ORIGINAL RESEARCH

JOURNAL OF PHARMACOLOGY AND BIOMEDICINE

Published by Educare Society for Science and Education

Development and Evaluation of a Nanoparticle-Based Transdermal Delivery System for Venlafaxine

Daya Shankar Yadav[1]*, Kamlesh Kumar Yadav[1]

[1] *R.K. Pharmacy College, Azamgarh, Uttar Pradesh, India*

Abstract

The present study was undertaken to develop and evaluate a nanoparticle-based transdermal delivery system for venlafaxine to overcome these limitations and provide sustained drug release. Gelatin nanoparticles containing venlafaxine were prepared using the desolvation method with different crosslinking agents, namely glutaraldehyde, PVP, PEG 2000, and PEG 10000. The prepared nanoparticles were evaluated for particle size, percentage yield, drug entrapment efficiency, and in vitro drug release. Among all formulations, the glutaraldehyde-crosslinked formulation (F1) exhibited the smallest particle size (217.2 nm), highest drug entrapment efficiency (61.6%), and sustained drug release up to 24 h. The optimized nanoparticles were further incorporated into transdermal patches prepared by the solvent casting method using HPMC and Eudragit polymers. The patches were evaluated for physicochemical characteristics including thickness, weight variation, drug content, surface pH, folding endurance, and in vitro permeation. All formulations demonstrated satisfactory mechanical properties, uniform drug distribution, and acceptable surface pH. In vitro permeation studies revealed sustained drug release over 24 h, with formulation P4 showing the highest cumulative drug release (87.33%). The findings suggest that nanoparticle-loaded transdermal patches can effectively enhance the controlled delivery of venlafaxine, potentially improving bioavailability, reducing dosing frequency, and increasing patient compliance. Thus, the developed nanoparticle-based transdermal system represents a promising alternative to conventional oral venlafaxine therapy.

Keywords: Venlafaxine; Gelatin Nanoparticles; Transdermal Drug Delivery; Sustained Release; Nanoparticle-Loaded Patch

*Corresponding author

Daya Shankar Yadav

Email id: ydayashankar726@gmail.com

JOURNAL OF PHARMACOLOGY AND BIOMEDICINE

ISSN No. 2456-8244

Publication Hosted by

www.jpbiomed.com

Cite this article as

Yadav DS, Yadav KK. Development and Evaluation of a Nanoparticle-Based Transdermal Delivery System for Venlafaxine. J Pharmacol Biomed. 2026; 10(4): 967-977

Received: 10.10.2026; Revised: 20.10.2026; Accepted: 22.10.2026

Introduction

Venlafaxine, a serotonin-norepinephrine reuptake inhibitor (SNRI), is widely prescribed for the management of major depressive disorder, generalized anxiety disorder, and panic disorder; however, its conventional oral administration is associated with significant limitations including extensive first-pass metabolism, short biological half-life, and dose-dependent gastrointestinal side effects, which collectively reduce bioavailability and patient compliance.[1,2] The therapeutic efficacy of venlafaxine is compromised by hepatic metabolism, leading to variable plasma concentrations and necessitating frequent dosing, which in turn increases the risk of adverse effects and poor adherence.

Transdermal drug delivery offers a promising alternative route by bypassing the gastrointestinal tract and hepatic first-pass metabolism, enabling direct absorption into systemic circulation through the skin.[3,4] Despite this advantage, the transdermal route faces challenges such as limited drug permeability. Nanoparticle-based drug delivery systems have emerged as innovative platforms capable of enhancing solubility, stability, and permeability of poorly bioavailable drugs like venlafaxine.

Incorporating mucoadhesive polymers into nanoparticle formulations further addresses the challenge of lower permeation by prolonging drug retention and facilitating sustained release. Such systems can potentially reduce dosing frequency, minimize systemic side effects, and improve therapeutic outcomes in patients requiring long-term antidepressant therapy.[5]

The development of a mucoadhesive nanoparticle-based transdermal delivery system aligns with the growing demand for patient-friendly, non-invasive, and efficient drug delivery strategies that enhance compliance and quality of life. Current literature reveals a paucity of optimized transdermal formulations for venlafaxine, highlighting a critical research gap in exploring advanced nanocarrier systems tailored for transdermal drug delivery.

