Section A -Research paper
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Formulation of a Transdermal Patch Containing Amlodipin Besylate and Its evaluation

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ABSTRACT

A transdermal patch is a medical-grade adhesive patch affixed to the skin to permit the absorption of a specific medication dose into the circulation via the skin. The transdermal drug administration system is a cutting-edge method of medication delivery that dispenses with conventional dosage forms. Prior to formulation, the drug's description,

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solubility, and melting point were evaluated and determined to be standard. Based on pre-formulation investigations, it was determined that the drug could be used to create a transdermal formulation. F5 exhibited a greater percentage of drug release in this transdermal medication delivery method. In comparison to other formulations, formulation F5 has a superior 24-hour prolonged release. It was determined that formulation F5, comprised of Eudragit RS100 and HPMC, was the optimal formulation for ensuring controlled drug release for up to 24 hours. Nevertheless, the optimal formulation, F-5, follows first order kinetics and the diffusion process. The findings of this study provide encouragement that it may be used as a controlled medication delivery system and that administration frequency may be reduced.
Keywords: Transdermal patch, Bioavailability, TDDS, Skin, Controlled release, Amlodipin besylate

INTRODUCTION

Transdermal drug delivery system (TDDS) established itself as an integral part of novel drug delivery system. Transdermal patches are polymeric formulation which when applied to skin deliver the drug at a predetermined rates across dermis to achieve systemic effect [1]. Transdermal dosage form, though a costly alternative to conventional formulations, are becoming popular because of their unique advantages. Controlled absorption, more uniform plasma levels, improved bioavailability, reduced side effect, painless, ease of application and flexibility of terminating drug administration by simply removing the patch from the skin are some of the potential advantages of transdermal drug delivery. Development of controlled release transdermal dosage form is a complex process involving extensive efforts [2].

Transdermal drug delivery can closely mimic the slow intravenous infusion, without its potential hazards and also offer another most important advantage in allowing the patient to terminate the drug therapy by simply removing the patch at any desired time if toxicity develops [3].

MATERIALS AND METHODS

I. MATERIALS

HPMC/Eudragit RS 100, distilled water, propylene glycol, Amlodipine besylate, Hydroxypropylmethylcellulose, ethaol.

II. EXPERIMENTAL WORK

1) **Preformulation Studies:**
   a) **Organoleptic properties of drug:** A small quantity of drug sample was taken on butter paper and viewed in well illuminated place. It results as it's shown as white powder. Very less quantity of drug was used to get taste as well as smelled to get the odor. It is bitter in taste and odorless.

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b) Determination of solubility: A qualitative determination of the solubility was made by adding solvent in small incremental amount to a test tube containing fixed quantity of solute and vice versa. After each addition, the system is vigorously shaken and observed visually. It is slightly soluble in distilled water and partially soluble in Methanol, Ethanol and Methylene Chloride.

c) **Determination of melting point:** Melting point of Amlodipine besylate was determined by using capillary method. In this method little amount of Amlodipine besylate was filled in capillary after that the capillary was tied to a thermometer with the help of a rubber band. The thermometer with capillary was placed into Theil's tube which was previously filled with paraffin oil. The paraffin oil in the tube was heated until the drug melts. The temperature at which drug begins to melt was recorded. The specified melting point is 190-200℃ and the observed melting point is 192-196℃**.**

d) **Partition Coefficient:** A partition coefficient (P) or distribution coefficient (D) is the ratio of concentrations of a compound in a mixture of two immiscible solvents at equilibrium. Partition coefficient are useful in estimating the distribution of drugs within the body.

The specified partition coefficient is 2.70 and the observed partition coefficient is 2.66.

5. Quantitative estimation of drug by Calibration Curve method

a) Calibration of Phosphate buffer pH 7.4

Various dilutions were prepared to get concentrations 2, 4, 6, 8, 10, 12, 14, 16, 18, 20 µg/ml. The graph of concentration v/s absorbance was plotted and data was subjected to linear regression analysis.

S. No.	Concentration (µg/ml)	Absorbance
1	2	0.054
2	4	0.121
3	6	0.192
4	8	0.255
5	10	0.321

Table No. 1: Calibration curve of Amlodipine besylate in phosphate buffer saline pH 7.4
(λmax 238nm)

