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Research Article

FORMULATION DEVELOPMENT AND EVALUATION OF PHENYLEPHRINE HYDROCHLORIDE TRANSDERMAL PATCHES BY USING SOLVENT EVAPORATION METHOD

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ABSTRACT

The purpose of this research work was to develop a matrix type transdermal therapeutic system containing a Phenylephrine hydrochloride with different ratios of HPMC K-100 and Eudragit L-100 by solvent evaporation technique. The physicochemical compatibility of drug and polymers was studied by FT-IR the results suggested no physicochemical incompatibility between the drug and polymers. Nine formulations are done with different ratios of polymers the total weight of polymers is maintained as the 1 gram. The PEG-400 used as plasticizer, SLS act as a penetration enhancers, chloroform: methanol (3:2) are used as an solvent mixture and aluminum foil act as backing film. The formulated patches will evaluated for physical appearance, thickness, folding endurance, weight uniformity, percentage moisture uptake, percentage moisture loss, drug content analysis and *In vitro* drug permeation study. The results are compared; from these nine formulations, the F5 shows better percentage content and percentage drug permeation than others.

INTRODUCTION:

A transdermal drug delivery system (TDDS) has many advantages over conventional modes of drug administration, in particular the avoidance of hepatic first-pass metabolism, a reduction in the frequency of drug administration, and an improvement of patient compliance.

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Thus, transdermal administration is a potential approach to overcoming these problems with Phenylephrine hydrochloride treatment. A TDDS consists of several components, including the active ingredient, a permeation enhancer, plasticizer, adhesive, backing membrane and so on. Permeation enhancers can overcome the intrinsic resistance of the stratum corneum, which results in an increase in the flux of the active ingredient, therefore we tried to design a matrix-type (drug in adhesive) patch, which is the simplest among the various patches used in the present study. Phenylephrine hydrochloride is the most widely prescribed drug for the treatment of nasal congestion.

Following oral administration the bioavailability remains low (38%) because of significant first-pass hepatic metabolism. Phenylephrine hydrochloride also has a short plasma half-life of 2-3 hours. So higher frequency of dosage administration is needed for better patient compliance because of low bioavailability and short plasma half-life. So an alternate route of administration is needed for Phenylephrine hydrochloride. The transdermal route is an alternative for administration of such drugs. This route offers many advantages over the oral dosage form, such as improving patient compliance in long-term therapy, bypassing first-pass metabolism, sustaining the drug delivery. Phenylephrine hydrochloride possesses ideal characteristics such as a smaller dose range (i.v 30 to 60 µg/min), short plasma half-life, and poor oral bioavailability for formulation as a transdermal patch. The aims of the present study were to develop different matrix type transdermal patches with various ratios of hydrophilic and hydrophobic polymer combinations such as Hydroxyl Propyl Methyl Cellulose (HPMC) and Eudragit-L-100, containing Phenyephrine Hydrochloride [1-4].

MATERIALS:

Phenylephrine HCl was obtained as a gift sample from Aurobindo Pharma limited, Chennai.HPMC K-100, Eudragit L-100, SLS, PEG-400 was obtained as a gift sample from saimeera life sciences pvt. Ltd, Chennai. Chloroform, Methanol was obtained as a gift sample from nice chemicals laboratory, Cochin. All the reagents used in this study were of analytical grade.

METHODS:

Solvent evaporation method: [5-11]

All the ingredients are weighed for the dispensed amount.Polymers are dissolved in a 5 ml of solvent mixture.Incorporate the required amount of PEG-400 & SLS and mixed well by uniform stirring.Then drug is slowly added to the above mixture and stirr . continuously for 30 mins. After 30 mins the above solution mixture is poured into the aluminium foil placed on the petridish. Then place the funnel over the petridish to control the rate of evaporation.

After evaporation the thin films are formed which is collected and stored in a suitable container. Nine formulations are done with difference in concentration of polymers used in formulation (total weight of polymers are maintained as 1g).Solvent system is chloroform: methanol (3:2). 20% of PEG-400 is used in formulation from total weight of drug and polymers.30% of SLS is used in formulation from total weight of drug and polymers.

Standard calibration curve of Phenylephrine HCl: [12,13]

Phenylephrine HCl can be estimated by UV spectrophotometry, in the present investigation, the Phenylephrine HCl was estimated by UV/Visble spectrophotometry in 0.5M H_2SO_4. Drug content analysis was also carried out in 0.5M H_2SO_4 & the Invitro drug permeation study was carried out in the phosphate buffer pH - 7.4.