Addressing this gap is essential to overcome pharmacokinetic limitations, achieve consistent therapeutic plasma levels, and reduce the burden of frequent oral dosing. Furthermore, the transdermal nanoparticle system offers translational potential for other CNS-active drugs with similar bioavailability challenges, thereby broadening its clinical relevance.

The study is therefore undertaken to design, develop, and evaluate a novel mucoadhesive nanoparticle-based transdermal delivery system for venlafaxine, with the aim of improving drug bioavailability, therapeutic efficacy, patient compliance, and overall treatment outcomes in depressive and anxiety disorders, while simultaneously contributing to the advancement of innovative drug delivery technologies in psychopharmacology.

Material and Methods

Materials

Venlafaxine was purchased from Yarrow Pharmaceuticals; gelatin, HPMC and other ingredients were obtained from Oxford Fine Chemicals.

Preformulation Studies

The color, odor and appearance of the obtained drug sample were observed with the help of the sensory organs. The drug was placed in a clean and dry watch glass and observed in well illuminated area. The texture was felt by rubbing between the fingers of hand. Solubility was observed in different solvents like water, HCl, ethanol and acetone.[6] Melting point was determined by open capillary method and is uncorrected. Partition coefficient was carried out using octanol and water by reported method.[7]

Preparation of Calibration Curve in phosphate buffer pH 6.8

Accurately weighed 10 mg of venlafaxine was taken in 10 mL volumetric flask and dissolved in water to the mark resulting in a stock solution of 1000 µg/mL. 1 mL of the above stock solution was taken in another 10 mL volumetric and volume was made up with phosphate buffer pH 6.8 to mark resulting in a solution of 100 µg/mL. Aliquots of 1-6 mL of stock solution were taken into a series of 10 mL volumetric flask and volume was made up to the mark using phosphate buffer pH 6.8 and were analyzed at 225 nm using UV spectrophotometer. A standard curve was constructed against absorbance and concentration.[8]

Formulation and characterization of gelatin nanoparticles

Four batches of gelatin nanoparticles of venlafaxine were prepared using four different crosslinking agents and a fixed amount of gelatin (Table 1)

Table 1 Composition of different batches of gelatin nanoparticles

S.No.	Ingredient	Batch Code			
		F1	F2	F3	F4
1	Venlafaxine (mg)	10	10	10	10
2	Gelatin (g)	1	1	1	1
3	Glutaraldehyde (g)	1	-	-	-
4	PVP K30 (g)	-	0.5	-	-
5	PEG 2000 (g)	-	-	1	-
6	PEG 10000 (g)	-	-	-	1
7	Deionized water	qs	qs	qs	qs

Gelatin (1 g) was dissolved in deionized water (20 mL) with stirring under gentle heating at 60°C. Acetone (20 mL) was quickly added to the gelatin solution as a de-solvating agent to precipitate the high molecular weight Gelatin (one-step de-solvation method). The obtained precipitated gelatin was redissolved by adding 20 mL of water with the aid of gentle heating to 60°C, adjusting the pH of the solution to 7.0 with phosphoric acid. Thereafter, the crosslinking agent (glutaraldehyde/PVP/PEGs) was added while stirring and the stirring was continued for further 1 h. Venlafaxine was added at this point to the mixture while stirring and acetone (75 mL) was added drop-wise under stirring at 500-1000 rpm to form the venlafaxine loaded gelatin nanoparticle. The solution was cooled to about 0°C and centrifuged at 1200 rpm for about 20 min. The solution was rinsed with distilled water and lyophilized to obtain powder of gelatin nanoparticle (two-step de-solvation method).[9,10]

Determination of Yield

The lyophilized nanoparticles were collected and weighed accurately. The percentage yield was then calculated using formulae given below:

$$\% \text{ yield} = \frac{\text{Mass of the lyophilized nanoparticles} * 100}{\text{Total weight of drug and polymer}}$$

Determination of particle size

The particle size of each formulation batch was determined using a laser diffraction particle size analyzer.

