Formulation Evaluation and Optimization of Proniosome Based Transdermal Patches of Ketorolac

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Abstract
Proniosomes are dry detailing of water-solvent bearer particles that are covered with surfactant and can be apportioned as required and dried out to frame niosomal scattering promptly before use on brief disturbance in hot fluid media inside of minutes. They have potential applications in the conveyance of hydrophobic and hydrophilic medications. Diverse clusters of proniosomes of Ketorolac tromethamine were readied by coacervation stage detachment strategy with distinctive proportions of polymers and surfactants. The physicochemical similarity of the medication and the polymers was considered by FTIR and DSC. The outcomes acquired demonstrated no physical-compound incongruently between the medication and the polymers. The readied frameworks were portrayed for embodiment effectiveness, shape, size and in vitro medication discharge. Release study was completed to research the draining of medication from the proniosomal framework amid capacity. On the premise of results acquired the gel KP 4 was upgraded and further utilized for the creation of transdermal patches with a backing layer (4% PVA) and a suitable rate controlling film. Distinctive rate controlling layers were readied with Eudragit RS-100 (ERS), Eudragit RL-100 (ERL) by mercury substrate method. The formulations were created and subjected to different physicochemical assessments and in vitro study. The patch manufactured with ERS (KTP 1) as rate controlling film was advanced as the best fix and further assessed for in vivo pervasion in rats. Investigation was completed to guarantee the connection between the in vitro and in vivo discharge design. The study exhibited that proniosomal transdermal patch in view of the ERS layer controlled discharge framework has the potential to deliver ketorolac tromethamine.

1 Introduction
Ordinary medication conveyance frameworks are known not a brief arrival of medication, to accomplish and additionally to keep up the medication fixation inside the restoratively successful extent required for treatment, it is regularly important to take this sort of medication conveyance framework a few times each day. These outcomes in a critical vacillation in medication levels, furthermore has a noteworthy downside like poor bioavailability because of hepatic digestion system (first pass)1. But late specialized progressions have brought about new procedures for medication conveyance, which will enhance the restorative viability and security of medications by more exact (i.e. site particular), spatial and worldly arrangement inside of the body consequently decreasing both the size and number of doses2. Colloidal particulate transporters, for example, liposomes or niosomes has been broadly utilized in medication conveyance frameworks and delivering them from proniosomes gives an unmistakable point of interest. These transporters can go about as medication repositories and change of their arrangement or surface can confirm the medication discharge rate and/or the proclivity for the objective site. Proniosomes offers an adaptable vesicle drug conveyance idea with potential for conveyance of medications by means of transdermal course3, 4.
Transdermal course of medication conveyance has numerous focal points as it dodges first-pass gut and hepatic digestion system and diminished symptoms and relative simplicity of the medication info end in hazardous cases. The vesicular medication conveyance is gainful as vesicles tend to circuit and stick to the cell surface. This is accepted to expand the thermodynamic movement angle of the medication at vesicle-stratum corneum interface hence prompting improved saturation rate.

Ketorolac (KT), a powerful pain relieving with moderate mitigating movement with antipyretic properties, used to treat osteoarthritis and control intense agony. It is directed by intramuscular and oral course in isolated numerous measurements for transient administration of post-agent pain. This incessant dosing is because of the short half-existence of medication, which brings about inadmissible patient consistence. Transdermal conveyance unquestionably gives off an impression of being an alluring course of organization to keep up the medication blood levels of KT for a developed timeframe. In this work, an endeavor was made to give proniosome based transdermal medication conveyance of KT.

2 Materials and Methods

2.1 Materials

Ketorolac Tromethamine was provided as gift sample by Ranbaxy Labs Limited, Goa, India. Eudragit was purchased from Evonik Degussa, Mumbai, India. Ethanol was procured from Poly Pharma Laboratories, Gujarat. Ethyl cellulose was purchased from High purityLab Chemicals, Mumbai. All other chemicals and reagents used were of laboratory or analytical grade.

