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Microwave non-destructive testing technique for characterization of HPMC-PEG 3000 films

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Abstract

The capacity of microwave non-destructive testing (NDT) technique to characterize the matrix property of binary polymeric films for use as transdermal drug delivery system was investigated. Hydroxypropylmethylcellulose (HPMC) and polyethylene glycol (PEG) 3000 were the choice of polymeric matrix and plasticizer, respectively with loratadine as the model drug. Both blank and drug loaded HPMC-PEG 3000 films were prepared using the solvent-evaporation method. These films were conditioned at the relative humidity of 25, 50 and 75% prior to physicochemical characterization using the established methods of ultra-violet spectrophotometry, differential scanning calorimetry and Fourier transform infrared spectroscopy methods, as well as, novel microwave NDT technique. Blank films exhibited a greater propensity of polymer–polymer interaction at the O–H domain upon storage at a lower level of relative humidity, whereas drug loaded films exhibited a greater propensity of polymer–polymer, polymer–plasticizer and/or drug–polymer interaction via the O–H, C–H and/or aromatic C=C functional groups when they were stored at a lower or moderate level of relative humidity. The absorption and transmission characteristics of both blank and drug loaded films for microwave varied with the state of polymer–polymer, polymer–plasticizer, and/or drug–polymer interaction of the matrix. The measurements of microwave NDT test at 8 and 12 GHz were sensitive to the polar fraction of film involving functional group such as O–H moiety and the less polar environment of matrix consisting of functional groups such as C–H and aromatic C=C moieties. The state of interaction between polymer, plasticizer and/or drug of a binary polymeric film can be elucidated through its absorption and transmission profiles of microwave.

Keywords: Hydroxypropylmethylcellulose; Loratadine; Microwave; Non-destructive testing technique; Polyethylene glycol 3000

1. Introduction

Transdermal drug delivery system delivers drugs into the systemic circulation via the penetration of drug molecules across the skin. Drug delivery by means of transdermal pathway has several advantages over the traditional mode of drug administration via the oral route such as reduction of side effects and offers multi-day dosing with a single administration, thereby leading to improved patient compliance (Paul et al., 1998; Narisetty and Ramesh, 2003; Ranade and Hollinger, 2004). Using transdermal drug delivery system, the drugs enter the systemic circulation without first passing through the gut wall and hepatic portal system. This aids to avoid the first-pass phenomenon of which the enzymes in liver and gut wall can significantly reduce the amount of intact drugs (Aqil and Ali, 2002; Aulton, 2002; Carmen and Angle, 2004).

Analysis of transdermal dosage form characteristics, such as state of polymer–polymer and drug–polymer interaction, is essential in examination of the drug delivery aspect of matrix. Practically, differential scanning calorimetry and Fourier transform infra-red spectroscopy have been employed to characterize the transdermal drug delivery system (Aarti et al., 1995; Emilio et al., 1997; Elka et al., 1998; Eun-Seok et al., 2000; Lodzki et al., 2003; Babu and Pandit, 2004; Satyanarayana et al., 2004; Biswajit et al., 2005; Siegfried and Reinhard, 2005). These techniques provide the physicochemical details of the matrix and add the depth of understanding to the delivery profiles of drugs.

The microwave non-destructive testing (NDT) techniques have been used to assess the physicochemical properties of non-metallic materials such as paper, rubber, circuit board and plastic

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composite in the engineering sector (Bois et al., 2000; Buldygin et al., 2000; Feng et al., 2000; Ju et al., 2001; Ciocan and Ida, 2004; Massood and Wang, 2004; Van Damme et al., 2004; Hughes and Zoughi, 2005; Park et al., 2005; Trabelsi and Nelson, 2006). Lately, a microwave NDT system has been built for use to characterize the hydroxypropylmethylcellulose (HPMC) films in our laboratory (Anuar et al., 2007). The results demonstrated that the microwave NDT test is potentially suitable for use as an apparent indicator of the state of polymer–polymer and drug–polymer interaction of the matrix, in addition to the existing DSC and FTIR techniques. Characterization of polymeric matrix using such technique does not require sample destruction during the process of measurement. The sample is recoverable from test and analysis of the entire batch of samples is possible without the need of solvents and chemical reagents. The present study sets to continue to explore the capacity of microwave NDT technique as an optional tool to characterize the matrix property of transdermal drug delivery system with binary polymers. In the present investigation, polyethylene glycol (PEG) 3000 was incorporated into the HPMC film. The changes of interaction profiles between the HPMC, PEG 3000 and drug molecules in the HPMC-PEG 3000 films, subjected to storage under different levels of relative humidity, were evaluated by microwave NDT technique with respect to data formerly obtained from the measurement of HPMC matrix.

2. Materials and methods

2.1. Materials

Hydroxypropylmethylcellulose (HPMC Methocel*K100 Premium LV, The Dow Chemical Company, USA) was used as a matrix polymer for the fabrication of film with loratadine (Morepen Laboratories, India) as the model drug. Polyethylene glycol (PEG 3000, Merck, Germany), a polymer with a nominal molecular weight of 3000 Da, was used as a plasticizer of film. Hydrochloric acid (HCl, Analytical Grade, Merck, Germany) was chemical employed in drug content assay. Lithium chloride (Acros Organics, USA), chromium(VI) oxide (Acros Organics, USA) and sodium chloride (Merck, Germany) were used as chemicals for the control of the relative humidity of storage chamber.