Determination of drug entrapment in the nanoparticles

The various formulations of the nanoparticles were subjected to drug content analysis. 50 mg of the microspheres of each batch were accurately and dispersed in 10 mL methanol and sonicated at 125 Watts power for 2 min. The suspension was then centrifuged at 6000 rpm for 2 min. The supernatant was diluted appropriately in water and analyzed using UV visible spectrophotometer at 225 nm. The percentage drug entrapment was calculated as follows:

$$\% \text{ Drug Entrapment} = \frac{\text{Calculated Drug Concentration}}{} * 100$$

In vitro release study

USP type II dissolution apparatus (paddle type) was performed at 50 rpm in 900 mL phosphate buffer pH 6.8, maintained at 37 ± 0.5°C. 50 mg of nanoparticles were placed in the dissolution vessel for studying the rate and extent and dissolution. 5 mL of the sample was withdrawn at a

predetermined interval and the volume of dissolution medium was maintained by adding equal volume of fresh dissolution medium. The absorption of the withdrawn sample was measured spectrophotometrically (225 nm) with suitable dilution and the corresponding concentration was determined from the calibration curve. The percentage of drug released at various time intervals was calculated and plotted against time.

Formulation of Transdermal Patches

Preparation of backing membrane

A weighed amount of PVA (2.5% w/v) was added to 100 mL of warm distilled water and a homogenous solution was made by constant stirring and intermittent heating at 60°C for a few seconds and poured into glass molds already wrapped with aluminum foil around open ends and were kept for drying at 60°C for 6 h, forming a smooth, uniform, and transparent backing membrane.[11]

Preparation of patches

The optimization of the polymer concentration for formulation of patch was done by using factorial approach to develop various patches and obtain the best polymer combination for patch with sustained release. The concentration of the polymers (HPMC, Eudragit) was varied at two different levels. The formulation table used for optimization of patch is presented in Table 2.

Table 2. Formulation table for optimizing transdermal patches

Ingredients	Venlafaxine nanoparticle	HPMC (mg)	Eudragit (mg)	Glycerine (%w/w)	Piperine (%w/w)
P1	113	750	500	40	10
P2	113	500	500	40	10
P3	113	750	250	40	10
P4	113	500	250	40	10

Venlafaxine nanoparticle loaded transdermal patches were formulated utilizing the solvent casting method. Polymers were accurately weighed and dissolved in 10 mL of chloroform-methanol (1:1) solution, stirrer for 30 min on a magnetic stirrer and kept aside to form clear solution. Venlafaxine nanoparticles was accurately weighed[12] and was dissolved in the above solution and mixed until clear solution was obtained. Glycerine (40% w/w of total polymer) was added to be used as plasticizer and piperine (10% w/w of total polymer) was added as the permeation enhancer. The resulted uniform solution was cast on the petri dish containing the backing membrane, which was lubricated with glycerin and dried at room temperature for 24 h. An inverted funnel was placed

over the petridish to prevent fast evaporation of the solvent. After 24 h, the dried patches were taken out and stored in a desiccator for further studies. The backing membrane with the patch was attached to suitable adhesive tape.[13]

Evaluation of Transdermal Patches[14]

Physical appearance

The formulated patches were evaluated for homogeneity, transparency, clarity, color, and smoothness.

Uniformity of weight test

The patches were subjected to mass variation by individually weighing each formulated patch and checking the weight of patch against the average weight of the formulated patches. Measurement of patch weight was carried out using a calibrated analytical balance. The determination was carried out for each formulation in triplicate.

Thickness

The thickness of each patch was measured by the use of vernier caliper at six different positions of the patch and the average was calculated.

Surface pH

The surface pH of the transdermal patches was measured using a calibrated pH meter. In a test tube, 1 mL of distilled water and a 1 cm^2 portion of transdermal patch was kept at room temperature (25 ± 2°C) for 2 h. The water from the test tube was decanted and the wet patch was used for surface pH analysis. The pH electrode was placed at three different places at the swollen part of the patch for calculating the average pH.

Folding endurance

Folding endurance was determined by repeatedly folding one patch from the same place till it cracked or broke. The number of times the film could be folded from the same place without breaking/ cracking represented the value of folding endurance.

Drug content

Three pieces of 4 cm^2 were collected by cutting off zones from different parts of patch from each patch. These pieces were dissolved in 10 ml methanol and were placed on vortex shaker for 1 h to dissolve completely the patches. The resultant solutions were filtered through the whatman paper and then 0.1 mL solution was withdrawn into another volumetric flask (10 mL) and dilution was made up to 10 mL with phosphate buffer pH 6.8. The absorbance of this solution was observed at 225 nm using UV-Visible spectrophotometer and the drug content was calculated.