2.2 Methods

2.2.1 Preformulation studies

2.2.1.1 Melting point determination

Melting point of the drug was determined by taking small amount of drug in a capillary tube closed at one end and placed in a melting point apparatus and the temperature at which the drug melts was recorded. The experiment was performed in triplicate, and average value was noted.

2.2.1.2 UV spectroscopy

Ketorolac was accurately weighed and dissolved in distilled water to a concentration 1 mg/ml. This solution was then suitably diluted to 100 ml using distilled water to a final solution of concentration 100 μg/ml. UV spectrum was recorded in the wavelength range 200-400 nm.

2.2.1.3 Determination of solubility of Ketorolac

Excess drug (50 mg) was added to 15 ml of each fluid taken in a 25 ml stoppered conical flask, and the mixtures were shaken for 24 h at room temperature (28±1°C) on Rotary Flask Shaker. After 24 h of shaking, 2 ml aliquots were withdrawn at 2 h interval and filtered immediately using a 0.45 μ disk filter. The filtered samples were diluted suitably and assayed for Ketorolac by measuring absorbance at 322 nm. Shaking was continued until two consecutive estimations are the same. The solubility experiments were replicated for four times each (n=4).

2.2.1.4 Determination of Partition coefficient

30 ml of water and 30 ml of n-octanol solution was taken in the separating funnel. 100 mg of Ketorolac was added and shaken for 1 h. 1 ml of aqueous layer was removed and transferred into a 100 ml standard flask and made up to the mark with water. The absorbance was measured at 322 nm by using water as the blank.

2.2.1.5 Drug lipid compatibility studies

Prior to formulation, to study the physical and chemical compatibilities of the drug with the lipids (Cholesterol and Lecithin) the following studies were conducted on the drug and lipid in the ratio 1:1. The physical mixtures were stored for 7 days at 50 °C before study. FTIR spectra of the mixture of drug and lipid were compared with the spectra of individual components.

The DSC thermogram of the physical mixture of drug and lipid (1:1 ratio) was obtained and compared with that of pure drug. 5 mg Samples were accurately weighed, sealed in an aluminium pan of 40 μL capacity and equilibrated at 25 °C, subjected to the DSC run over the temperature range of 25 to 200°C at the heating rate of 5 °C/min.

2.2.2 Formulation development of Ketorolac proniosomes

Proniosomes were prepared using coacervation phase separation method. Using a wide-mouth glass tube, 100 mg of Ketorolac with surfactant (span 60 or tween 80), lecithin, and cholesterol were mixed with 2.5 ml of absolute ethanol. The open end of the glass tube was covered with a lid and the tube was warmed in a water bath at 65± 8°C for 5 min. 1.6 ml of PBS was added, and the mixture was further warmed in the water bath for about 2 min so that a clear solution was obtained. The mixture was allowed to cool to room temperature until the dispersion was converted to proniosomal gel. Table 1 explains the formulation of Ketorolac proniosomes.

2.2.2.1 Evaluation of Proniosomes

2.2.2.1.1 Measurement of Proniosomal gel pH and viscosity

The pH of the gel was measured using pH meter before and after incorporation of the drug. Viscosity of the gel was determined using a Brook field viscometer.

2.2.2.1.2 Determination of encapsulation efficiency

0.2 g of proniosome gel was weighed in a glass tube; 10 ml of pH 7.4 phosphate buffer (to convert to niosomal dispersion) was added. The
aqueous suspension was sonicated in a sonicator bath. The Ketorolac containing niosomes was separated from untrapped drug by centrifugation at 25,000 rpm at 20 °C for 30 min. The supernatant was recovered and assayed spectrophotometrically at 322 nm.

