CHAPTER-7

PHYSICOCHEMICAL STUDY OF THE TRANSDERMAL PATCHES

7.1 Experimental:

7.1.1 Percent moisture content (% MC) [1]:

The patches were weighed individually and kept in a desiccator containing 10 gm of calcium chloride as desiccant at 37°C for 24 hours. The patches were weighed again and again at an interval of 2 hours individually until it showed a constant weight. The final weight was noted when there was no further change in the weight of individual patch. The percentage of moisture content was calculated as the difference between initial and final weight with respect to final weight.

$$\% MC = \frac{X - Y}{Y} \times 100$$

Where, X = initial weight
Y = final weight

7.1.2 Percentage moisture uptake (% MU) [1]:

The patches were weighed accurately and placed in a desiccator where a humidity condition of 75 % RH was maintained by using saturated solution of sodium chloride. The patches were taken out and weighed periodically at an interval of 6 hours and for a period of 72 hours. The percentage of moisture uptake was calculated as the difference between final and initial weight of the patch with respect to initial weight.

$$\% MU = \frac{Y - X}{X} \times 100$$

Where, X = initial weight
Y = final weight

7.1.3 Tensile strength:

The tensile strength measurement was done using an instrument assembled in the laboratory and following the method used by *Sadhna et al.* [2]. According to the method, the films were fixed individually to the assembly where one end of the film was tied with a fixed hook1 and the other end was fixed with hook2 to which the weight holder was attached. When the weight onto the small holder which is attached to the hook2 was increased

gradually, the stretching of the film also found to be increased. The required weights to break the films were then noted for individual film and were considered as the tensile strength of the respective film.

7.1.4 Water vapour transmission (WVT) rate:

For this study glass vials of equal diameter (1.4 mm) were used as transmission cells. These cells were washed thoroughly and dried in a woven. The transdermal patch of known thickness was fixed over the mouth of the glass vial containing 3 gm of fused calcium chloride as a desiccant by using an adhesive. Then the transmission cells were weighed accurately and initial weight was recorded. The cells were then kept in a desiccator containing saturated solution of potassium chloride (200 ml). The humidity inside the desiccator was maintained at 80-90 % RH. The cells were taken out periodically at an interval of 4 hours and weighed for a period of 72 hours. The water vapour transmission rate values of the transdermal patches were calculated by the following formula[3,4].

$$\text{WVT rate} = WL/S$$

Where, W = water vapour transmitted in gm,

L = thickness of the transdermal patch in cm,

S = exposed surface area in cm^2.

7.1.5 Drug content study [5,6]:

This test provides the means for measuring the amount of drug that is actually present in each transdermal patch formulations. Transdermal patches were taken individually, crushed and taken in a 100 ml volumetric flask. The volume was made up to 100 ml with distilled water and kept for 48 hours at room temperature with occasional shaking. After 48 hours, samples are withdrawn, suitably diluted and analyzed using UV-visible spectrophotometer at 290 nm for the actual amount of drug present in the patches.

7.1.6 Surface topography by selective electron microscopy (SEM):

The surface morphologies of the transdermal patch were investigated by using a JEOL JSM 6360 Scanning Electron Microscope at 7 kV. Prior to examination, samples were gold coated to make them electrically conductive.

7.2 Results of the physicochemical studies of the transdermal patches:

In the present study transdermal patches of propranolol hydrochloride were prepared as monolithic matrices by solvent casting technique employing glass moulds of known diameter into which polyvinyl alcohol (PVA) backing membrane was cast previously. Both side opened glass moulds were wrapped with aluminium foil at one end and PVA backing as well as drug-polymer matrix was prepared. Transdermal patches were formulated by using three polymers in two combinations and in different proportions like ethyl cellulose (EC) with polyvinyl pyrrolidone (PVP) (Table 6.1, Chapter 6) and ethyl cellulose (EC) with hydroxypropyl methyl cellulose (HPMC) (Table 6.2, Chapter 6). Dibutyl phthalate (30 % w/w of polymer) and propranolol hydrochloride (20 % w/w of polymer) in ethanol (10 ml) along with the polymers in requisite ratios were prepared as the casting solution to formulate the transdermal patches.

The physical appearances of the formulated transdermal patches were evaluated by visualization. The patches prepared with EC and PVP in different proportions employing aluminium foil as backing support were semi clear but found flexible, smooth and were removed easily from the mould (Table 5.7, Chapter 5). The patches prepared with EC and HPMC in different proportions employing aluminium foil as backing support were found transparent, flexible, smooth and were removed easily from the mould (Table 5.9, Chapter 5). The patches were found apparently satisfactory in respect to there physical appearance.