In-vitro release study

In-vitro permeation studies of the transdermal patches were carried out by using Franz diffusion cell with a receptor compartment capacity of 30 ml. The formulated patch of surface area of 4 cm^2 was placed in between the dialysis membrane and the donor compartment and then dialysis membrane was mounted between the donor and receptor compartment of diffusion cell. The receptor compartment of diffusion cell was filled with phosphate buffer saline pH 6.8. The whole assembly was fixed on a magnetic stirrer and the solution in the receptor compartment was constantly and continuously stirred magnetic beads at 50 rpm; the temperature was maintained at 37±0.5ºC. The 1 ml aliquots were withdrawal at different time intervals (0, 2, 4, 6, 8, 12 and 24 h) and analyzed the drug content by UV at 225 nm by appropriated dilution with methanol. The receptor phase was replenished with an equal volume of phosphate buffer (37ºC) at each sample withdrawal, the cumulative amount of drug released was plotted against time.

Results and Discussion

Venlafaxine was white, odorless, crystalline powder with a melting temperature of 217-218°C. It was soluble in water, ethanol, methanol and chloroform and had a partition coefficient of 0.264. A linear calibration curve in the range of 10-50µg/mL was obtained with a regression coefficient of 0.9979 (Figure 1).

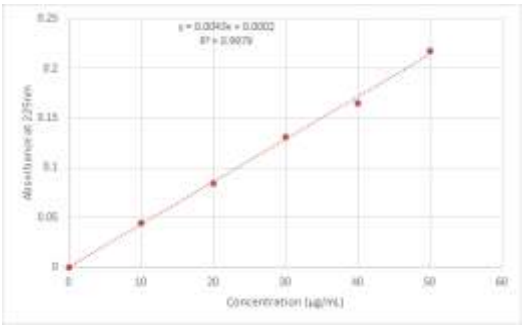

Figure 1. Calibration curve of venlafaxine

Evaluation of venlafaxine nanoparticles

Particle Size

The particle size of various formulations was determined Malvern particle size analyzer (Table 3). The particles size was widely influenced by the choice of the cross-linking agent. It was observed that the smallest particles were obtained from the use of glutaraldehyde. The order of the particle size was glutaraldehyde < PVP < PEG2000 < PEG 10000.

Table 3. Various characters of the nanoparticles

Formulation	Average Particle Size (nm)	Percent Yield (%)	Drug entrapment (%)
F1	217.2	77.3	61.6
F2	363.8	73.6	61.2
F3	643.2	78.9	47.5
F4	688.7	77.4	46.2

Percentage Yield of nanoparticles

The various formulations of the prepared nanoparticles were evaluated for the percentage process yield. The percentage yield ranged between 70-80% (Table 3). The yield of the nanoparticles was also affected by the choice of the crosslinking agent suggesting glutaraldehyde and PEG 2000 to be better cross linkers in comparison to the PVP used in the study.

Determination of entrapment of drug

The drug entrapment of various formulations of venlafaxine was carried out as per the procedure. The drug entrapment efficiencies of different formulations were in the range of 46-62 %. Glutaraldehyde and PVP were able to entrap the drug in efficient amounts owing to their good crosslinking capabilities. On the other hand, the PEGs used in the study exhibited poor entrapment of venlafaxine.

***In vitro* drug release study**

The *in vitro* drug release study of the nanoparticles was evaluated in phosphate buffer pH 6.8. The % release, % cumulative drug release calculated and the cumulative release data was subjected to kinetic modeling studies. From the release data it could be inferred that only glutaraldehyde and PVP were able to sustain the relesae of venlafaxine for upto 24 h and 12 h respectively whereas PEG 2000 and PEG 10000 formualations released drug within 8 and 6 h of the study respectivley (Figure 2).