2.2. Methods

2.2.1. Preparation of film

An accurately weighed amount of 2.5% (w/w) of HPMC solution, with or without PEG 3000 and loratadine, was transferred into a glass petri dish (internal diameter = 3 cm). The theoretical content of HPMC in each blank HPMC film (A0), blank HPMC-PEG 3000 film (B0) and drug loaded HPMC-PEG 3000 films (B1, B2, B3 and B4) was kept at 37.5 mg. The amount of PEG 3000 incorporated in the HPMC-PEG 3000 film was kept at 3.75 mg. In the case of drug loaded HPMC-PEG 3000 films, 5, 10, 20 and 40 mg of loratadine were added into the formed films denoted as B1, B2, B3 and B4, respectively. The solution was then subjected to hot air drying at $40 \pm 0.5\,^{\circ}C$ for 24 h. The formed film was collected and further conditioned in a desiccator at $25 \pm 1\,^{\circ}C$ and at a pre-set level of relative humidity for at least 5 days prior to physicochemical characterization. At least triplicates were carried out for each formulation. The pre-set levels of relative humidity were kept at 25 ± 5, 50 ± 5 and $75 \pm 5\%$ using the saturated solutions of lithium chloride, chromium(VI) oxide and sodium chloride, respectively.

2.2.2. Characterization of film

The drug content of film was examined using ultra-violet spectrophotometry method, while the matrix characteristics of film were assessed using differential scanning calorimetry (DSC), Fourier transform infra-red spectroscopy (FTIR) and microwave non-destructive testing (NDT) techniques.

2.2.2.1. Drug content analysis. An accurately weighed fraction of a film was dissolved in 0.1 M HCl solution. The content of loratadine embedded in the sample was determined spectrophotometrically at a ultra-violet wavelength of 275.1 nm (Cary 50 Conc, Varian Australia Pty Ltd., Australia). A total of five fractions from each film were assayed for the drug content. The drug content was defined as the percentage loratadine embedded in a unit weight of film. Triplicates were carried out and the results averaged.

2.2.2.2. DSC analysis. DSC thermograms were obtained using a differential scanning calorimeter (Pyris 6 DSC, Perkin-Elmer, USA). Three milligrams of sample were crimped in a standard aluminium pan and heated from 30 to 300 °C at a heating rate of 10 °C/min under constant purging of nitrogen at 40 ml/min. The characteristic peaks and specific heat of the melting endotherm were recorded. At least triplicates were carried out for each batch of sample and the results averaged.

2.2.2.3. FTIR analysis. 2.5% (w/w) of sample, with respect to the potassium bromide (KBr) disc, was mixed with dry KBr (FTIR grade, Aldrich, Germany). The mixture was ground into a fine powder using an agate mortar before compressing into a disc. Each disc was scanned at a resolution of $4\,cm^{-1}$ over a wavenumber region of 450–4000 cm^{-1} using a FTIR spectrometer (Spectrum RX1 FTIR system, Perkin-Elmer, USA). The characteristic peaks of IR transmission spectra were recorded. At least triplicates were carried out for each batch of sample and the results averaged.

2.2.2.4. Microwave NDT analysis. The microwave NDT technique employed a rectangular dielectric waveguide (RDWG) system of which the set up was consisted of RDWGs, standard-gain horn antennas, coaxial cables and a vector network analyzer (VNA, WILTRON 37269B, USA) (Fig. 1). The RDWG was made of polytetrafluoroethylene (PTFE). Each RDWG had a length of 37.5 cm and was equipped with a standard metallic TE_{10} waveguide (WR-90) of which acted as a microwave launcher for the RDWG. The RDWG was inserted into the WR-90 waveguide through a standard-gain horn antenna of which functioned to contain and minimize the losses of microwave from RDWG. At the point of insertion into each WR-90

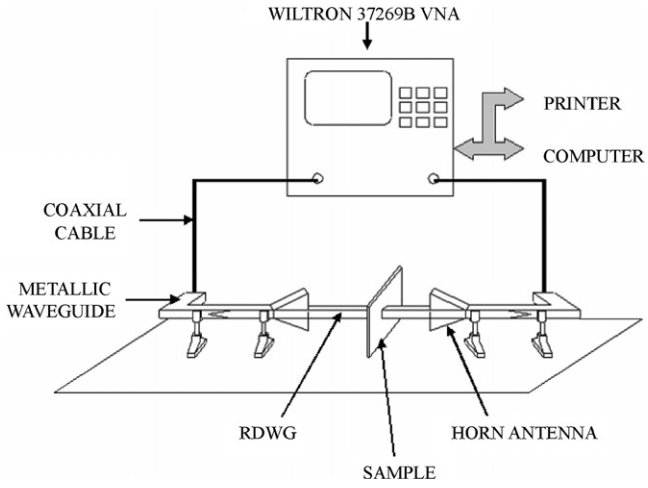

Fig. 1. Schematic diagram of RDWG measurement system.

waveguide, the edge of RDWG was double-tapered to direct the transmission of microwave across the RDWG. The contact area of RDWG with film had a cross sectional area of 22.86 mm × 10.16 mm. It had a smooth surface in order to avoid the formation of air pockets between the surfaces of RDWG and film.

The measurement system of RDWG was calibrated using the internal TRL (Through, Reflect and Line) model of VNA. The amplitudes of forward transmission coefficient (S_{21}) and forward reflection coefficient (S_{11}) were characterized. The accuracy of RDWG system was verified through the measurement of complex permittivities of samples with known dielectric properties such as PTFE and plexiglass prior to its application in film characterization (Robert et al., 1989; Zulkifly et al., 1998).