The thickness of the patches prepared with EC and PVP were found in between 0.00114 cm to 0.00206 cm (Table 5.11, Chapter 5). Patches containing EC and HPMC were found to show the thickness range in between 0.00129 cm to 0.00214 cm (Table 5.13, Chapter 5). Low standard deviation values observed in the thickness profile of the patches of both the

combination ensure uniformity of the formulated patches and less batch variation. Moreover less thickness imparts elegance to the patches, patient's compliance and acceptability.

Transdermal patches showed less weight variation as well as low standard deviation and the range was in between 0.122 gm to 0.141 gm for the patches composed of EC and PVP (Table 5.15, Chapter 5), whereas it was 0.126 gm to 0.143 gm for the patches containing EC and HPMC (Table 5.17, Chapter 5). The folding endurance values of all the patches were found satisfactory which indicates that the dibutyl phthalate (30 % w/w of polymer) used as the plasticizer for the transdermal patches, rendered good flexibility and restricted brittleness (Table 5.19 and 5.21, Chapter 5).

7.2.1 Percent moisture content and moisture uptake:

The percent moisture content (% w/w) and percent moisture uptake (% w/w) of the patches prepared with different proportion of EC and PVP were found in between 0.9 to 6.25 (% w/w) and 1.12 to 5.34 (% w/w) (Table 7.1, figure 7.1 and figure 7.2) respectively. Whereas it was found to be 1.64 to 5.79 (% w/w) and 1.45 to 5.03 (% w/w) for the formulations prepared with EC and HPMC in different ratios (Table 7.2, figure 7.3 and figure 7.4). It was observed that the moisture content increases gradually with the increase of hydrophilic polymer concentration. Moisture uptake profile of the transdermal patches was also found to be increased with the increase in hydrophilic polymer concentrations. Formulations containing higher proportions of PVP and HPMC blended with EC (TTS5 > TTS4 > TTS3 and TDS5 > TDS4 > TDS3) were thereby found to show higher moisture content and moisture uptake in comparison to the patches containing lesser proportions of PVP and HPMC (TTS6 < TTS7 < TTS8 < TTS9 < TTS10 and TDS6 < TDS7 < TDS8 < TDS9 < TDS10). Little moisture content of the formulations helps them not to become completely dried and brittle patches. Again low moisture uptake restricts the microbial contamination and bulkiness of the transdermal patches.

7.2.2 Tensile strength:

The tensile strength of the patches containing EC with PVP and EC with HPMC in different proportions were found to be in between 211.45 gm/cm^2 to 280.89 gm/cm^2 and

195.47 gm/cm^2 to 276.32 gm/cm^2 (Table 7.3 and 7.4) respectively. It was observed that with the increase in PVP and HPMC concentration, the tensile strength of the patches gradually decreased.

7.2.3 Water vapour transmission rate:

The water vapour transmission was found to be least with the formulations containing less amount of hydrophilic polymer. Thus formulations TTS6, TTS7, TTS8, TTS9, TTS10 and TDS6, TDS7, TDS8, TDS9, TDS10 have shown lesser affinity towards water in comparison to the formulations TTS1, TTS2, TTS3, TTS4, TTS5 and TDS1, TDS2, TDS3, TDS4, TDS5; where proportions of PVP and HPMC were more (Table 7.5 and 7.6). Patches containing EC with PVP and EC with HPMC showed a water vapour transmission profile within the range of 0.51852 × 10^{-4} gm/cm/h to 3.09965 × 10^{-4} gm/cm/h and 0.90838 × 10^{-4} gm/cm/h to 2.95309 × 10^{-4} gm/cm/h respectively. Thus amongst all the formulations TTS6 and TDS6 have shown the least water vapour transmission profile may be due to having lesser concentrations of PVP and HPMC with highest concentration of hydrophobic polymer EC.

7.2.4 Drug content:

The drug content of the patches prepared with EC and PVP was found to be 19.86 mg to 19.94 mg and it was 19.82 mg to 19.93 mg for the patches prepared with EC and HPMC (Table 7.7 and 7.8) respectively.

7.2.5 Selective electron microscopy:

The scanning electron microscopic (SEM) examination of the patches showed best performances by the formulation code TTS6 and TDS6. Transdermal patches at different conditions like blank patch without drug, drug loaded patch and patch after skin permeation were taken for the study. Blank patches (Figure 7.5 and 7.6) and drug loaded patches (Figure 7.7a and 7.7b and figure 7.8a and 7.8b) were seemed to be formed uniformly. Patches after skin permeation study has appeared with the void space in the film, which indicate the release of the drug from the patches (Figure 7.9a and 7.9b and figure 7.10a and 7.10b).

