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Original Research Article

Pharmaceutics for enhanced drug delivery

Invitro Evaluation Of Transdermal Patch For Edivoxetine Hydrochloride

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Abstract: The aim of this study was to create a transdermal patch of Edivoxetine hydrochloride which has an appreciable mechanical properties. The transdermal patches were prepared using solvent casting method . Various groups of patches with medication were prepared using diverse inclusion of polymers, for example, HPMC (different grades)), Polyox303, Eudragit RL 100.Considering solubility of drug and polymer, the solvent system of water: ethanol was chosen. *Invitro* release of drug substance was performed using phosphate buffer (PBS) pH 7.4. Compatibility of drug with various excipients (drug: excipient in the proportion 1:1) was studied using Fourier Transform Infra-Red Spectroscopy (FTIR). Assessment test, weight variation, content uniformity, drug content, collapsing perseverance, thickness, invitro disintegration and invitro crumbling were completed. The folding endurance of all batches found less than 500 times . The rates of medication dispersion was found between 72 and 100%.The formulation F4 containing a combination of HPMC and Eudragit showed maximum drug release of 94.23%. The method employed to prepare patches was capable of producing patches with almost uniform drug distribution. Stability studies were conducted as per ICH guidlines (40±2?C at 75±5% RH) for optimized formulations and was found to be stable.

Keywords: Edivoxetine hydrochloride, Transdermal Patch HPMC, Polyox303, Eudragit RL 100

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1. INTRODUCTION

Transdermal drug delivery system (TDDS) is one of the drug delivery under the class of controlled medication in which to the drug has to traverse the medication through skin in a foreordained and controlled rate. TDDS are glue sedate containing devices of characterized surface zone that convey a foreordained measure of medication to the outside of unblemished skin at a customized rate to arrive at the foundational dissemination[1,2] . The epic medication conveyance framework will be helpful for improving the solvability, steadiness and organic existence of the medications. The robustness of the strip relies upon the sort of polymer utilized in the formulation[3.] Medications which are inclined to significant first pass digestion or debased in acidic condition of stomach are inadequately assimilated from the GIT or transdermal course is utilized when the treatment requests fast beginning of activity[4.]The exact system by which Edivoxetine produces its restorative impacts in Attention-Deficit/Hyperactivity Disorder (ADHD) is obscure, however it is believed to be identified with specific hindrance of the presynaptic norepinephrine transporter, as decided in ex vivo take-up and synapse consumption considers. The medication is utilized for the treatment of Attention deficiency hyperactivity issue (ADHD) and also in antidepressant. Attention-deficit/hyperactivity disorder (ADHD) is a common psychological diagnosis in children. It belongs to BCS class 1, and it experiences first pass digestion. EdivoxetineHCl seems to have negligible proclivity for other noradrenergic receptors.And drug is quickly retained after oral administrationso the medication is delievered via transdermal formulation. [5,6] The objective of this work was to prepare a transdermal patch of Edivoxetine HCl which has good mechanical properties and to evaluate the patch for its appearance, weight consistency, drug content, drug release , elasticity, collapsing continuance, thickness and stability[7].

2. MATERIAL AND METHODS[6-10]

Edivoxetine hydrochloride was acquired from Ra ChemPharma ltd, and all the excipients from Asian Scientifics Hyderabad

2.1 Preparation of medicated films[6]

The polymer was broken down in 15ml methanol and water in receptacle A. In B measuring glass , 15ml ethanol, water, polyethylene glycol 450 was dissolved. And in a vial propylene glycol was taken and the drug is dissolved using ultrasonicator. Mix solution A into B and to this solution in vial is added with the help of mechanical stirrer for 2-4 hrs.

2.2 Planning of non-sticky petri plate

The silicon emulsion was used to prepare the non- sticky petri plates of diameter of 9.6 cm for casting of plates. Initially, the silicon emulsion was poured and spread to have uniform surface. The plates were then kept in oven for 12 hours at 120 ^{0}c. The dried plates were used to cast the films.

2.3 Casting and drying of films

The blend was poured into the petri plates which were pretreated with silicon emulsion. The petriplates were kept in a closed box with inverted funnel for the controlled dissipation of natural solvents used. The controlled evaporation is required for uniform drying of patches. The drying was completed at room temperature in 24 hours. At that point the patches were cut into little fixes of 2cm × 2cm for Evaluation of Patches and subjected to physicochemical assessments of oral patches .

2.4 Visual assessment and appearance

The patches were assessed outwardly for its clearness, transparency and tenacity. Patches that were acceptable were assessed further and if they were unsatisfactory they were discarded.