The characterization of film using the microwave NDT technique proceeded by first placing the test sample directly in contact with two RDWGs on the opposite sides of the film. S_{11} and S_{21} values of the film were determined at various spots of the same sample using microwave at the frequencies of 8 and 12 GHz. The power transmission coefficient (nPTC), power reflection coefficient (nPRC) and power absorption coefficient (nPAC) of samples were calculated using the following equations:

$$\text{nPTC}\ (\%) = \frac{|S_{21}|^2_{\text{linear}} \times 100}{d} \quad (1)$$

$$\text{nPRC}\ (\%) = \frac{|S_{11}|^2_{\text{linear}} \times 100}{d} \quad (2)$$

$$\text{nPAC}\ (\%) = \frac{[1 - |S_{11}|^2_{\text{linear}} - |S_{21}|^2_{\text{linear}}] \times 100}{d} \quad (3)$$

where $|S_{11}|_{\text{linear}} = 10^{(|S11|\text{dB}/20)}$, $|S_{21}|_{\text{linear}} = 10^{(|S21|\text{dB}/20)}$ and d = film thickness of which was measured using a digital micrometer (Mitutoyo, Japan). Triplicates were carried out for each batch of sample and the results averaged. Principally, microwave possesses both electrical and magnetic properties (Wong, in press). The contact of microwave with an object results in vibration of molecules by induced or permanent dipoles. The intensity of vibration is a function of the quantity of microwave energy absorbed by the object (Wong et al., 2005). This depends on the size, shape and polarizability of the molecules, as well as, extent of intermolecular interaction of the object. Apparently, materials with a high level of molecular interaction are expected to absorb more microwave energy, thereby giving rise to a more intense vibration.

3. Results and discussion

Table 1 showed the contents of loratadine embedded in HPMC-PEG 3000 films determined using the ultra-violet spectrophotometry technique. The drug content of films was not affected by the level of relative humidity in the storage chamber (ANOVA; $p > 0.05$). Generally, a thicker film was formed in sample containing a higher content of drug load (Table 1).

In the present investigation of the capacity of microwave NDT technique to characterize the matrix property of the polymer film, the nPTC, nPRC and nPAC values of each film were computed. The magnitude of nPTC, nPRC and nPAC represented the propensity of microwave being transmitted through, reflected from and absorbed into the film. Their applicability in characterization of films, subjecting to different storage conditions, was assessed in relation to thermograms and spectra of the same samples obtained from DSC and FTIR analysis, respectively.

3.1. DSC analysis

PEG 3000 is a hydrophilic waxy polymer. It is commonly employed as a plasticizer in the preparation of pharmaceutical films. The unprocessed PEG 3000 had a melting endotherm at 61.9 ± 0.2 °C and an exotherm at 151.0 ± 0.2 °C attributing to polymer volatilization (Fig. 2b). The incorporation of PEG 3000 into film A0 resulted in an increase in melting peak temperatures of film A0 (Figs. 2e, 3b and 4b). This observation indicated that the polymer–plasticizer interaction was effected in the matrix. Practically, both HPMC and HPMC-PEG 3000 films stored under a lower level of relative humidity had higher melting peak temperatures, but lower endothermic enthalpy values at specific domains of film (Figs. 2–4). The strength of polymer–polymer and/or polymer–plasticizer interaction was greater in samples stored at a lower level of relative humidity but the extent of polymer–polymer and/or polymer–plasticizer

Table 1
Empirical film thickness and loratadine content of HPMC-PEG 3000 films

Sample	Film thickness (mm)	Loratadine content (%w/w)		
		25%[a]	50%[a]	75%[a]
A0	0.031 ± 0.006	0	0	0
B0	0.036 ± 0.003	0	0	0
B1	0.064 ± 0.015	12.15 ± 0.32	13.59 ± 0.36	13.06 ± 0.16
B2	0.068 ± 0.008	23.04 ± 0.91	23.47 ± 0.92	21.77 ± 0.45
B3	0.114 ± 0.033	39.06 ± 0.93	35.06 ± 1.14	38.04 ± 1.34
B4	0.143 ± 0.014	58.40 ± 1.12	56.35 ± 2.74	55.88 ± 1.28

The values represent mean ± standard deviation.
[a] Relative humidity.

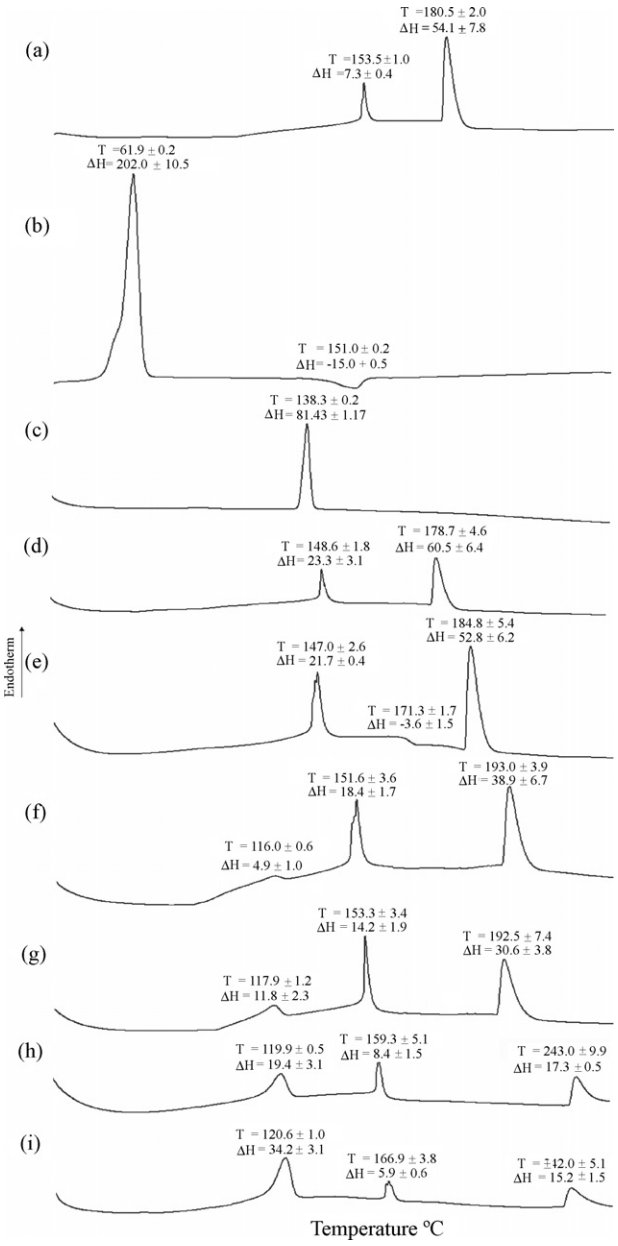

Fig. 2. DSC thermograms of (a) unprocessed HPMC, (b) PEG 3000, (c) loratadine, (d) A0-25% RH, (e) B0-25% RH, (f) B1-25% RH, (g) B2-25% RH, (h) B3-25% RH and (i) B4-25% RH. *T*: endothermic/exothermic peak temperature (°C); Δ*H*: enthalpy (J/g).