The percentage of drug encapsulation (EP %) was calculated by the following equation:

\[
EP(\%) = \left( \frac{C_t - C_r}{C_t} \right) \times 100\%
\]

Where

- \(C_t\) is the concentration of total Ketorolac
- \(C_r\) is the concentration of free Ketorolac

Table 1: Preparation of proniosomal formulation

<table>
<thead>
<tr>
<th>Proniosomal code</th>
<th>Drug</th>
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<th>Tween 80</th>
<th>Lecithin</th>
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</table>

2.2.2.1.3 Optical microscopy and vesicle size determination

A drop of niosomal dispersion prepared from proniosomes was spread on a glass slide and examined for the vesicle structure and presence of insoluble drug crystals under the light microscope with varied magnification.

The proniosomal gel (100 mg) was hydrated with PBS (10 ml) in a small test tube by manual shaking for 5 min and the resulting niosomes were observed under an optical microscope at 100 X magnification. The average size of 100 vesicles was measured using calibrated ocular and stage micrometer in the microscope.

2.2.2.1.4 In vitro release study

In vitro diffusion study of proniosomal gel was performed in Franz diffusion cell that has a receptor compartment with an effective volume, approximately 25 ml and an effective surface area of permeation of 3.14 sq cms. The egg membrane or cellulose membrane was mounted between the donor and receptor compartment. A weighed amount of proniosomal gel was placed on one side of the skin, and the receptor medium was phosphate buffer pH 7.4. The receptor compartment was surrounded by a water jacket to maintain the temperature at 37±0.5 °C. Heat was provided using a thermostatic hot plate with a magnetic stirrer. The receptor fluid was stirred by a teflon coated magnetic bead fitted to a magnetic stirrer. At each sampling interval, sample was withdrawn and replaced by equal volume of fresh receptor fluid. Samples were analyzed spectrophotometrically at 322 nm.

2.2.2.1.5 Stability studies

The stability studies were conducted according to ICH guidelines. The stability of vesicles to retain the drug was assessed by keeping the proniosomal gel at different temperature conditions like refrigeration temperature (4-8 °C), room temperature (25±2 °C) in aluminum foil sealed glass vials. The samples were withdrawn at different time intervals over a period of one month. They were observed visually and under the optical microscope for the change in consistency and appearance of drug crystals upon storage point and drug leakage from the formulations by analyzing drug content.

2.2.2.1.6 Optimization of prepared proniosomes

Optimization of proniosomes was done based on the evaluated parameters such as particle size, %EE, drug release profile and stability study. One of the criteria in optimizing proniosome was a drug release, i.e., the proniosomes with high cumulative drug release will be selected as the best batch.

2.2.3 Formulation and evaluation of transdermal patches by using optimized ketorolac proniosomal gel

2.2.3.1 Development of membrane controlled transdermal systems

2.2.3.1.1 Backing Layer

4 gm of Poly vinyl alcohol was dissolved in 100 ml water, and the solution was poured on to the mercury surface and dried at 60°C for 6 h.

2.2.3.1.2 Rate Controlling Membrane

ERL and ERS rate controlling membranes were prepared by dissolving 300 mg of respective polymers in 5 ml solvent (Chloroform). Di-n-Butyl phthalate (30% w/w of polymer) was used as the plasticizer to optimize the best rate controlling membrane with flexibility, elegance, uniformity, etc.
2.2.3.1.3 Fabrication of Pronosome drug reservoir

2×3 cm backing membrane was cut out; three edges of the backing layer were then sealed with the edges of rate controlling membrane using adhesive tape. The weighed quantity (1 g) of gel was transferred into the reservoir patch. After filling, the unsealed edge was sealed using adhesive tape. The obtained reservoir patch was then pasted to an adhesive plaster (The backing layer should face to the plaster). A release liner was placed over the adhesive coated rate controlling membrane.

