	Yes	No	-	Yes
7	Straw, uniform	Yes	Yes(+)	No	Yes
*8	Straw, uniform	Yes	Yes	No	No
9	Straw, uniform	Yes	Yes	Yes	No
10	Straw, uniform	Yes	No	-	Yes
11	Whitish-straw, uniform	Yes	Yes	No	Yes
*12	Whitish-straw, uniform	Yes	Yes	No	No
13	Whitish-straw, uniform	Yes	No	Yes	No
14	Whitish-straw, uniform	Yes	No(-)	-	No
15	Whitish-straw, uniform	Yes	Yes	Yes	No
*16	Whitish-straw, uniform	Yes	Yes	No	No
17	Whitish-straw, uniform	Yes	No(+)	No	Yes

(+) = Rubbery in nature , (-) = Cracked

TABLE III: COMPOSITIONS OF CHLORPHENIRAMINE MALEATE TABLETS

Product No.	Amount of mixture (g)	Quantity of dispersion (mL)	% Dry solid basis	Talc (g)	Average weight of tablet (mg)
A1	50	15.0	7.820	0.540	109
A2	50	20.0	10.160	0.556	112
A3	50	25.0	12.395	0.570	115
A4	50	30.0	14.515	0.584	118
A5	50	35.0	16.530	0.600	121
B1	50	15.0	9.231	0.550	110
B2	50	20.0	11.940	0.560	113
B3	50	25.0	14.490	0.580	116
B4	50	30.0	16.902	0.600	120
B5	50	35.0	19.178	0.610	121
C1	50	17.4	9.020	0.550	111
C2	50	25.0	12.470	0.570	115
C3	50	30.0	14.602	0.580	118
C4	50	35.0	16.630	0.590	120
C5	50	40.0	18.560	0.610	129

* Formulation no. 8 was used in A1-A5.
* Formulation no. 12 was used in B1-B5.
* Formulation no. I6 was used in C1-C5.

hours. The dried granules were passed through 20# screen and mixed with talc in polyethylene jars to obtain granules ready for compression. The granules were then compressed using 8/32 inch dies and punches set to produce tablets having 2-3 Kg/cm^2 hardness.

Dissolution Studies of Chlorpheniramine Maleate Tablets:

Each batch of chlorpheniramine maleate tablet were subjected to dissolution studies using U.S.P. apparatus 2 at 50 RPM using 500 mL distilled water as dissolution media. The drug content in the medium was estimated by withdrawing aliquots at an interval of sixty minutes upto four hundred and eighty minutes and measuring the absorbance at 261 nm[3].

RESULT AND DISCUSSION

Physical properties of the formulation and cast films are shown in Table II . Three formulations namely 8, 12 and 16 were selected for further studies as they gave films with desirable characteristics such as flexibility, transperancy, non-stickiness and easy removability, solid contents were found to be 28.3, 28.5 and 33.9%w/v in the formulations respectively. Films containing higher percentages of castor oil or n-dibutyl phthalate were sticky in nature. Formulations containing higher percentage of Sodium Lauryl Sulphate exhibited excessive foaming tendency. Such type of formulations may be difficult to handle while

processing. Therefore, it is concluded that desirable properties and film characteristics can be achieved by optimising the formulation of dispersion.

The in-vitro dissolution of chlorpheniramine maleate, shown in Figure.1, 2 and 3, from the tablets was found to be dependant on the amount of binder present in the formulations. It has been reported[6] that ethyl cellulose provides a membrane which remains intact throughout the GI tract. However, it does permit water to permeate the film, dissolves the drug and permits the diffusion of drug solution. The relatively slow release from the product containing higher % of ethyl cellulose may be because of reduced permeability.

The release of the drug from each batch, was releatively rapid in the first sixty minutes and it declined in the later period. The release rate of the drug decreased after three hours. The release of the drug from all tablets in the first hour, was in between thirty and forty percent of the total drug present. The release of drug from all tablets after three hours was in between fifty and sixty percent of the total drug. After three hours the release of drug was of controlled type till eighth hours. Increase in the total dry solids of the dispersions in the tablet formulation showed increased retardation of the drug release. Therefore, it is concluded that a desired dissolution pattern can be achieved by selecting