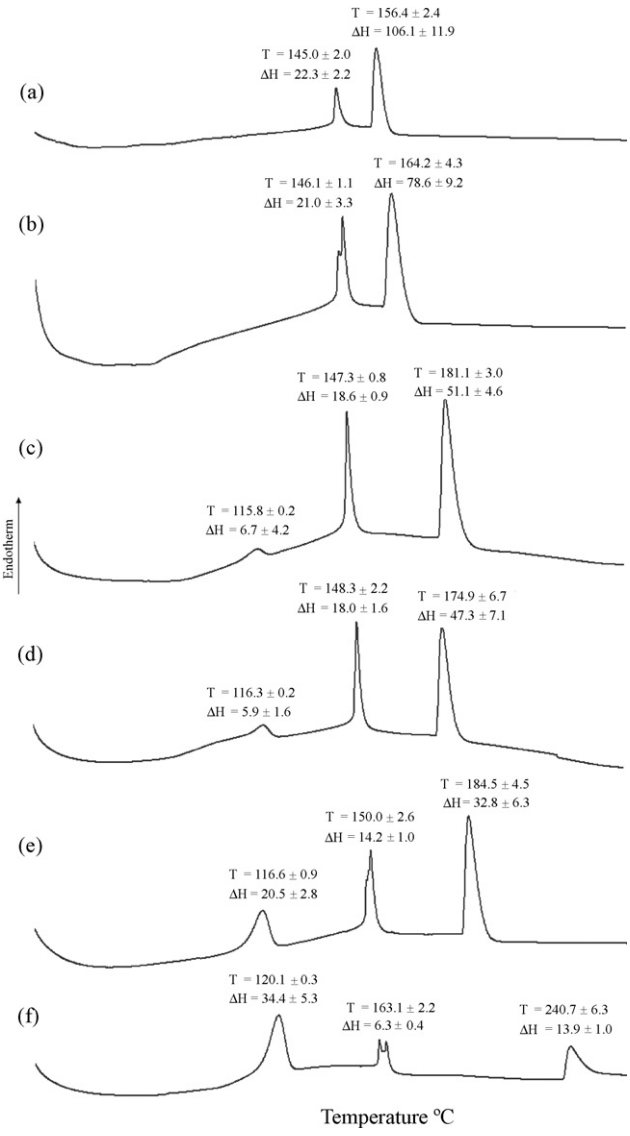

Fig. 3. DSC thermograms of (a) A0-50% RH, (b) B0-50% RH, (c) B1-50% RH, (d) B2-50% RH, (e) B3-50% RH and (f) B4-50% RH.

interaction was higher in samples stored at a higher level of relative humidity. The latter may ascribe to a higher containment of moisture in films stored at a higher level of relative humidity as inferred from the changes in capacitance values obtained using the skin hydration measurement device (Corneometer® CM825, Cologne, Germany) of which a higher moisturization value represented a higher content of sorbed moisture in the test samples. Apparently, the samples stored at the relative humidity of 25% had a lower moisturization value of 4.09 ± 0.39 than that of samples stored at the relative humidity of 75% of which had a moisturization value of 4.51 ± 0.94. Unlike films stored at the relative humidity of 50 and 75%, an exotherm which was characterized by a peak temperature at 171.3 ± 1.7 °C and an enthalpy value of -3.6 ± 1.5 J/g was found in the thermogram of film B0 stored at the relative humidity of 25% (Fig. 2e). The formation of an exotherm in the latter was probably ascribed to the loss of PEG 3000 following the treatment of film sample at high temperatures. The similar exotherm was not found in the thermograms of films stored at the higher levels of relative humidity, as it was probably masked by the melting endotherms of the same thermogram. The overlap of exotherm and endotherm in the same thermogram would give rise to an inaccurate computation of the enthalpy value. It was envisaged that the endothermic enthalpy values in samples stored at the higher levels of relative humidity could have been underestimated, albeit such incidence did not affect the interpretation of the trend of DSC study.

Similar to those of HPMC films (Anuar et al., 2007), the incorporation of loratadine into the HPMC-PEG 3000 films brought about the formation of new endotherms at 111–121 °C (Figs. 2–4). Apparently, the loading of loratadine into the