2.2.4 Evaluation of patches

2.2.4.1 Percentage of moisture content

The films were weighed individually and stored in desiccator containing activated silica at room temperature for 24 h. Individual films were weighed repeatedly until they showed a constant weight. The percentage of moisture content was calculated as the difference between initial and final weight with respect to final weight.

2.2.4.2 Percentage moisture uptake

The films were weighed accurately and placed in the desiccators containing 100 mL of saturated solution of potassium chloride, which maintains 80-90% RH. After 3 days, the films were taken out and weighed. The study was performed at room temperature. The percentage moisture absorption was calculated using the formula:

\[ \text{% moisture absorption} = \frac{\text{Final weight} - \text{Initial weight}}{\text{Initial weight}} \times 100 \]

2.2.4.3 Mass Variation

The patches were subjected to mass variation by individually weighing 10 randomly selected patches.

2.2.4.4 In vitro drug release study23-26

In vitro drug diffusion study was carried out by using Franz diffusion cell. In this method pre hydrated cellophane was used as the model membrane. The membrane was placed between the donor compartment and the reservoir compartment (phosphate buffer pH7.4). The patch was placed on the membrane, and the compartments clamped together. The receptor compartment was filled with phosphate buffer pH 7.4 and hydrodynamics in the receptor compartment was maintained by stirring with a magnetic bead at 100 rpm. Samples were withdrawn and replaced with receptor medium and assayed spectrophotometrically at 322 nm and the amount of drugs released at various time intervals were calculated.

2.2.4.5 Optimization of Ketorolac patches

Optimization of the best patch was done based on the drug release profile i.e. the patch with the highest cumulative drug release in 24 h in a controlled manner and also based on other evaluated parameters such as moisture absorption, moisture loss and mass variation.

2.2.5 Curve fitting analysis

In order to understand the mechanism of drug release, in vitro drug release data were treated to kinetic models such as zero order, first order, Higuchi model and Korsemeyerpeppa's model.

2.2.5.1 Zero order kinetics

It describes the system where the drug release rate is independent of its concentration of the dissolved substance. A graph was plotted between time taken on x-axis and the cumulative percentage of drug release on y-axis, if the plot is linear then the data obeys zero-order kinetics. The equation for zero order release is

\[ Q_0 = Q + K_0 t \]

\[ Q_0, \text{initial amount of drug, } Q, \text{cumulative amount of drug release at time } t, K_0, \text{zero order release constant, } t=\text{time in hours.} \]

2.2.5.2 First order kinetics

A graph was plotted between the time taken on x-axis and the log cumulative percentage of drug remaining to be released on y-axis, if it yields a straight line, it indicates that the release follows first order kinetics. The constant ‘k’ can be obtained by multiplying 2.303 with the slope values. The first order release equation is

\[ \log Q_0 = \log Q + K_1 / 2.303 \]

\[ Q_0, \text{initial amount of drug, } Q, \text{cumulative amount of drug release at time } t, K_1, \text{first order release constant, } t=\text{time in hours.} \]

2.2.5.3 Higuchi model

The Higuchi equation suggests that the drug release mechanism is diffusion. A graph was plotted between the square root of time taken on x-axis and cumulative percentage of drug release on y-axis. If it yields a straight line, it indicates that the drug was released by diffusion mechanism. The slope is equal to ‘K’. The Higuchi release equation is

\[ Q = K H t^{1/2} \]

\[ Q, \text{cumulative amount of drug release at time } t, \text{ K, Higuchi constant, } t=\text{time in hours.} \]

2.2.5.4 Korsemeyerpeppa’s equation model

To the study the mechanism of drug release from the formulation, the released data were fitted to exponential equation which is often used to describe the drug release behavior from polymeric system.

\[ F = (M_0/M) = K_e t^n \]

\[ F=\text{fraction of drug released at time } t', M_0=\text{amount of drug released at time } t', M=\text{total amount of drug in dosage form, } K_e=\text{kinetic constant,} \]
Behin et al. Formulation evaluation and optimization of transdermal patches of Ketorolac overnight. The dorsal surface of the rat was clean shaved, and the optimized transdermal patch was fixed. Blood samples (200 µl) were drawn by retro-orbital plexus puncture with the aid of the capillary tube at 1, 2, 4, 6, 8, 12, 16, 20 and 24 h. The samples were collected in heparinized eppendorf tubes containing 3.8% trisodium citrate (100 µl) which acts as a complexing agent and centrifuged at 5000 rpm for 6 min, and collected the plasma and stored at -20°C until analysis (Fig-1).