Table 7.1: Percent moisture content (% MC) and Percent moisture uptake (% MU) data of drug loaded transdermal patches of EC and PVP:

Sl. No.	Formulation	% MC (w/w)	% MU (w/w)
1	TTS1	4.17	3.86
2	TTS2	4.24	3.93
3	TTS3	4.34	4.05
4	TTS4	5.17	4.67
5	TTS5	6.25	5.34
6	TTS6	0.9	1.12
7	TTS7	1.1	1.37
8	TTS8	2.05	1.82
9	TTS9	2.98	2.75
10	TTS10	3.21	3.01

Table 7.2: Percent moisture content (% MC) and Percent moisture uptake (% MU) data of drug loaded transdermal patches of EC and HPMC:

Sl. No.	Formulations	% MC (w/w)	% MU (w/w)
1	TDS1	4.32	3.67
2	TDS2	4.86	3.98
3	TDS3	5.13	4.15
4	TDS4	5.34	4.49
5	TDS5	5.79	5.03
6	TDS6	1.64	1.45
7	TDS7	1.87	1.92
8	TDS8	2.09	2.17
9	TDS9	2.31	2.54
10	TDS10	2.84	2.96

Table 7.3: Tensile strength data of the drug loaded transdermal patches of EC and PVP:

Sl. No.	Formulations	Tensile strength (gm/cm^2) n = 3
1	TTS1	251.36
2	TTS2	243.67
3	TTS3	221.54
4	TTS4	215.58
5	TTS5	211.45
6	TTS6	280.52
7	TTS7	280.89
8	TTS8	261.48
9	TTS9	257.60
10	TTS10	253.52

n = number of repeated observation.

Table 7.4: Tensile strength data of the drug loaded transdermal patches of EC and HPMC:

Sl. No.	Formulations	Tensile strength (gm/cm^2) n = 3
1	TDS1	234.45
2	TDS2	221.67
3	TDS3	204.12
4	TDS4	198.53
5	TDS5	195.47
6	TDS6	276.32
7	TDS7	271.68
8	TDS8	256.21
9	TDS9	237.16
10	TDS10	238.04

n = number of repeated observation.

Table 7.5: Water vapour transmission rate (WVTR) profile of the drug loaded transdermal patches of EC and PVP:

Sl. No.	Formulations	WVTR (gm/cm/h)
1	TTS1	1.01754×10^{-4}
2	TTS2	1.12437×10^{-4}
3	TTS3	1.56959×10^{-4}
4	TTS4	2.38791×10^{-4}
5	TTS5	3.09965×10^{-4}
6	TTS6	0.51852×10^{-4}
7	TTS7	0.91033×10^{-4}
8	TTS8	1.21636×10^{-4}
9	TTS9	1.27758×10^{-4}
10	TTS10	1.30719×10^{-4}

Table 7.6: Water vapour transmission rate (WVTR) profile of the drug loaded transdermal patches of EC and HPMC:

Sl. No.	Formulations	WVTR (gm/cm/h)
1	TDS1	1.33853×10^{-4}
2	TDS2	1.47524×10^{-4}
3	TDS3	1.85419×10^{-4}
4	TDS4	1.90409×10^{-4}
5	TDS5	2.95309×10^{-4}
6	TDS6	0.90838×10^{-4}
7	TDS7	0.97355×10^{-4}
8	TDS8	1.09766×10^{-4}
9	TDS9	1.10472×10^{-4}
10	TDS10	1.10648×10^{-4}

Table 7.7: Drug content study of the transdermal patches containing EC and PVP:

Sl. No.	Formulations	Drug content (mg)
1	TTS1	19.93
2	TTS2	19.92
3	TTS3	19.94
4	TTS4	19.91
5	TTS5	19.89
6	TTS6	19.92
7	TTS7	19.88
8	TTS8	19.90
9	TTS9	19.88
10	TTS10	19.86

Table 7.8: Drug content study of the transdermal patches containing EC and HPMC:

Sl. No.	Formulations	Drug content (mg)
1	TDS1	19.87
2	TDS2	19.82
3	TDS3	19.87
4	TDS4	19.86
5	TDS5	19.87
6	TDS6	19.88
7	TDS7	19.90
8	TDS8	19.93
9	TDS9	19.82
10	TDS10	19.84