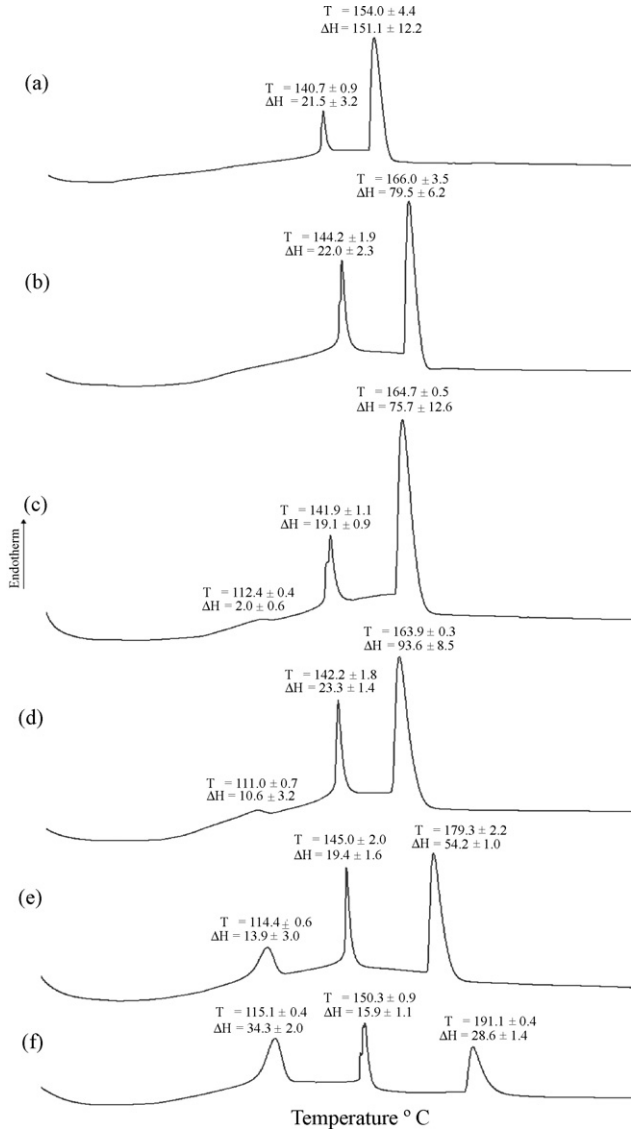

Fig. 4. DSC thermograms of (a) A0-75% RH, (b) B0-75% RH, (c) B1-75% RH, (d) B2-75% RH, (e) B3-75% RH and (f) B4-75% RH.

HPMC-PEG 3000 film brought about a reduction in the melting peak temperature of the unprocessed drug at $138.3 \pm 0.2\,^{\circ}C$, owing to probable interruption of drug crystals by HPMC and/or PEG 3000 (Fig. 2c). An increase in drug content of film from samples B1–B4 was reflected by an increase in the enthalpy value of these endotherms (Figs. 2–4). In addition to the newly formed endotherm, two different melting endotherms attributed to different domains of HPMC and/or PEG 3000 molecules were found in the thermogram of drug loaded film (Figs. 2–4). Similar to blank HPMC-PEG 3000 films B0, the melting peak temperatures were higher in films stored at a lower level of relative humidity (Figs. 2–4). Keeping the drug content similar, higher endothermic enthalpy values were obtained at various domains of HPMC and/or PEG 3000 particularly in the case of samples B2, B3 and B4 kept at a higher level of relative humidity, unlike those of films B0 of which the changes of enthalpy were restricted to the specific domain of HPMC and/or PEG 3000 molecules in film (Figs. 2–4).

Table 2
FTIR peak wavenumber values of blank HPMC, blank HPMC-PEG 3000 and loratadine loaded HPMC-PEG 3000 films

Sample	Wavenumber (cm^{-1})			Functional group
	RH (%)			
	25	50	75	
A0	1450.4 ± 1.4	1449.6 ± 1.5	1452.4 ± 1.0	C–H
	2924.5 ± 5.2	2917.7 ± 8.4	2926.1 ± 9.7	C–H
	3372.5 ± 69.7	3296.9 ± 50.7	3461.0 ± 8.8	O–H
B0	1449.5 ± 1.4	1457.5 ± 2.4	1451.0 ± 2.1	C–H
	3419.5 ± 12.6	3442.3 ± 9.7	3446.1 ± 7.8	O–H
B1	1438.4 ± 3.1	1444.2 ± 1.5	1439.1 ± 4.4	Aromatic C=C
	3407.3 ± 15.8	3414.4 ± 8.0	3417.7 ± 6.3	O–H
B2	1436.5 ± 1.3	1438.6 ± 2.1	1440.7 ± 0.4	Aromatic C=C
	3430.2 ± 6.0	3434.0 ± 4.5	Band broadening	O–H
B3	2905.0 ± 1.8	2905.4 ± 0.7	2918.2 ± 10.1	C–H
	3378.0 ± 8.4	3420.9 ± 4.5	Band broadening	O–H
B4	1435.3 ± 0.2	1438.0 ± 0.7	1436.0 ± 0.3	Aromatic C=C
	3410.3 ± 25.3	3444.0 ± 8.4	3428.3 ± 2.6	O–H

3.2. FTIR analysis

The addition of PEG 3000 into the film A0 induced polymer–plasticizer interaction via the O–H moiety. Evidence of this was shown by the FTIR wavenumbers of B0 films at 3419.5 ± 12.6 and $3446.1 \pm 7.8\,cm^{-1}$ in the respective samples stored at the relative humidity of 25 and 75% of which were intermediate between those of A0 film and PEG 3000 (Table 2; Figs. 5e and 7b). Under the relative humidity of 25%, a greater strength of interaction between the HPMC and/or PEG 3000 molecules in films B0 was effected via the polymeric O–H functional groups than films stored at the relative humidity of 50 and 75% (Table 2; Figs. 5e, 6b and 7b). The observation was in agreement with the DSC findings of which the film B0 stored under a lower level of relative humidity had higher melting peak temperatures when compared to those of films stored under a higher level of relative humidity (Figs. 2e, 3b and 4b).

With the incorporation of loratadine into film B0, the propensity of polymer–polymer, polymer–plasticizer and/or drug–polymer interaction via the O–H functional group was greater in samples stored at a lower level of relative humidity, particularly when samples B1, B2 and B3 were concerned (Table 2; Figs. 5–7). In samples B2 and B3 which were stored at the relative humidity of 75%, it was possible that the PEG 3000 molecules had interacted with HPMC chains via the O–H moiety in a selective manner thereby leading to the formation of FTIR bands with dual peak characteristics (Fig. 7d and e).