Fig 1: Different stages of animal study (A-Shaved to remove the dorsal hair, 2- Adhered patch on dorsal skin, 3- Retro orbital blood collection)

The plasma samples were taken in a centrifuge tube containing equivalent quantity of 10M K₂CO₃, in order to precipitate the whole blood proteins, and centrifuged again at 5000 rpm for 6 min. 2 ml of ethyl acetate was added to the supernatant and centrifuged again at 5000 rpm for 5 min. The separated organic phase was transferred into clean glass tubes in order to evaporate from the organic solvent by keeping it inside a vacuum oven. After the organic phase was completely evaporated, about 300 µl of phosphate buffer pH 7.4 was added and centrifuged at 6000 rpm for 5 min. The supernatant solution was analyzed at 322 nm.

Institution Animal Ethics committee Approval Number: SDCP/IAEC-07/2011-12

3 Results and Discussions

3.1 Preformulation studies of ketorolac

3.1.1 Melting point determination
The melting point of unadulterated ketorolac tromethamine was resolved utilizing melting point contraption and was observed to be 163-167°C.

3.1.2 UV Spectroscopy
The λₘₐₓ of ketorolac was determined by using UV spectrophotometer. The λₘₐₓ was found out to be 322 nm, similar to the previous reported literature.

3.1.3 Determination of solubility of Ketorolac
Ketorolac was freely soluble in water & methanol, slightly soluble in tetrahydrofuran and insoluble in acetone & toluene.

3.1.4. Determination of partition coefficient
The partition coefficient was found to be 2.32.

3.1.5 Drug-Excipient compatibility studies

Infrared spectra of Ketorolac as well as its proniosome showed characteristic peaks at 1699 cm\(^{-1}\) (C=O stretch in acid), 3299 cm\(^{-1}\) (OH in acid), 3504 cm\(^{-1}\) (NH stretch), and 1646 cm\(^{-1}\) (diaryl ketone). There were no changes in the major peaks of Ketorolac in the presence of lecithin and cholesterol. So the drug and the excipients are compatible with each other. The FTIR and DSC results are shown in figure 2.4. DSC bend for the medication demonstrates an endothermic crest at 163 \(^\circ\)C identified with medication dissolving point. The nonattendance of a liquefying crest of the medication in the proniosomes was taken as a sign that the medication was entangled by the polymer. Similar result was reported by Nanda\(^27\) exhibiting the endothermic peak at 161.39°C.

![Fig 2: A) FTIR spectrum of pure Ketorolac tromethamine B) Ketorolac+cholesterol](image)

3.2 Evaluation of proniosomes

The formulations were studied for physical characteristics like colour and appearance, determination of viscosity and were found to be within the acceptable limits as indicated in table 2.

3.2.1 Colour and appearance

All the formulations had a yellowish brown to slight yellow colour and had semisolid consistency. The gel definitions displayed great spreadability and thickness.

3.2.2 Optical microscopy and vesicle size determination

The span of 100 particles was dictated by optical microscopy, and the particles uncovered unilamellar vesicles with no agglomeration or total. The mean particle size was in the range of 2.98 to 5.01 \(\mu\)m. The mean particle sizes of all the hydrated proniosomal formulations showed that the niosomes prepared with Tween 80 were significantly larger than those prepared with Span 60. The relationship saw between niosome size and Traverse hydrophobicity has been ascribed to the decline in surface vitality with expanding hydrophobicity, bringing about the little vesicles. This would likewise clarify the vast vesicle size of niosomes arranged with Tween which has a much lower hydrophobicity than spans. It was observed that the gel formulation showed good spreadability, and viscosity.