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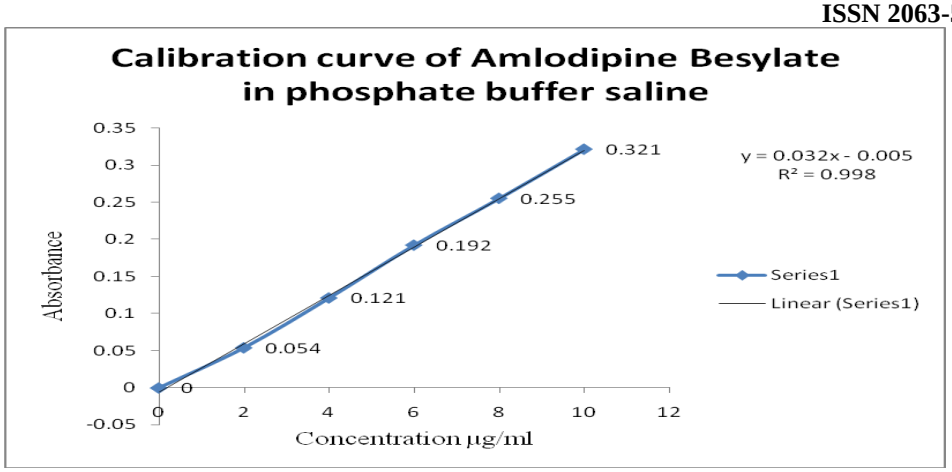

Fig. No. 1 Calibration curve of in Amlodipine Besylate in phosphate buffer saline pH 7.4

b) UV spectroscopic studies

The maximum wavelength of Amlodipine besylate was found to be 245 nm which matches the reported wavelength.

S.No.	Solvent	Peak Point Observed	Peak Point specified
1	Phosphate Buffer pH 7.4	245 nm	230-250 nm

Table No. 2 UV spectroscopic studies of Amlodipine Besylate

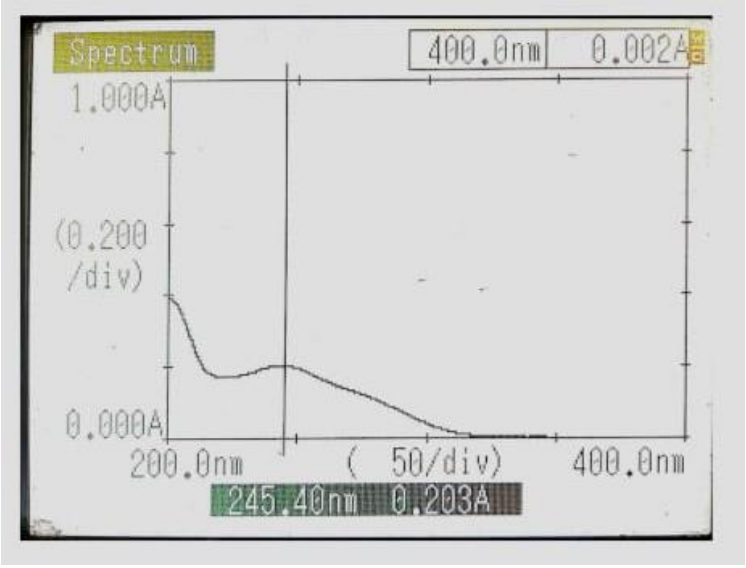

Fig no. 2 UV Spectra of Amlodipine Besylate sample in Phosphate buffer saline pH 7.4

FORMULATION AND EVALUTION OF TRANSDERMAL PATCH OF AMLODIPINE BESYLATE:

The Transdermal patch were prepared by solvent casting method. The different concentration of polymer (Eudragit RS 100 and HPMC) were weighed and used in suitable solvent of ethnol 20ml and known volume of PG (Propylene Glycol). As an Permeation enhancer PEG- 400 (polyethylgycol)was used in the preparation.

PROCEDURE

Transdermal patch of Amlodipine besylate was prepared by solvent casting method. The polymer (for example HPMC/Eudragit RS 100) was taken in a beaker with a minimum quantity of the solvent. Then 2/3rd of the solvent was mixed with the polymers and was added firstly with stirring at lower rpm and later at a higher speed. The plasticizer was added and homogeneously mixed, the drug was included with enduring agitation and the volume was made up. The patches were cast onto a suitably designed and fabricated glass mould and then dried in oven at 40°C. The patches were removed by using sharp blade by inserting along the edges of the patch. The dried patches were wrapped in butter paper and stored in a closed container away from light and in cool place.

RESULT

1 Drug content determination

From all the optimized patches, the formulation of batch F5 was highest drug content.

S.NO.	Formulation	Drug Content
1	F1	93.43%
2	F2	93.90%
3	F3	90.00%
4	F4	95%
5	F5	95.62%
6	F6	92.32%

Table No. 3: Drug Content

2 Percentage Cumulative Drug Release of Formulation F1 to F6, n=6

S. NO.	Time	FORMULATION					
		F1	F2	F3	F4	F5	F6
1	0	0.0 ±0.00	0.0±0.0	0.0±0.0	0.0±0.00	0.0±0.0	0.0±0.0
2	1	1.0±0.15	3.8±0.36	0.0±0.0	3.5±0.21	5.0±0.10	7.3±0.61
3	2	1.3±0.15	6.7±0.25	7.7±0.30	5.4±0.40	5.5±0.50	8.8±0.54
4	3	2.0±0.26	8.8±0.41	14.5±0.25	7.4±0.31	7.4±0.48	10.8±0.43
5	4	6.2±0.25	11.4±0.4	15.6±0.4	7.8±0.34	10.2±0.	13.6±0.1