Under the relative humidity of 25%, the propensities of drug–polymer interaction in sample B2 via the aromatic C=C moiety, as well as, polymer–polymer, polymer–plasticizer

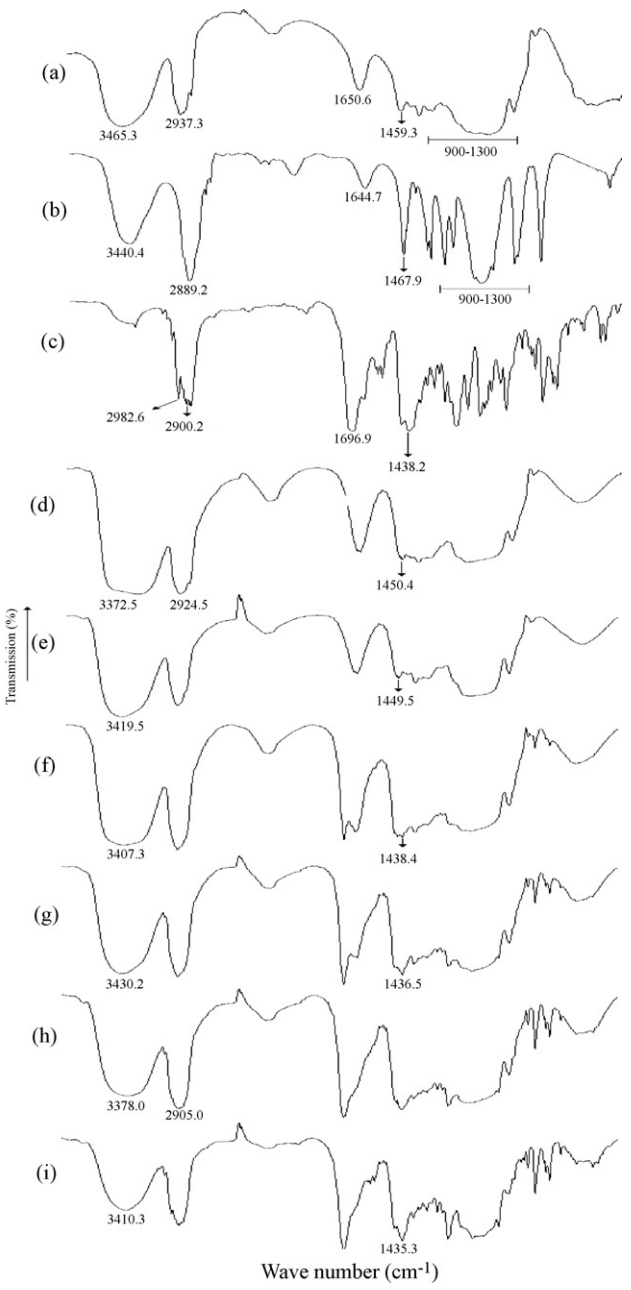

Fig. 5. FTIR spectra of (a) unprocessed HPMC, (b) PEG 3000, (c) loratadine (d) A0-25% RH, (e) B0-25% RH, (f) B1-25% RH, (g) B2-25% RH, (h) B3-25% RH and (i) B4-25% RH.

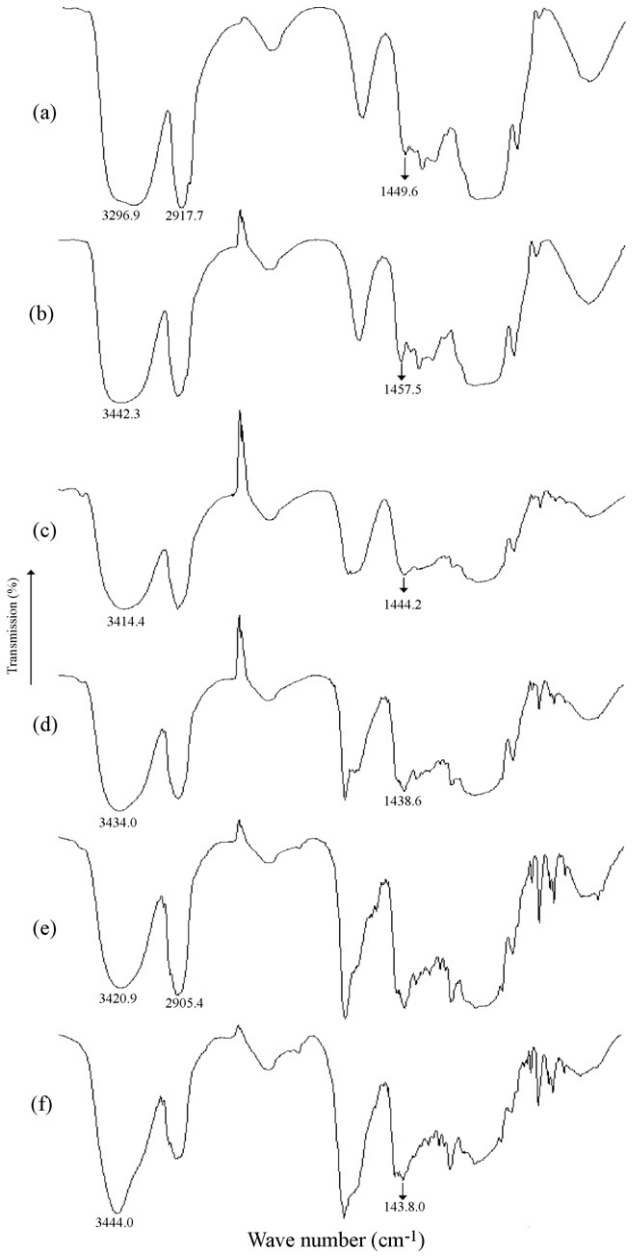

Fig. 6. FTIR spectra of (a) A0-50% RH, (b) B0-50% RH, (c) B1-50% RH, (d) B2-50% RH, (e) B3-50% RH and (f) B4-50% RH.