3.2.3 Determination of encapsulation efficiency

The encapsulation efficiency of the formulated proniosomes were determined and tabulated in table 2. The EE were determined for all proniosomal formulations stored at 4-8 \(^\circ\)C and 25\(\pm\)2 \(^\circ\)C, approximately 87\% of ketorolac was retained in all proniosomal formulations.
formulations after the one-month period. Thus, both Span 60 and Tween 80 based proniosomes of ketorolac seemed to exhibit good stability at low temperatures. The entrapment efficiency of our proniosomes ranged between 80-90\% compared to the 40-70\% reported by Mishra for proniosomes of Naproxen.

3.2.4 In vitro release study

The in vitro releases from ketorolac proniosomes were investigated by using Franz diffusion cell. The percentage of the drug released after 24 h from the proniosomal vesicles are shown in table 3. In vitro diffusion studies of proniosomal transdermal gel studies showed the cumulative percentage permeation 79.66\%, 82.02\%, 87.01\%, 91.73\%, 70.56\%, 74.65\%, 67.03\%, 77.84\% in 24 h from the formulations KP I, KP 2, KP 3, KP 4, KP 5, KP 6, KP7 and KP8 respectively.

3.2.5 Stability studies

Physical stability of proniosomal formulations were studied for a period of one month. The EE were determined (table 4) for all proniosomal formulations stored at 4-8 °C and 25±2°C, which indicates insignificant decrease in EE of proniosomes stored at 4-8 °C. Thus, both tween 80 and Span 60 proniosomes of ketorolac seemed to exhibit good stability. The result is similar to proniosomal transdermal system of granisetron hydrochloride stable at 4-8°C, reported by Patil.

3.2.6 Optimization of Pronosome Gel

KP4 was optimized by considering particle size (2.98±0.45), % EE (93.53), % CDR (91.73) and stability. Therefore KP 4 was selected for fabricating transdermal patches.

3.3 Evaluation of transdermal patches of ketorolac

Two formulations of Ketorolac transdermal patches were formulated using KP 4 as optimized proniosome gel and ERL & ERS as rate controlling membranes. The prepared transdermal patches were transparent, smooth, and uniform.

3.3.1 Percentage moisture content

The percentage moisture content was found to be 5.13\% and 6.96\% for KTP1 and KTP2 respectively. The lowest percentage moisture loss was found in patches fabricated with ERS as rate controlling membrane.
3.3.2 Percentage moisture uptake

The percentage moisture uptake was found as 1.76% and 2.48% for KTP 1 and KTP 2 respectively. The lowest percentage moisture uptake was found in patches fabricated with ERS as rate controlling membrane.

3.3.3 Mass variation

The mass was found to be uniform in the prepared batches and varied from 0.063%±0.07 mg to 0.068%±0.09.

3.3.4 In vitro study

Table 5 explains the % CDR of patches after 24 h. KPT1 was the best with 88% drug release compared to 82% of KPT2.

3.3.5 Optimization of best patch

Out of two formulations KTP 1 (ERS as RC membrane) exhibited good mechanical properties and release pattern. Hence KTP 1 had been optimized as the best patch.

3.4 Curve fitting analysis

In this study, two formulations released variable amounts of ketorolac through semi permeable membrane in the in vitro fluid. To examine the drug permeation kinetics and mechanism, the data of KTP 1 were fitted to models representing zero-order, first-order, Higuchi and Korsemeyer-Peppas. The graphs are shown in figure 5 and 6.