Preparation of stock solution:

Phenylephrine HCl (100 mg) was accurately weighed and transferred into a 100ml volumetric flask it was dissolved in 0.5M H_2SO_4 & the volume is made upto the mark which 0.5M H_2SO_4 to get a1000 µ/ml solution, 10 ml of the above solution was further diluted with 0.5M H_2SO_4 up to 100ml to get a stock solution of 100 µg/ml.

UV absorption maxima of Phenylephrine HCl:

UV scanning was done for 100 µg/ml drug solution 200-400 nm in 0.5M H_2SO_4 as a blank using UV/Visible spectrophotometer. The wavelength maxima were found to be at 273 nm.

Preparation of standard curve:

From stock solution 2, 4, 6, & 8ml were transferred into a separate 10ml volumetric flask and were diluted with the 0.5M H_2SO_4 upto the mark obtain Phenylephrine HCl concentration 20, 40, 60, 80 µg/ml respectively. The stock solution (100µg/ml) are also utilised for standard curve preparation. Absorbance of each solution was measured at 273 nm.

Evaluation of formulated Phenylephrine HCl transdermal patches

1.Physical appearance:[14]

All the formulated PE HCl was visually inspected for colour, shape, clarity, opaque, transparency, flexibility and smoothness.

2. Interaction studies:[14, 15]

The physicochemical compatibility between PE HCl & polymers (HPMC K-100 & Eudragit L-100) was studied by using fourier transform infrared spectroscopy (FT-IR). The infrared spectra were recorded using an FTIR spectrophotometer in KMCH college of pharmacy by the KBr pellet method and spectra were recorded in the wavelength region between 4000-400 cm^{-1}. The spectra obtained for PE HCl & polymers (HPMC K-100 & Eudragit L-100) and physical mixtures of PE HCl with polymers (HPMC K-100 & Eudragit L-100) were compared.

3.Thickness of patch:[16]

The thickness of the film was determined by measuring the thickness at random sites on formulated films using vernier callipers. The average thickness and standard deviation for the same ensure the thickness of the formulated patch.

4. Weight uniformity:[16]

Before done the weight uniformity test the formulated patches were dried at 60°c for 4 hours. A specified area of the patch is to be cut in different parts of patch and it is weighed in digital balance. The average weight is calculated from individual weights.

5. Folding endurance:[16]

A specific area of the film is cut evenly (1 cm^2 area) and folds it repeatedly at the same place till it broke. The number of folding is noted before the breaking of patch. It will give the folding endurance.

6. Percentage moisture loss:[16]

The formulated patches are weighed individually and kept in desiccators containing anhydrous calcium chloride at room temperature for 24 hours. After the 24 hours the patches are weighed at a specific time interval until the constant weight is obtained. The percentage moisture content is calculated by using following formulae,

Percentage moisture loss = (Initial wt - final wt)/initial wt) X 100

7. Percentage moisture uptake:[16]

Formulated patches are weighed individually and kept in a desiccators containing saturated potassium chloride. The RH is maintained as 84%. After 24 hours the patches are reweighed at a specific time intervals till the constant weight is attained.

Percentage moisture uptake = (final wt - initial wt)/initial wt) X 100

8. **Drug content analysis:[17]**

The accurately weighed pieces patches equivalent to 50 mg of PE HCl and add sufficient 0.5 M H_2SO_4 to produce 100 ml. Dilute 10 ml of this solution to 100 ml with 0.5 M H_2SO_4 and measure the absorbance of the resulting solution at the maximum wavelength 273 nm, calculate the % drug content using calibration curve of PE HCl.

***9. In-vitro* drug permeation studies:[14]**

In-vitro drug permeation was carried out with SPM. The SPM was collected from egg shell. Then it was tied at one end of the pipette. Other end was open at top and was exposed to atmosphere. The diffusion medium used was phosphate buffer (pH-7.4) 1 ml of the phosphate buffer (pH-7.4) was transferred into a pipette via other end the temperature is maintained at 37±0.5 ºC. Then [lace this pipette on the beaker containing the phosphate buffer (pH-7.4). The formulated patch equivalent to 50 mg is placed on the beaker containing phosphate buffer. After 6 hrs the concentration of drug in phosphate buffer present in inside of pipette was determined by UV spectrophotometry at 273 nm.