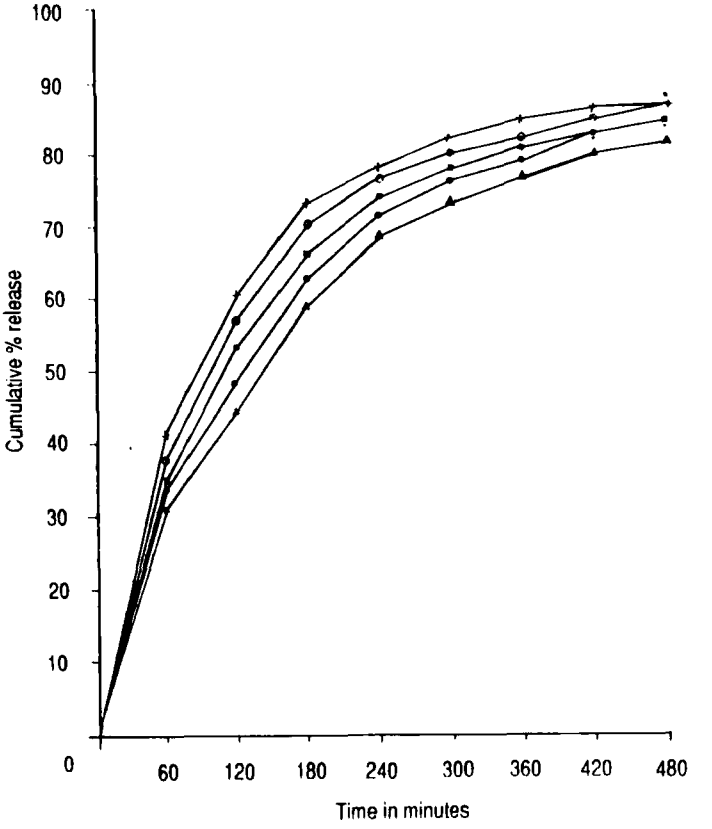

FIGURE 1 Chlorpheniramine Maleate Release in Distilled Water.

Key : + A_1 = 7.82 % (DSB)
○ A_2 = 10.16 % (DSB)
■ A_3 = 12.39 % (DSB)
● A_4 = 14.51 % (DSB)
▲ A_5 = 16.53 % (DSB)

(DSB) = Dry solid basis

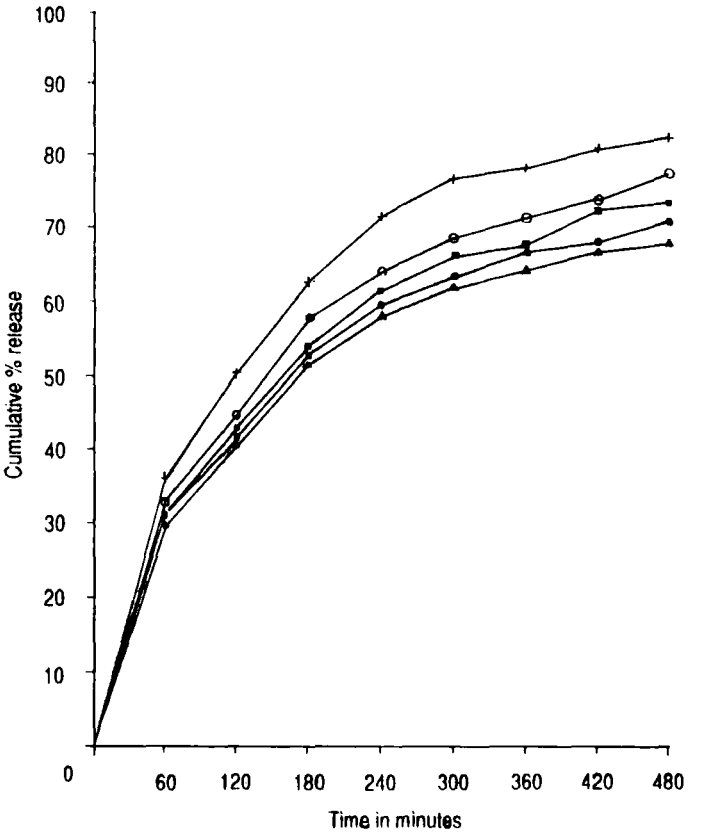

FIGURE 2 Chlorpheniramine Maleate Release in Distilled Water.

Key : + B_1 = 9.231 % (DSB)
○ B_2 = 11.94 % (DSB)
■ B_3 = 14.49 % (DSB)
● B_4 = 16.92 % (DSB)
▲ B_5 = 19.17 % (DSB)
(DSB) = Dry solid basis