and/or drug–polymer interaction in sample B3 via the C–H moiety were greater than those of stored at a higher level of relative humidity (Table 2; Figs. 5–7). Practically, the wavenumbers attributing to the aromatic C=C and C–H functional groups of drug, polymer and/or plasticizer were relatively small for the respective samples of B2 and B3 kept at lower levels of relative humidity. Unlike films B1, B2 and B3, the strength of polymer–polymer, polymer–plasticizer and/or drug–polymer interaction of sample B4 via the O–H and aromatic C=C functional groups was lower when the sample was stored at 50% relative humidity (Table 2; Figs. 5i, 6f and 7f). Analysis of FTIR spectra indicated that there was a higher propensity of drug–polymer interaction in film B1 stored at 50% relative humidity and in film B2 stored at 75% relative humidity via the C=O of polymer and C=O, C–N and/or unconjugated C=C of drug as the dual crest of FTIR peak at the wavenumber between 1600 and 1700 cm^{-1} became inconspicuous when compared to the same samples stored under different levels of relative humidity (Figs. 5–7).

3.3. Microwave NDT analysis

The microwave NDT analysis indicated that nPAC, nPTC and nPRC values of both blank and drug loaded films obtained at the frequency bands of 8 and 12 GHz varied with the profiles of polymer–polymer, polymer–plasticizer and/or drug–polymer

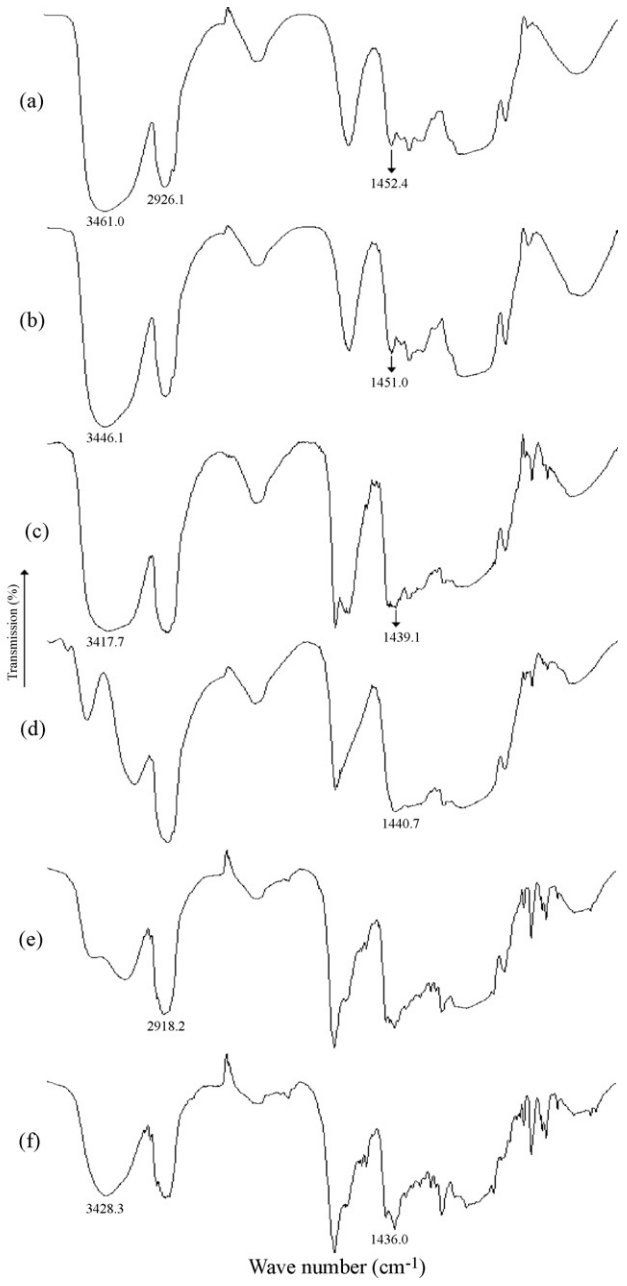

Fig. 7. FTIR spectra of (a) A0-75% RH, (b) B0-75% RH, (c) B1-75% RH, (d) B2-75% RH, (e) B3-75% RH and (f) B4-75% RH.

interaction in films. As the values of nPRC were relatively small and susceptible to erroneous variation, the subsequent discussion would thus focus on the measurements of nPTC and nPAC as the indicators of matrix characteristics in addition to thermal and molecular spectroscopy profiles obtained using the DSC and FTIR techniques, respectively.

Under the microwave frequency of 8 GHz, it was found that higher nPAC, but lower nPTC values were obtained for samples A0, B0, B1, B2 and B3 stored at a lower level of relative humidity (Table 3a). Similar observation was found for the same samples in the case of microwave NDT test conducted at the frequency of 12 GHz (Table 3b). In the case of samples B4 stored at the relative humidity of 50%, it effected lower nPAC, but higher

Table 3
nPTC, nPRC and nPAC values of blank HPMC, blank HPMC-PEG 3000 and loratadine loaded HPMC-PEG 3000 films determined at microwave frequency bands of (a) 8 GHz and (b) 12 GHz