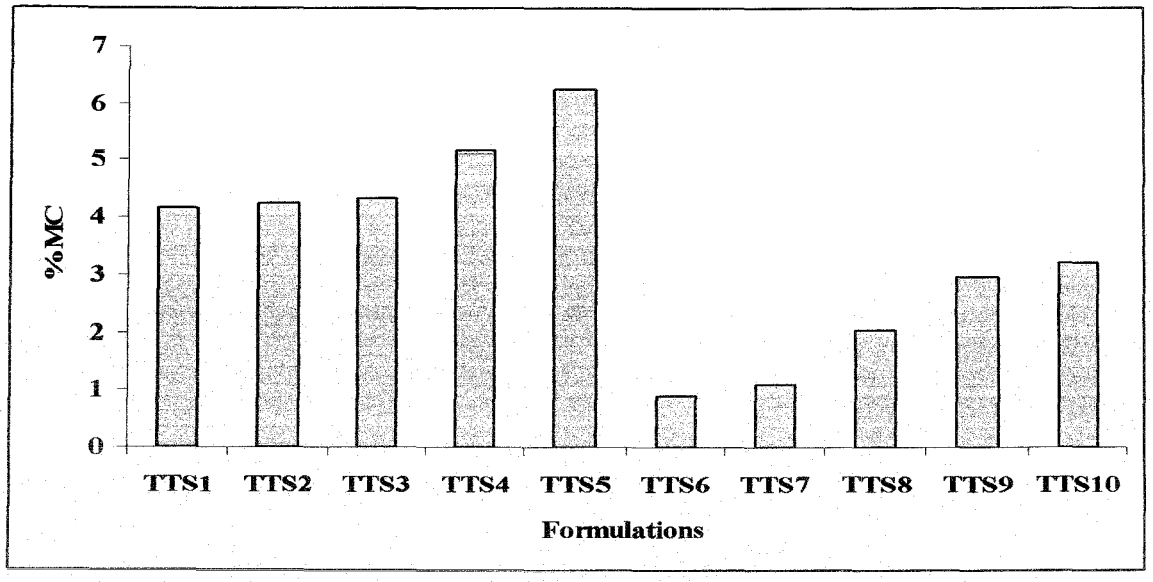


Figure 7.1: Comparative percent moisture content profile of different formulations of EC and PVP:

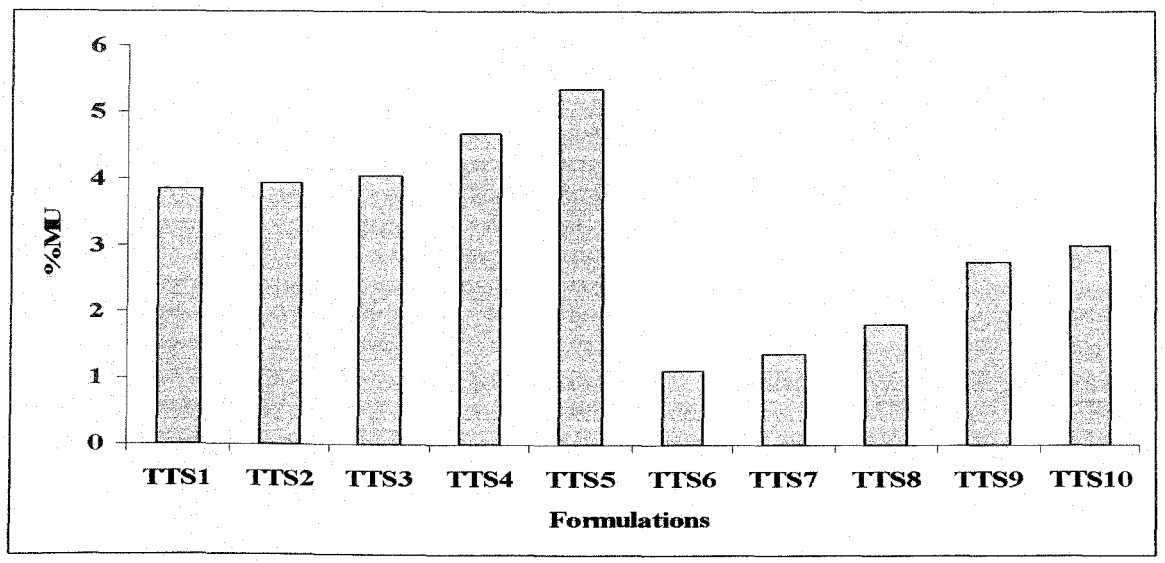


Figure 7.2: Comparative percent moisture uptake profile of different formulations of EC and PVP:

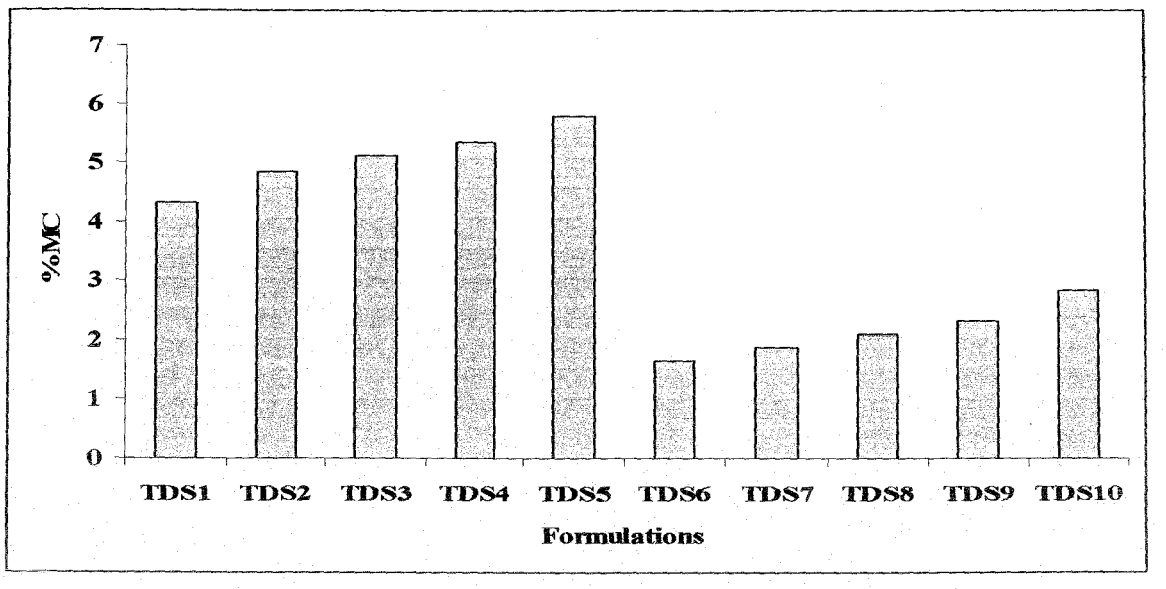


Figure 7.3: Comparative percent moisture content profile of different formulations of EC and HPMC:

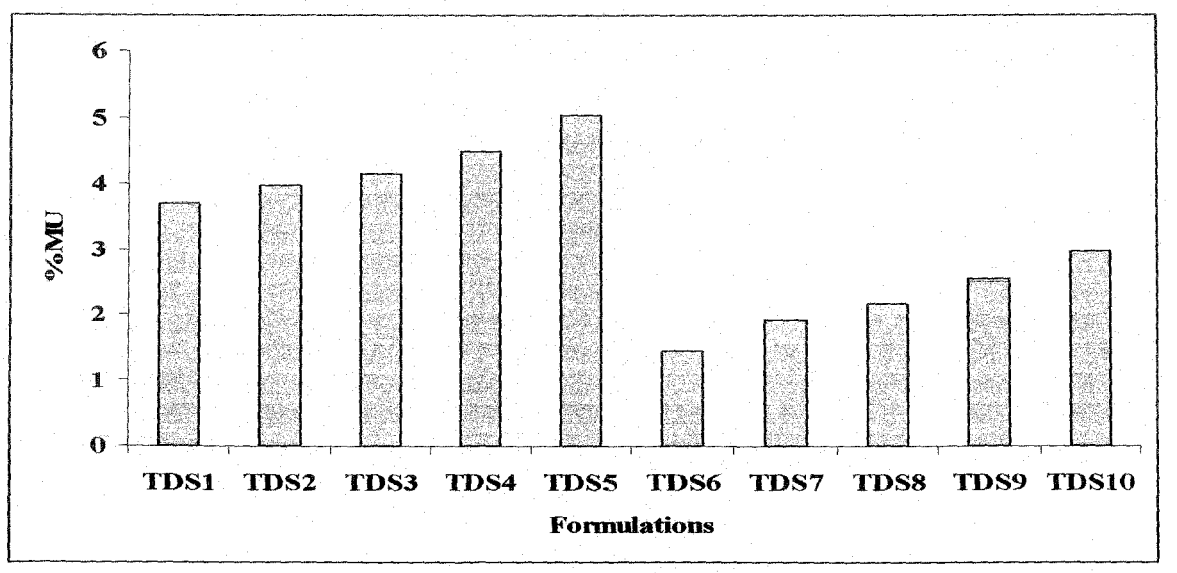


Figure 7.4: Comparative percent moisture uptake profile of different formulations of EC and HPMC:

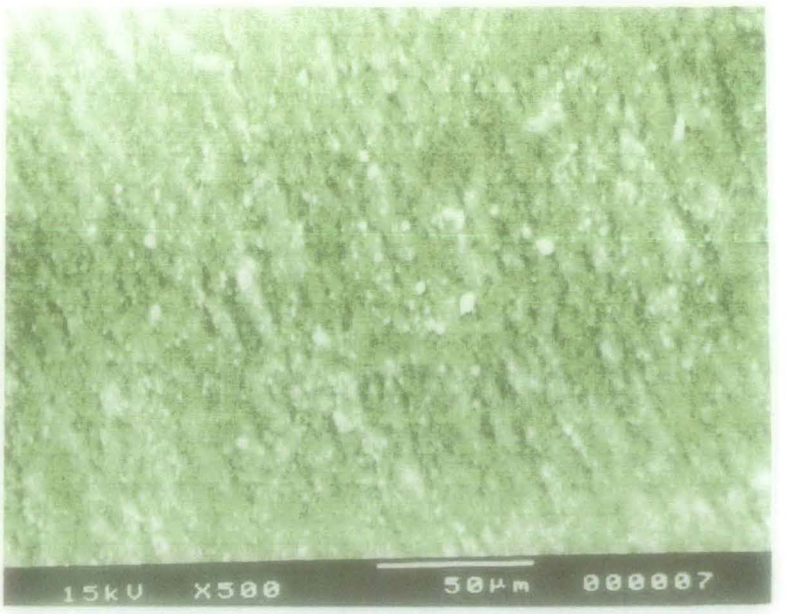


Figure 7.5: SEM photograph of the blank film containing ethyl cellulose and poly vinyl pyrrolidone:

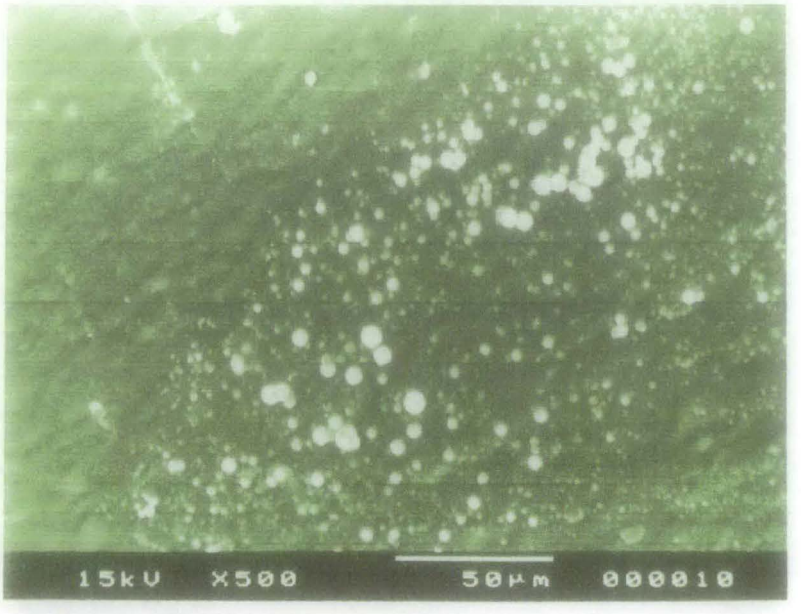
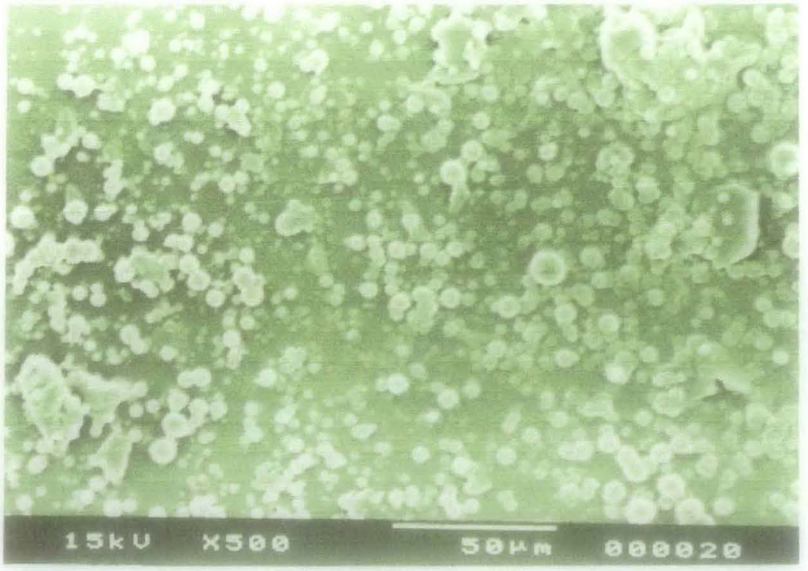


Figure 7.6: SEM photograph of the blank film containing ethyl cellulose and hydroxypropyl methyl cellulose:



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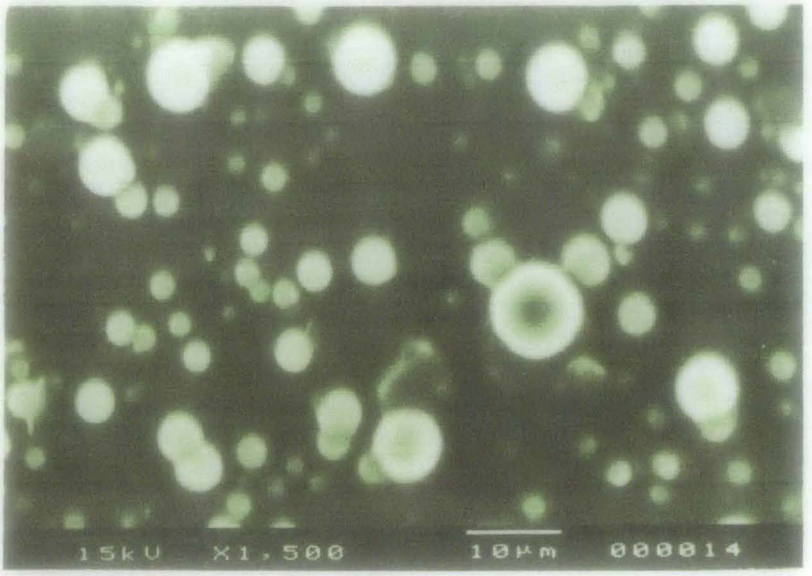
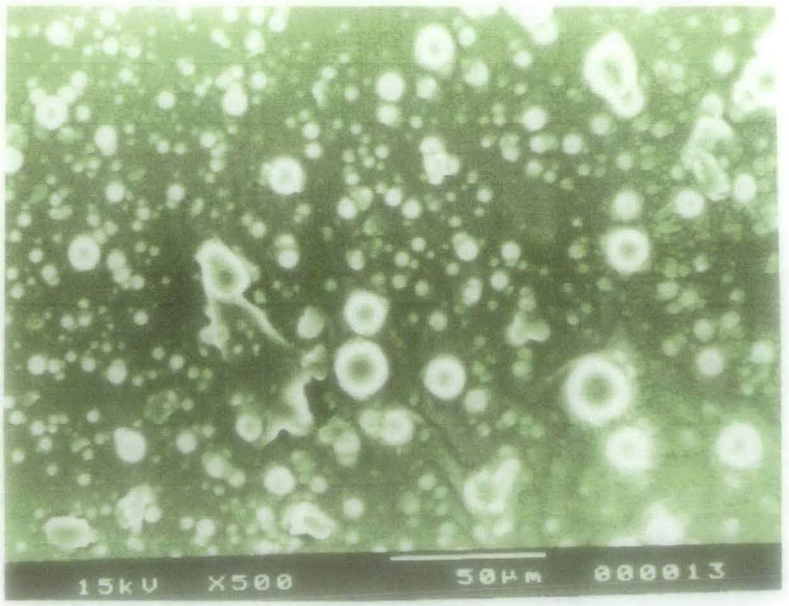


(b)

Figure 7.7 (a, b): SEM photograph of the drug-loaded film of ethyl cellulose and poly vinyl pyrrolidone before skin permeation study:



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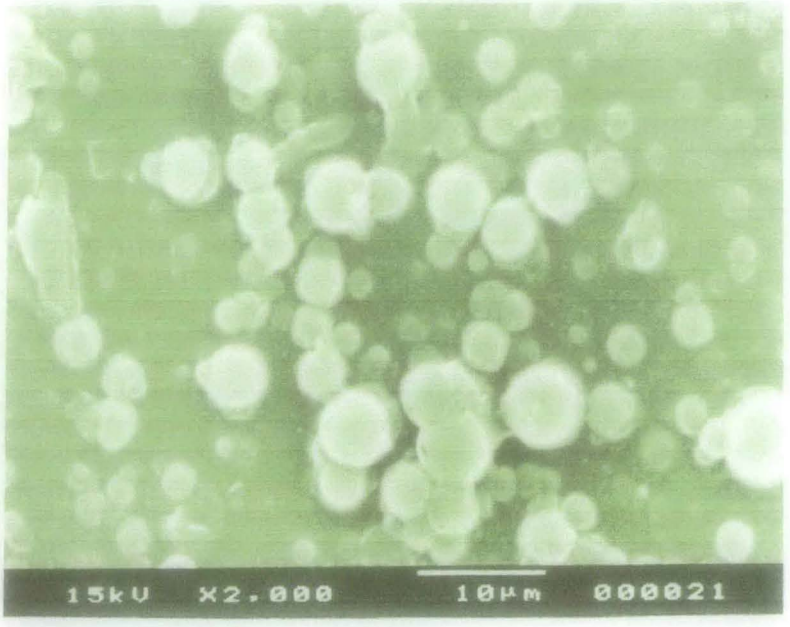
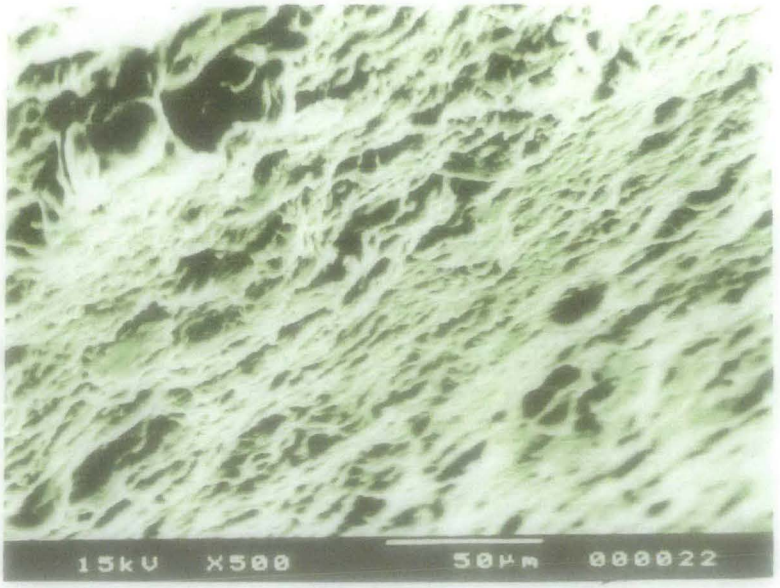