			0	0		26	2
6	5	6.7±0.36	13.4±0.15	16.3±0.26	8.3±0.56	11.4±0.22	14.2±0.65
7	6	7.6±0.30	15.4±0.47	17.6±0.10	10.1±0.10	13.7±0.48	17.0±0.68
8	7	9.0±0.25	19.2±0.45	21.4±0.32	11.3±0.75	15.6±0.38	18.7±0.20
9	8	11.1±0.35	21.0±0.20	23.6±0.35	13.4±0.86	19.9±0.67	20.7±0.17
10	9	12.8±0.40	21.8±0.35	26.1±0.55	14.9±0.62	24.1±0.36	21.8±0.35
11	10	15.2±0.45	25.3±0.50	27.9±0.40	16.0±0.28	33.0±0.15	26.5±0.30
12	11	18.1±0.40	27.7±0.30	29.6±0.68	16.7±0.15	33.8±0.10	28.0±0.22
13	12	21.4±0.75	35.4±0.92	31.9±0.45	21.4±0.12	37.3±0.67	28.5±0.15
14	24	61.4±0.45	56.4±0.75	51.8±0.50	24.1±0.76	69.3±0.78	58.4±0.90

Table No. 4 % CDR of Formulation F1, F2, F3,F4,F5,F6

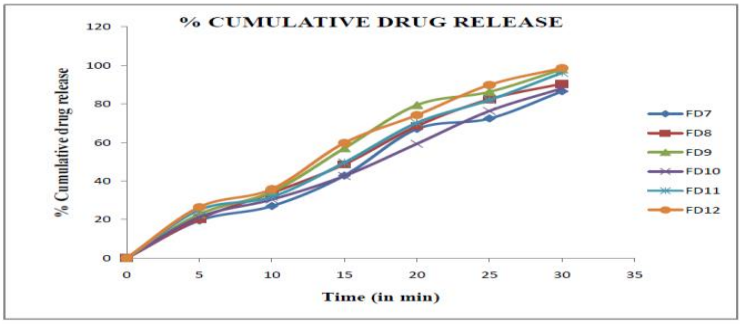

Fig.No. 3 Percentage Cumulative Drug Release

Based on all these factors the transdermal drug delivery system F5 is having greater % drug release. The formulation F5 shows better extended release up to 24hrs when compared to other formulations. So it was concluded that the formulation F5 prepared by using Eudragit RS100 and HPMC is the better formulation for control release of drug up to 24hrs of time.

S. NO.	Batch No.	Evaluation Parameters	Results
1	F5	Thickness	0.23+0.01
2	F5	Weight variation	230±0.3

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3	F5	Moisture Content	4.39 ± 0.04
4	F5	Moisture Uptake	4.02±0.06
5	F5	Folding Endurance	24.1±1.52

8 *In-vitro* Drug Release Studies

S. No.	Time (hrs)	Absorbance
1	**0**	**0.00±0.0**
2	**1**	**5.0±0.1**
3	**2**	**5.5±0.5**
4	**3**	**7.4±0.48**
5	**4**	**10.2±0.26**
6	**5**	**11.4±0.22**
7	**6**	**13.7±0.48**
8	**7**	**15.6±0.38**
9	**8**	**19.9±0.67**
10	**9**	**24.1±0.36**
11	**10**	**33.0±0.15**
12	**11**	**33.8±0.10**
13	**12**	**37.3±0.67**
14	**24**	**69.3±0.78**

Table No. 5 Drug release studies of Optimized Batch F5

CONCLUSION

The transdermal route is practical, safe, and may be superior to conventional routes in a number of ways, including avoiding first pass metabolism, extending the duration of action, minimising unwanted side effects, using drugs with short half-lives, improving physiological and pharmacological response, preventing fluctuations in drug levels, avoiding inter- and intra-patient variations, and, most importantly, increasing patient compliance because the drug delivery is more convenient. When applied to intact skin, transdermal therapy systems are self-contained, discrete dose forms that deliver the drug(s) to the systemic circulation at a regulated rate via the skin. Using two polymers, HPMC and Eudragit RS100, transdermal patches containing amlodipine besylate were designed and evaluated in an effort to develop a controlled release formulation. The transdermal patch was produced through a method known as solvent evaporation. The constant weight and thickness of the manufactured patches indicated that the drug was equitably distributed throughout the polymeric solution. The created patches were stable,

and the prepared formulation could be applied transdermally due to the low absorption values for moisture content.

Conflicts of Interest: No conflicts of interest to reveal.

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