RESULTS:

The results of evaluation parameters of formulated Phenylephrine HCl Transdermal patches are shown below

Table 1: Formulation Composition

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
PE HCl	0.2 g	0.2 g	0.2 g	0.2 g	0.2 g	0.2 g	0.2 g	0.2 g	0.2 g
HPMC K-100	0.5 g	0.6 g	0.7 g	0.8 g	0.9 g	0.4 g	0.3 g	0.2 g	0.1 g
Eudragit L-100	0.5 g	0.4 g	0.3 g	0.2 g	0.1 g	0.6 g	0.7 g	0.8 g	0.9 g
PEG-400	0.13 ml	0.13 ml	0.13 ml	0.13ml	0.13ml	0.13ml	0.13 ml	0.13 ml	0.13 ml
SLS	0.195 g	0.195 g	0.195 g	0.195 g	0.195 g	0.195 g	0.195 g	0.195 g	0.195 g
$CHCl_3$:CH_3OH	3:2	3:2	3:2	3:2	3:2	3:2	3:2	3:2	3:2

Table 2: Standard curve of Phenylephrine HCl

S.no	Concentration (mcg/ml)	Absorbance
1	20	0.1070
2	40	0.1940
3	60	0.2720
4	80	0`3320
5	100	0.3720

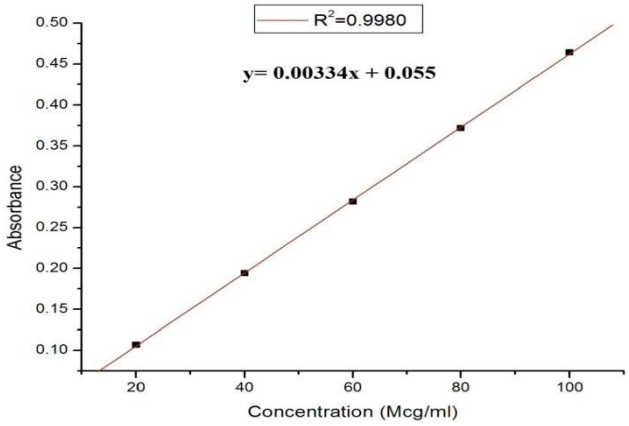

Fig 1: Calibration Curve of PE HCl

Table 3: Physical appearance of formulated Phenylephrine HCl Transdermal patches

Formulation	Appearance
F1	White, clear, transparent, slightly flexible.
F2	White, clear, transparent, slightly flexible.
F3	White, clear, transparent, slightly flexible.
F4	White, clear, transparent, flexible.
F5	White, clear, transparent, flexible.
F6	White, clear, transparent, flexible.
F7	White, clear, transparent, flexible.
F8	White, clear, transparent, flexible.
F9	White, clear, transparent, flexible.

Table 4: Other Evaluation parameters of formulated Phenylephrine HCl Transdermal patches

Formulations	Thickness Mean ± S.D	Weight uniformity avg wt in g	Folding endurance (no of Folds)	% Moisture loss	% Moisture uptake	% Drug Content	% Drug Permeation (in 6 hrs)
F1	0.5±0.001	0.06	114	28.57 %	150 %	97.60 %	27.26 %
F2	1±0.001	0.0275	158	9.09 %	92.30 %	85.44 %	27.24 %
F3	1±0.001	0.0400	249	6.25 %	100 %	86.40 %	27.30 %
F4	1±0.001	0.075	329	6.45 %	87.17 %	90.58 %	27.42 %
F5	1.5±0.001	0.0725	360	13.79 %	115.38 %	97.12 %	27.60 %
F6	0.5±0.001	0.03	142	23.07 %	107.14 %	92.52 %	26.94 %
F7	0.5±0.001	0.0225	135	27.27 %	37.5 %	96.22 %	26.76 %
F8	1±0.001	0.0325	148	33.33 %	53.84 %	85.92 %	26.46 %
F9	0.5±0.001	0.0475	251	20 %	47.36 %	85.02 %	26.34 %

CONCLUSION:

- The TDDS will become most popular dosage form because of accurate dosage, self medication, painless parenteral therapy and convenient to use.
- The most common solid dosage forms are tablets and capsules, one of the main drawback of this dosage form is reduction in bioavailability due the first pass metabolism.
- The PE HCl is selective α_1-adrenoreceptor agonist, used as an nasal decongestant & mydriatics.
- The PE HCl has low oral bioavailability (38% only), can able to given in the form of IV infusion (30-60 µg/min) which needs hospitalization. So to overcome these problems, there is a need to develop the Transdermal patches of PE HCl.
- The drug polymers compatibility studies were carried out by FT-IR analysis; it showed there is no interaction between drug and polymers chosen in this formulation.
- The transdermal patches of Phenylephrine HCl were prepared by solvent evaporation method. Phenylephrine HCl, HPMC K-100, EL-100, PEG-400, and SLS, chloroform & methanol, aluminium foil is used in this formulation.
- Then the formulated Phenylephrine HCl Transdermal patches were evaluated by physical appearance, thickness, weight uniformity, folding endurance, percentage moisture loss, percentage moisture content, drug content, % drug permeation,
- From the results it was conclude that the successful formulation of Phenylephrine HCl transdermal patches are **[F5]** because it has better % drug content and % drug permeation than other formulations.

REFERENCES:

1. Chein YW. Transdermal drug delivery and delivery system. In, novel drug delivery system, vol. 50, Marcel Dekkar, Inc., New York, 1992; 031-381.
2. Jalwal P, Jangra1 A, Dahiya L, Sangwan Y, Saroha R. A Review on Transdermal Patches. The Pharma Research. 2010; 3: 139- 149.
3. Gordon RA, Peterson TA. Four myths about transdermal drug delivery. Drug Delivery Technology. 2003; 3: 1-7.
4. Walters KA. Transdermal drug delivery systems In:Swarbick K., Boylan J.C, eds. Encyclopedia of pharmaceutical technology. New York, Marcel Dekker Inc; 1997. p. 253-293.
5. Bagyalakshmi J, Vamsikrishna RP, Manavalan R, Ravi TK, Manna PK. Formulation development and invitro and invivo evaluation of membrane moderated transdermal systems of ampicilline sodium in ethanol: pH 4.7 buffer solvent system AAPS PharmSciTec. 2007, 8, Article7.
6. Baker W and Heller J. ”Material Selection for Transdermal Delivery Systems”, In Transdermal Drug

Delivery: Developmental Issues and Research Initiatives, J.Hadgraft and R.H.Guys, Eds. Marcel Dekker, Inc.,New york 1989 pp. 293-311.

7. Al- Khamis K, Davis S.S and Hadgraft J. Microviscosity and drug release from topical gel formulations. Pharm. Res. 1986; 3: 214-217.
8. Anon. Transdermal delivery systems-general drug release standards. Pharmacopeial Forum, 1980; 14: 3860-3865
9. Mayorga P, Puisieux F and Couarraze G. Formulation study of a Transdermal delivery system of primaquine. Int. J. pharm. 1996; 132: 71-79 Deo M.R, Sant V.P,Parekh S.R, Khopade A.J an Banakar U.V. Proliposome-based Transdermal delivery of levonorgestrel. Jour. Biomat. Appl. 1997; 12: 77-88.
10. Yan-yu X, Yun- mei S, Zhi-Peng C and Qi-nerg P. Preparation of silymarin proliposomes; A new way to increase oral bioavailability of silymarin in beagle dogs. Int. pharm. 2006; 319: 162-168.
11. Crawford R.R and Esmerian O.K. Effect of plasticizers on some physical properties of cellulose acetate phthalate films. J. Pharm. Sci. 1997; 60: 312-314.
12. Indian Pharmacopoeia, Govt. of India published by the controller of publication, Delhi. Vol. II: 1996. A-90.
13. Indian Pharmacopoeia."Government of India ministry of health and family welfare". The Controller of Publication, Delhi. Vol. (1): 1996. 424-425.
14. Singh J, Tripathi K.T and SakiaT.R. Effect of penetration enhancers on the *invitro* transport of ephedrine through rate skin and human epidermis from matrix based Transdermal formulations. Drug Dev.Ind. Pharm. 1993; 19: 1623-1628.
15. Wade A, Weller P.J. Handbook of pharmaceutical Excipients. Washington, DC: American Pharmaceutical Publishing Association; 1994: 362-366.
16. Rhaghuram reddy k, Muttalik S and Reddy S. Once daily sustained-release matrix tablets of nicorandil: formulation and invitro evaluation. AAPS Pharm.Sci.Tech. 2003; 4:4.
17. Shaila L, Pandey S and Udupa N. Design and evaluation of matrix type membrane controlled Transdermal drug delivery system of nicotin suitable for use in smoking cessation. Indian Journal. Pharm. Sci. 2006; 68: 179-184.