(b)

Figure 7.8 (a, b): SEM photograph of the drug-loaded film of ethyl cellulose and hydroxypropyl methyl cellulose before skin permeation study:



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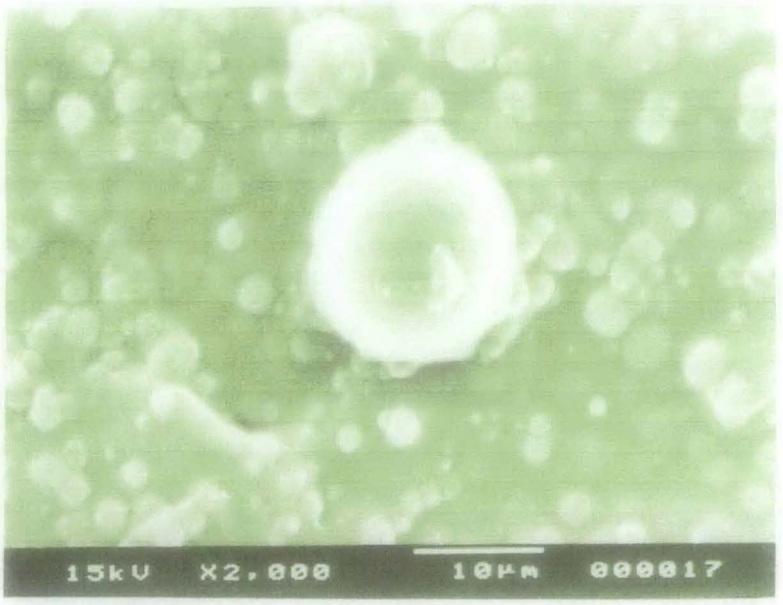
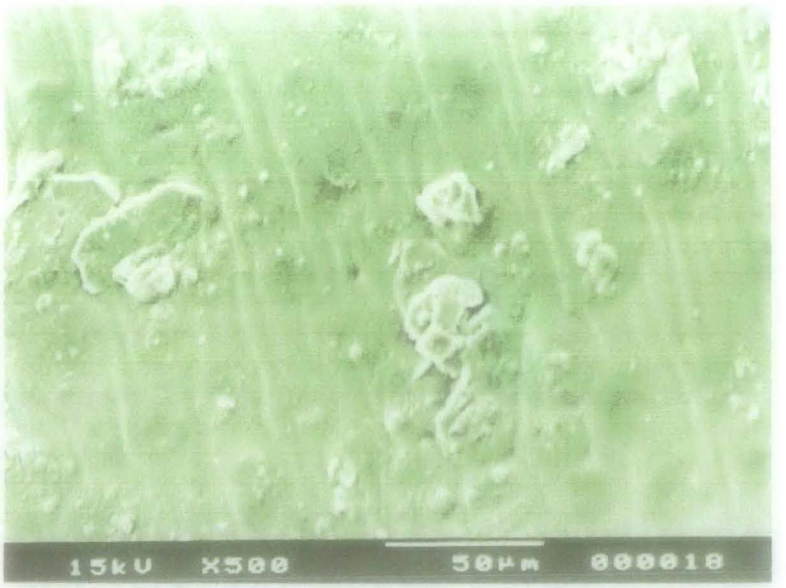


(b)

Figure 7.9 (a, b): SEM photograph of the exhausted film of ethyl cellulose and poly vinyl pyrrolidone after skin permeation study:



(a)

(b)

Figure 7.10 (a, b): SEM photograph of the exhausted film of ethyl cellulose and hydroxypropyl methyl cellulose after skin permeation study:

REFERENCE

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