ANALYSIS OF NIFEDIPINE CONTENT IN TRANSDERMAL DRUG DELIVERY SYSTEM USING NON-DESTRUCTIVE VISIBLE SPECTROPHOTOMETRY TECHNIQUE.

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Abstract

The applicability of visible spectrophotometry technique as a tool to determine the drug content of polymeric film for use as a transdermal drug delivery system was investigated. Hydroxypropylmethycellulose (HPMC) was selected as the matrix polymer and nifedipine as the model drug. Blank and nifedipine-loaded HPMC films were prepared using the solvent evaporation method. The absorbance spectra of these films under the visible wavelengths between 400 and 800 nm were assessed and compared against the drug content values obtained by means of the conventional destructive UV-spectrophotometry technique. The latter required the use of a solvent system which contained methanol, a harmful organic component in pharmaceutical applications. The results indicated that the absorbance values, attributed to nifedipine, at the wavelengths of 545, 585, 638 and 755nm were significantly correlated to the drug content values obtained using the chemical assay method (Pearson correlation value: $r \geq 0.990$ and $p < 0.01$). The visible spectrophotometry technique is potentially suitable for use to determine the nifedipine content of films owing to its nature of characterization of transdermal drug delivery system which does not require sample destruction during the process of measurement. The samples are recoverable from test and analysis of the entire batch of samples is possible without the need of solvents and chemical reagents.

Keywords: Hydroxypropylmethycellulose; Nifedipine; Visible Spectrophotometry; UV Spectrophotometry

Introduction

Transdermal drug delivery system has been developed for delivery of therapeutic agents owing to it represents a safe administration system and has gained a higher level of patient compliance when compared to other routes of administration [1]. Practically, there are several advantages of drug administration by means of transdermal drug delivery system over conventional oral dosage forms. The use of transdermal drug delivery system avoids the chemically and biochemically hostile gastrointestinal environment and first pass metabolism which could bring about inactivation of drugs [2]. In the pharmaceutical industry, the drug content of transdermal drug delivery system dictates the dosage of drug administered to each patient. A high level of consistency in intra-batch and inter-batch drug content of transdermal drug delivery system is utmost important in avoidance of adverse effects following excessive or sub-therapeutic doses. Analytical techniques, such as ultraviolet (UV) spectrophotometry, have long been employed to determine the drug content of transdermal drug delivery system. The technique results in sample being unrecoverable from test and disposal of a large amount of solvents and reagents owing to the destructive nature of the test. The objective of the present study was to explore the applicability of non-destructive visible spectrophotometry technique as an optional tool to determine the drug content of polymeric film for use as transdermal drug delivery system.

Materials and methods

Materials

Hydroxypropylmethylcellulose (HPMC, Dow Chemical Company, USA) was used as matrix polymer with nifedipine (Kothari Phytochemicals International Nagari, India) as the model drug.

Sample Preparation

An accurately weighed quantity of 2.5% w/w of HPMC solution, with or without nifedipine, was transferred into a glass petri dish. The solution was subjected to hot air drying at $40 \pm 0.1\ ^0$C for 24 hours. The formed film was conditioned in a desiccator at the relative humidity of $50 \pm 5\%$ for at least 5 days prior to physicochemical characterization. The contents of HPMC and nifedipine in each film are shown in Table 1.

Table 1: Contents of HPMC and nifedipine in film.

Film	HPMC (mg)	Nifedipine (mg)
N0	37.5 ± 0.01	0 ± 0.01
N1	37.5 ± 0.01	5 ± 0.01
N2	37.5 ± 0.01	10 ± 0.01
N3	37.5 ± 0.01	20 ± 0.01
N4	37.5 ± 0.01	40 ± 0.01

UV Spectrophotometry Analysis

The drug contents of HPMC and HPMC-nifedipine films were examined using the UV spectrophotometry technique (Cary 50 Conc, Varian Australia Pty Ltd., Australia). Five fractions of each film were accurately weighed, and dissolved in the respective solvent systems of each consisted of 50 ml mixture of methanol and deionized water in a volume ratio of 3:2. The solutions were then filtered through a 0.45μm cellulose acetate membrane and subjected to spectrophotometric assay at the wavelength of 235 nm. The drug content of film was defined as the ratio of drug amount embedded in film to the total film weight expressed in the unit of percentage. Triplicates were carried out and the results averaged.