Sample	RH (%)								
	25			50			75		
	nPTC (%/mm)	nPRC (%/mm)	nPAC (%/mm)	nPTC (%/mm)	nPRC (%/mm)	nPAC (%/mm)	nPTC (%/mm)	nPRC (%/mm)	nPAC (%/mm)
(a) 8 GHz									
A0	3088.50 ± 5.84	0.07 ± 0.01	114.28 ± 5.84	3127.79 ± 8.50	0.09 ± 0.02	74.96 ± 8.51	3172.94 ± 13.74	0.13 ± 0.02	29.78 ± 13.75
B0	2725.26 ± 8.86	0.08 ± 0.01	61.03 ± 8.86	2752.82 ± 12.73	0.11 ± 0.02	33.49 ± 12.75	2792.25 ± 11.28	0.21 ± 0.05	0.13 ± 0.09
B1	1534.69 ± 2.30	0.05 ± 0.01	33.20 ± 2.30	1533.05 ± 5.83	0.05 ± 0.01	34.84 ± 5.83	1569.60 ± 5.20	0.16 ± 0.02	0.51 ± 0.11
B2	1446.87 ± 5.86	0.06 ± 0.01	21.26 ± 5.86	1453.77 ± 5.10	0.07 ± 0.00	14.35 ± 5.10	1466.36 ± 4.71	0.14 ± 0.02	1.69 ± 4.73
B3	851.15 ± 3.06	0.02 ± 0.00	24.32 ± 3.06	862.89 ± 4.60	0.04 ± 0.01	12.55 ± 4.61	866.81 ± 4.87	0.05 ± 0.01	8.63 ± 4.88
B4	683.88 ± 2.84	0.01 ± 0.01	13.79 ± 2.84	690.13 ± 2.87	0.06 ± 0.00	7.48 ± 2.87	681.69 ± 2.30	0.05 ± 0.00	15.93 ± 2.30
(b) 12 GHz									
A0	3074.47 ± 4.49	0.11 ± 0.04	128.27 ± 4.48	3114.06 ± 8.41	0.27 ± 0.05	88.52 ± 8.44	3155.45 ± 12.79	0.39 ± 0.13	47.00 ± 12.90
B0	2709.75 ± 5.83	0.26 ± 0.04	76.36 ± 5.83	2733.38 ± 12.69	0.42 ± 0.12	52.58 ± 12.77	2775.57 ± 6.22	0.79 ± 0.25	10.02 ± 6.36
B1	1525.49 ± 1.90	0.20 ± 0.03	42.26 ± 1.90	1525.53 ± 5.18	0.16 ± 0.03	42.25 ± 5.20	1560.87 ± 4.28	0.65 ± 0.07	6.43 ± 4.31
B2	1447.68 ± 4.80	0.19 ± 0.04	20.32 ± 4.82	1448.38 ± 4.16	0.24 ± 0.04	19.56 ± 4.17	1457.56 ± 2.53	0.59 ± 0.08	10.04 ± 2.58
B3	851.43 ± 1.66	0.03 ± 0.01	24.03 ± 1.66	858.57 ± 4.69	0.19 ± 0.04	16.72 ± 4.71	860.62 ± 4.24	0.21 ± 0.07	14.66 ± 4.31
B4	681.48 ± 2.64	0.01 ± 0.01	16.18 ± 2.64	686.87 ± 2.11	0.27 ± 0.02	10.53 ± 2.10	677.54 ± 2.07	0.17 ± 0.01	19.97 ± 2.08

nPTC values than those of stored at 25 or 75% relative humidity with respect to microwave NDT measurement conducted at both 8 and 12 GHz (Table 3). The microwave NDT test of samples B0, B1, B2 and B3 stored at the lower level of relative humidity gave rise to higher nPAC, but lower nPTC values regardless of the test frequencies employed when compared to samples stored at the higher level of relative humidity. This was attributed to a greater strength of polymer–polymer, polymer–plasticizer and/or drug–polymer interaction was mediated in the former at O–H, C–H and/or aromatic C=C domains of films. A lower propensity of polymer–polymer, polymer–plasticizer and/or drug–polymer interaction was effected via the O–H and aromatic C=C moieties in sample B4 stored at 50% relative humidity than those of stored at 25 and 75% relative humidity, and this led to lower nPAC but higher nPTC values when tests were conducted at the microwave frequencies of 8 and 12 GHz.

From the previous study of our laboratory, it was found that the measurement of microwave NDT test at 8 GHz was sensitive to the chemical environment involving polar moiety such as O–H functional group, while it was greatly governed by the less polar C–H moiety in test conducted at 12 GHz (Anuar et al., 2007). The present findings indicated that the changes of both polar and apolar environments of HPMC-PEG 3000 films were reflected accordingly by the microwave NDT measurements conducted at the frequency bands of 8 and 12 GHz, respectively. Pearson correlation study indicated that the nPAC values of films measured at 8 GHz (B0: $r = -0.9$; B1: $r = -0.7$; B2: $r = -1.0$; B3: $r = -1.0$; B4: $r = -0.7$) and 12 GHz (B2: $r = -1.0$; B3: $r = -0.7$; B4: $r = -0.9$), as well as, the nPTC values of films determined at 8 GHz (B0: $r = 0.9$; B1: $r = 0.7$; B2: $r = 1.0$; B3: $r = 1.0$; B4: $r = 0.7$) and 12 GHz (B2: $r = 1.0$; B3: $r = 0.7$; B4: $r = 0.9$) were well described by the changes in FTIR profiles of matrices stored under various levels of relative humidity. Apparently, the FTIR wavenumbers ascribing C–H and aromatic C=C moieties of the respective film samples of B0 and B1 varied with the measurements of nPAC and nPTC (Tables 2 and 3; Figs. 5–7) though the trend was less marked unlike film samples B2, B3 and B4.

4. Conclusions

Apparently, the absorption and transmission characteristics of both blank and drug loaded HPMC-PEG 3000 films for microwave varied with the state of polymer–polymer, polymer–plasticizer and/or drug–polymer interaction at O–H, C–H and/or aromatic C=C domains. The measurements of microwave NDT test at 8 and 12 GHz were sensitive to the changes of chemical environment in matrix involving polar functional group such as O–H moiety and less polar functional groups such as C–H and aromatic C=C moieties, respectively. The present investigation verified that the microwave NDT technique has the capacity to evaluate the state of interaction between polymer, plasticizer and/or drug of a binary polymeric matrix, in addition to the existing DSC and FTIR techniques. It is potentially useful for the characterization of transdermal drug delivery system made up of complex formulation.

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