### Table 2: characterization of ketorolac proniosomal gel

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<tr>
<th>Formulation code</th>
<th>pH</th>
<th>Viscosity</th>
<th>Vesicle size in µm</th>
<th>Encapsulation efficiency (%)</th>
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Results are mean±SD (n=3)

3.4.1 Zero order kinetics of KTP 1

It was found that 88.91% of drug was released within 24 h from KTP-1 (ERS as rate-controlling membrane) and 82.323% of drug released from KTP2 after 24h. A higher drug release pattern was exhibited by KTP 1 at each time intervals. This release is optimum and significant and followed zero-order kinetics (By Zero order plot). The zero-order plot of KTP 1 was found to be fairly linear and had high regression values. Therefore, the drug permeation from this formulation could follow zero-order kinetics.

3.4.2 First order kinetics of KTP 1

The log % CDR at 24 h was 1.948951 %

3.4.3 Higuchi model

By plotting Higuchi’s plot, it was found that the release obeys diffusion mechanism. The square root time of 88.91% CDR was 4.898979

3.4.4 Korsemeyerpeppa’s model

Hence, to confirm the exact mechanism of drug permeation from these patches, the data were fitted according to the Korsmeyer-Peppas model indicated by R² value closer to 1(0.98) and the n<1.0 confirmed that the drug permeation from transdermal patches followed diffusion and Non-Fickian transport. The log time was 1.380211 and the log % CDR was 1.948951
**Table 3: % CDR of proniosomes of KP₁ - KP₈**

<table>
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<tr>
<th>S.no</th>
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**Fig 5:** Graph indicating A) Zero order kinetics B) First order kinetics of KPT₁

**Fig 6:** Graph indicating A) Higuchi Model B) Korsmeyerpeppa’s model
Table 4: Entrapment efficiency of formulations in various temperatures after 1 month

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<th>Formulations</th>
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3.5 In vivo Study

KTP 1 (with ERS rate controlling membrane) exhibited good mechanical properties and optimum release after in vitro release study. So the bioavailability study was conducted with KTP 1 in 6 Male wistar rats. Blood samples were analyzed UV spectrophotometrically at 322 nm. Table 6 explains the % CDR of samples 1-6 after 24 h. The in vitro and in vivo correlation of formulation KTP1 after 24 h is shown in figure 7.

The system shows 78.66% of drug release in in vivo method and then to determine the correlation between the in vitro data the release pattern analysis was carried out, which revealed that they were well related and followed zero order release in a biological system also.

Table 5: % CDR of Formulated patches after 24 hrs

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4 Conclusions

Ketorolac (KT), presently controlled by intramuscular and oral course in partitioned various measurements for transient administration of post-agent agony makes inadmissible patient consistence. So in this work an endeavor was made to give proniosome based transdermal medication conveyance. Ketorolac was effectively ensnared inside of the lipid bilayers of the vesicles with high effectiveness and displays noteworthy in vitro discharge example and great steadiness too. The detailing having best attributes was chosen to manufacture transdermal patch utilizing ERS and ERL as RC films.

The patch with ERS as RC film demonstrated great mechanical properties and ideal medication discharge pattern. The active information investigation uncovered that the defined TDDS takes after zero request discharge energy. Higuchi’s plot for the plan demonstrated that the overwhelming component of medication discharge is dispersion, and the information were fitted by Korsmeyer-Peppas model showed that the medication penetration from transdermal patches took after dissemination transport. The in vivo discharge example indicated the relationship with the in vitro discharge design. The above result prompts the decision that proniosomes are a promising bearer for ketorolac.
Table 6: %CDR of sample 1-6 after 24 hrs

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Fig 7: Graph indicating *in vitro* and *in vivo* correlation of KTP 1 after 24 hrs

5 Acknowledgements

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6 Conflicts of interests

The authors declare that they have no competing interests.

7 Authors contributions

BS and PIS carried out literature review and preparation of the manuscript. Vidya participated in the collection of data. All authors read and approved the final manuscript.

8 References