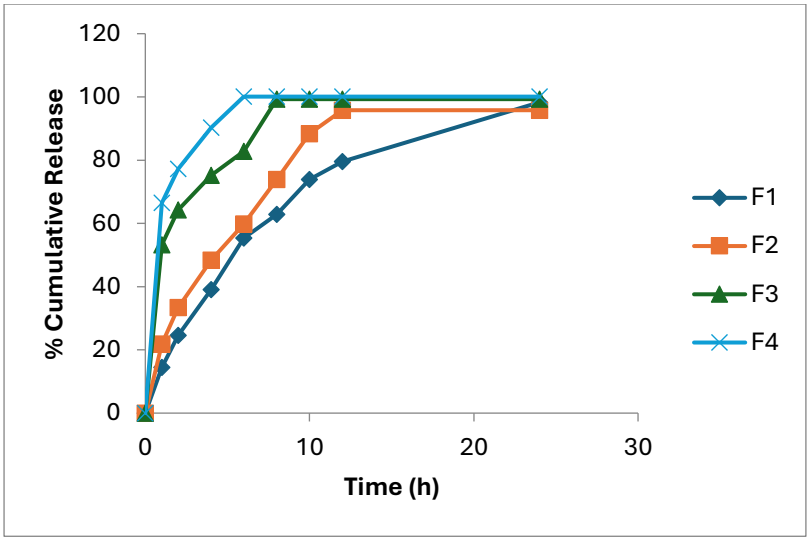

Figure 2. *In vitro* release of venlafaxine from nanoparticles

F1 with lowest particle size, highest entrapment efficiency and maximum sustained release of drug was used for formulation of transdermal patches.

Evaluation of transdermal patch

Physicochemical features

Transdermal patches containing venlafaxine nanoparticles were prepared using Hydroxy propyl methyl cellulose (HPMC) and Eudragit using PVA 2.5%w/v as the backing membrane. The elasticity of the patches was attained using glycerine (40% polymeric weight) as the plasticizer and piperine (10% polymer weight) was used as the permeation enhancer to assist permeation of drug into the dermis. Solvent casting method is the most widely used and the simplest method for formulation of transdermal patches. The use of inverted funnel allowed for the controlled evaporation of the solvents from the patch.

The evaluation of the patches was done for various physical parameters as per procedure and the results are reported in Table 4.

All the prepared patches were subjected to visual inspection for examining the physical appearance. The physical appearance of the patches gave satisfactory results. All the prepared patches were found to be smooth, non-sticky, opaque, homogeneous, and flexible in nature.

Table 4. Characterization of nanoparticle loaded transdermal patches

	Thickness (mm)	Average weight (mg)	Drug content (%)	Folding Endurance	Surface pH
P1	0.514 ± 0.0011	318.67 ± 2.082	94.47 ± 0.289	272 ± 3.055	5.32 ± 0.006
P2	0.540 ± 0.0017	341.67 ± 1.155	95.37 ± 0.451	253 ± 3.512	5.35 ± 0.012

P3	0.533 ± 0.004	370.33 ± 1.526	96.20 ± 0.300	269 ± 4.726	5.60 ± 0.012
P4	0.548 ± 0.0021	381.67 ± 1.155	95.53 ± 0.252	261 ± 2.646	5.56 ± 0.017

In vitro release from transdermal patch

The amount of drug that released from the transdermal patches was determined using Franz diffusion cell. The *in vitro* drug release study depicted that the highest amount of drug was released from **P4** (87.33 ± 0.551 %) while the lowest was released from **P1** (62.2 ± 0.964 %) at the end of 24 hours of release study. Faster drug release was observed from formulated patches containing lower amounts of the Eudragit and HPMC (Figure 3).

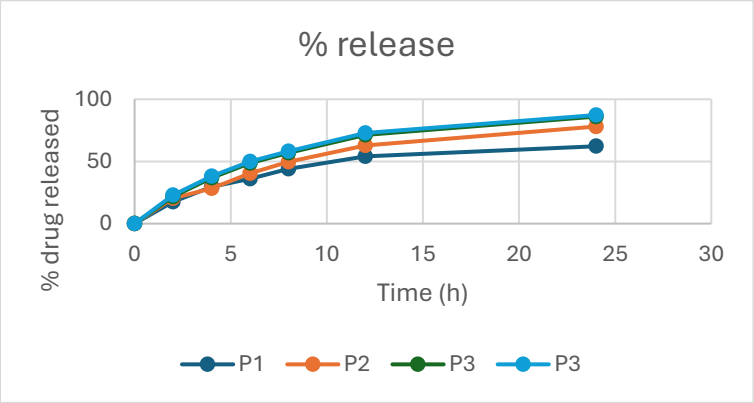

Figure 3. % release of venlafaxine from nanoparticle loaded transdermal patches

Conclusion

In conclusion, the present work successfully demonstrated the formulation and evaluation of a nanoparticle-loaded mucoadhesive transdermal delivery system for venlafaxine. Nanoparticles prepared using glutaraldehyde as a cross-linking agent showed the most favorable characteristics, including the smallest particle size, highest entrapment efficiency, and sustained drug release for up to 24 hours.