Visible Spectrophotometry Analysis

The absorbance spectra of film with respect to visible waves were examined using a non-destructive visible spectrophotometer (Figure 1). The set up of non-destructive visible spectrophotometer consists of tungsten halogen light source (Ocean Optics LS-1, USA), illumination fiber, sample holder, bifurcated fiber, detector (S2000) and spectra recording system. The absorbance measurement of film proceeded by placing the film in the sample holder and subjected it to scanning by visible waves in the wavelength ranged between 400 and 800nm. At least triplicates were carried out and the results averaged.

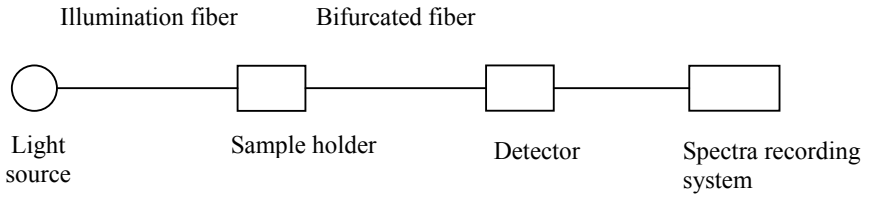

Figure 1: Schematic diagram of non-destructive visible spectrophotometer.

Results and discussion

Table 2 shows the drug content values of films (N0-N4) measured using the UV spectrophotometry technique. The N0 was blank HPMC film without the drug. HPMC-nifedipine films, N1, N2, N3 and N4 contained drug loads amounting to those of introduced during the preparation of film samples (Tables 1 and 2).

Table 2: Drug contents of films determined using the UV spectrophotometry technique.

Film	Drug content (% w/w)
N0	0
N1	11.05 ± 0.33
N2	20.32 ± 0.09
N3	34.60 ± 0.02
N4	49.01 ± 0.03

Using visible spectrophotometry technique, it was found that peaks of absorbance was noted in nifedipine-loaded HPMC films at 545, 585, 638 and 755 nm but no absorbance peak was observable in the visible spectrum of blank HPMC film. In the latter, a consistent absorbance value of 110 was attained at all tested visible wavelengths. At all visible wavelengths, a higher absorbance intensity was obtained with film containing a higher drug load (Tables 2 and 3). Pearson correlation study indicated that there was a significant relationship between the drug content of film with the absorbance intensity of the same sample (Table 4; $r \geq 0.990$ and $p < 0.01$).

Table 3: Visible absorbance values of HPMC and HPMC-nifedipine films.

Film	Absorbance intensity (counts)			
	λ_{545}	λ_{585}	λ_{638}	λ_{755}
N0	110 ± 0.01	110 ± 0.01	110 ± 0.01	110 ± 0.01
N1	510 ± 4.62	538 ± 6.03	517 ± 5.69	247 ± 3.61
N2	979 ± 4.16	1150 ± 27.47	1221 ± 11.36	578 ± 4.04
N3	2028 ± 19.30	2290 ± 7.23	2226 ± 2.89	855 ± 12.77
N4	2451 ± 18.04	2829 ± 5.13	2883 ± 15.70	1247 ± 13.75

Table 4: Pearson correlation between visible absorbance value and drug content of films.

	Pearson correlation			
	Absorbance intensity (counts)			
	λ_{545}	λ_{585}	λ_{638}	λ_{755}
Drug content (%w/w)	0.990*	0.992*	0.995*	0.994*

* Level of significance at $p < 0.01$

Conclusion

The present study demonstrated the applicability of visible spectrophotometry technique to assess the drug content of transdermal drug delivery system without subjecting the dosage form to destruction by solvents and reagents such as methanol, water and 4-(methylamino) phenol. Visible spectrophotometry technique is potentially useful as an optional tool to characterize transdermal drug delivery system formulated in the form of a polymeric film.

References

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