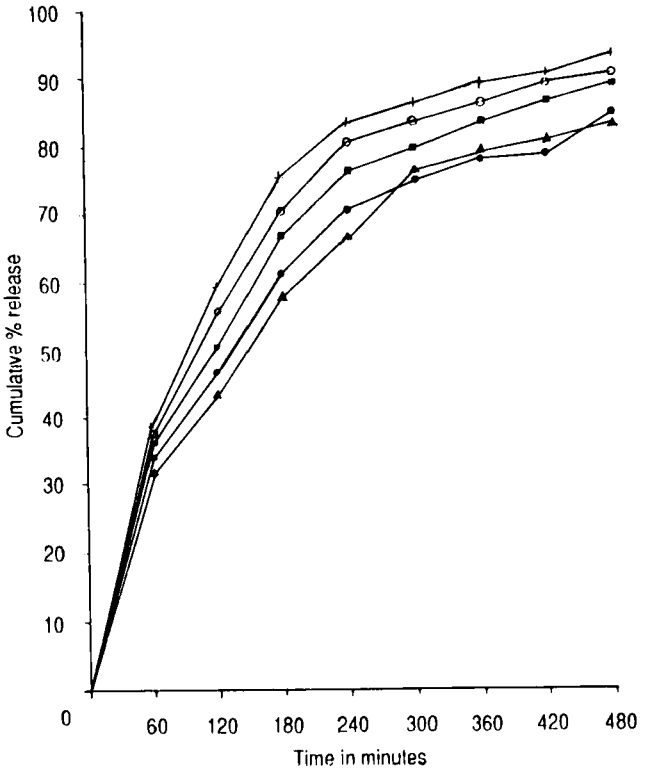

FIGURE 3 Chlorpheniramine Maleate Release in Distilled Water.

Key : + C_1 = 9.02 % (DSB)
○ C_2 = 12.47 % (DSB)
■ C_3 = 14.60 % (DSB)
● C_4 = 16.63 % (DSB)
▲ C_5 = 18.56 % (DSB)

(DSB) = Dry solid basis

TABLE IV: CORRELATION COEFFICIENT SQUARE USING VARIOUS EQUATIONS

Product No.	1	2	3	4	5	6	7	8
A1	Ø.73Ø3	Ø.73Ø3	Ø.9168	Ø.9168	Ø.8631	Ø.9352	Ø.7944	Ø.9861
A2	Ø.7641	Ø.7641	Ø.9381	Ø.9381	Ø.8887	Ø.95Ø7	Ø.818Ø	Ø.9779
A3	Ø.7927	Ø.7927	Ø.9485	Ø.9485	Ø.9Ø56	Ø.9631	Ø.8425	Ø.9775
A4	Ø.8316	Ø.8316	Ø.9698	Ø.9698	Ø.9346	Ø.9781	Ø.885Ø	Ø.987Ø
A5	Ø.8486	Ø.8486	Ø.9683	Ø.9683	Ø.9376	Ø.9817	Ø.8927	Ø.9843
B1	Ø.7953	Ø.7953	Ø.9397	Ø.9397	Ø.9ØØØ	Ø.966Ø	Ø.8625	Ø.9926
B2	Ø.823Ø	Ø.823Ø	Ø.9494	Ø.9494	Ø.9144	Ø.9779	Ø.9Ø01	Ø.9936
B3	Ø.8269	Ø.8269	Ø.9425	Ø.9425	Ø.91Ø1	Ø.9797	Ø.9Ø66	Ø.9959
B4	Ø.8114	Ø.8114	Ø.9164	Ø.9164	Ø.8855	Ø.9736	Ø.8892	Ø.9954
B5	Ø.824Ø	Ø.824Ø	Ø.927Ø	Ø.927Ø	Ø.9Ø5Ø	Ø.9724	Ø.9Ø81	Ø.99Ø1
C1	Ø.77Ø5	Ø.77Ø5	Ø.97Ø3	Ø.97Ø3	Ø.9192	Ø.9513	Ø.8Ø81	Ø.9754
C2	Ø.7921	Ø.7921	Ø.9671	Ø.9671	Ø.9224	Ø.9618	Ø.8376	Ø.9796
C3	Ø.8199	Ø.8199	Ø.9756	Ø.9756	Ø.9374	Ø.9734	Ø.8737	Ø.9864
C4	Ø.8Ø37	Ø.8Ø37	Ø.94Ø8	Ø.94Ø8	Ø.9Ø37	Ø.9629	Ø.8425	Ø.973Ø
C5	Ø.866Ø	Ø.866Ø	Ø.974Ø	Ø.974Ø	Ø.9489	Ø.9851	Ø.9Ø92	Ø.9878

1: Time versus cumulative release
2: Time versus cumulative % unreleased
3: X versus log % Y left
4: Time versus in % unreleased.
5: Hixon-Crowell relationship
6: Higuchi square root equation
7: Time versus cumulative % release excluding time = Ø or concentration = Ø
8: 1/ square root of t versus % cumulative release/time.

appropriate concentrations of formulation additives and the amount of dispersion added as a binder.

It was difficult to predict the exact mechanism of the drug release from the figures 1, 2, and 3 and various equations were tried to interprete the data. From the values of square of correlation coefficient shown in Table IV, it can be concluded that good correlation is observed in the case of Higuchi square root model (equation 6) and also in the case of 1/sqaure root of time versus rate of drug release (equation 8). Relatively poor correlation was noticed in the rest of the cases.

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