The transdermal patches prepared with venlafaxine nanoparticles exhibited desirable physicochemical properties such as uniform thickness, high drug content, appropriate surface pH, and good mechanical strength. In vitro release studies revealed that drug release was influenced by polymer composition, with Carbopol-rich formulations showing faster release. Among the patches, BP3 demonstrated the highest drug release (87.33% at 24 hours), indicating its potential for sustained therapeutic action and improved patient compliance.

Overall, the study highlights that nanoparticle-loaded transdermal patches can effectively overcome the limitations of conventional oral delivery of venlafaxine, such as low bioavailability and extensive first-pass metabolism. The optimized formulation not only ensures controlled and prolonged drug release but also enhances patient convenience. This approach offers a promising alternative for the systemic delivery of venlafaxine and may serve as a platform for developing transdermal delivery systems of other drugs with similar pharmacokinetic challenges. assessment, and targeted delivery strategies to translate these findings into clinical and industrial applications.

References

1. https://go.drugbank.com/drugs/DB00285; assessed on 19/04/2026
2. https://pubchem.ncbi.nlm.nih.gov/compound/Venlafaxine; assessed on 19/04/2026
3. Pastore MN, Kalia YN, Horstmann M, Roberts MS. Transdermal patches: history, development and pharmacology. British Journal of pharmacology. 2015; 172: 2179-2209
4. Ghodke SD, Kalamkar VM, Musmade SR, Jori DK, Chaudhari ML. Formulation and evaluation of transdermal patch for pain management. Int J Creative Res Thoughts. 2025;13(5):837-846.
5. Karnakoti A, Borade A, Birajdar P, Bodke V, Dagale M, Badekar R. Formulation and evaluation of transdermal patch. Int J Sci Res Technol. 2025;2(2):77-86.
6. Khare R, Tripathi D, Lal M, Kondalkar A. Formulation and evaluation of transdermal patches of etodolac for topical application. Journal of Pharmaology and Biomedicine. 2022; 7(2): 589-597
7. KB, Hoff DJ, Lahren TJ, Mount DR, Squillace AJ, Burkhard LP. Estimating n-octanol-water partition coefficients for neutral highly hydrophobic chemicals using measured n-butanol-water partition coefficients. Chemosphere. 2019; 218: 616-623.
8. Sowmya C, Reddy YP, Kiran Kumar M, Santhosh Raja M. Development and validation of spectrophotometric method for the estimation of venlafaxine in bulk and formulations. International Journal of Chemical Sciences. 2011; 9(1): 52-58
9. Elzoghby AO. Gelatin-based nanoparticles as drug and gene delivery systems: Reviewing three decades of research. Journal of controlled release, 2013; 172: 1075-1091.
10. Sailaja KA, Amareshwar P, Chakravarty P. Different techniques used for the preparation of nanoparticles using natural polymers and their application. International Journal of Pharmacy and Pharmaceutical Sciences. 2011;3(2): 45-50.
11. Trivedi D, Goyal A. Formulation and evaluation of transdermal patches containing dexketoprofen trometamol. International Journal of Pharmaceutical Chemistry and Analysis. 2020;7(2): 87–97
12. Gupta A, Mehta P. Formulation and evaluation of transdermal patches of Lamotrigine. Journal of Pharmacology and Biomedicine. 2021; 5(1): 242-248
13. Sheth NS, Mistry RB. Formulation and evaluation of transdermal patches and to study permeation enhancement effect of eugenol. J. Appl. Pharm. Sci. 2011; 1 (3); 96-101
14. Mutalic S, Udupa N. Glibenclamide transdermal patches: physicochemical, pharmacodynamic, and pharmacokinetic evaluations. Journal of Pharmaceutical Sciences 2004; 93: 1577-1594.