2.5 IR Spectrum

IR retention range of EdivoxetineHCl was recorded by potassium bromide scattering strategy in which dry examples and potassium bromide were keptin a test holder and infrared range was recorded utilizing FTIR spectrophotometer.

2.6 Determination of λ max [6]

About 5 mg of Edivoxetine HCL was precisely weighed and was crushed in 100 ml methanol to get a 100 µg/ml arrangement and absorption is measured at UV range at a wavelength of 200-400nm.

2.7 Weight variation [7,8]

The patches were subjected to weight variation by individually weighing five different randomly selected patches. Such determination was carried out for each formulation. The test ensures the uniformity of the formed film. From the whole film three small pieces, each of 2×2 cm^2 area and were weighed individually.

2.8 Water vapor transmission rate[: 9,10]

About 2 gm. of combined calcium chloride as desicant was taken in vials and polymeric fix fixed over the vial by sticky tape. The vial is weighed and kept in to the dampness chamber at a RH 75% and temperature at 35^0 C. The vial is taken out and weighed at regular intervals.

2.9 Collapsing perseverance [11]

This was controlled by over and over collapsing the film at a similar spot until it broke. The occasions the films could be collapsed at a similar spot without breaking/splitting gave the benefit of collapsing perseverance. Collapsing perseverance was determined by more than once collapsing a little piece of the film at a similar spot until it breaks. The number of times the film collapsed at explicit spot without breaking gives the collapsing perseverance.

2.10 Thickness of film [12]

Appearances of the patches were checked for consistency and for the nearness of air bubbles. The thickness of patches was estimated at five better places utilizing a Vernier caliper with least check 0.01mm and mean qualities were determined.

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2.11 Tensile strength [13]

Tensile strength was dictated by the elasticity contraption and the elasticity was determined using the following equation Tensile stress (S) = Applied force/cross sectional area = (mxg)/(bxt)

where,

S = pliable worry in 970 dynes/cm2 m = mass in grams
g = increasing speed because of gravity (970 dynes/cm2)
b = broadness of strip in centimeters
t = thickness of strip in centimeters

2.12 *In vitro* dissolution [14]

Phosphate buffer at pH 7.4was used as the disintegration medium for the *in vitro* disintegration study. The temperature was kept at 37±0.5°C with a speed of 100 rpm. Tests samples were withdrawn at 0, 1, 3, 5, 10 intervals and replaced by equivalent volumes of medium. The samples were examined by UV Visible spectrophotometer.(Table 1)

2.13 Stability study [15]

Stability studies are conducted according to theICH guidelines at 40°C and 75% RH .The samples are analyzed for the drug content.

Table 1: Formula of medicated patches

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8
HPMC E 50	400mg	-	-	-	500mg	450mg	-	500mg
HPMC E 30	-	-	-	400mg	-	-	400mg	-
Eudragit RL 100	-	500mg	-	50mg	-	-	-	50mg
Polyox 303	-	-	-	-	100mg	50mg	100mg	-
HPMCK 100	-	-	500	-	-	-	-	-
PEG 400	200mg	200mg	200mg	200mg	200mg	200mg	200mg	200mg
Propylene glycol	1 ml	1 ml	1 ml	1 ml	1 ml	1 ml	1 ml	1 ml
Edivoxetine HCL	200mg	200mg	200mg	200mg	200mg	200mg	200mg	200mg
Water: ethanol(1:2)	30ml	30ml	30ml	30ml	30ml	30ml	30ml	30ml

3. RESULT AND DISCUSSION

3.1 Visual Appearance

Each formulations were found transparent, thin and smooth . A portion of the polymers were used alone and some of them were used in blends .The patches which has great appearance and smooth were used for further assessments.

3.2 FTIR studies

The IR spectra of unadulterated EdivoxetineHCl indicated absorbances at 3295, 3385,1619, 2629, 733 for C-CH stretch, N-H stretch, N-H stretch (Secondary amine), N-H stretch, C-O stretch.

3.3 UV spectroscopic studies

The UV absorbance at 258nm and concentration estimates of un adulterated Edivoxetine HCL indicated great linearity (r^2=0.9973) over the concentration range of 1-15 µg/ml. Consequently the given example of un adulterated EdivoxetineHCl was found to obey Beer-Lambert's law over this range.

3.4 Thickness of the film

The thickness of film was found to be 0.3 to 0.7 mm which implies uniform thickness found in every one of the batches

3.5 Folding endurance

The folding endurance of all the batches was seen multiple times. Patches didn not demonstrate any breaks even in collapsing of upto multiple times which demonstrated an appreciable adaptability of the patches.

3.6 Weight Variation

Uniform weight was seen as in single polymer batches and further more in mixed batches. The range of weight variation was found in the middle of 45 to 72 mg, implies uniform weight was found.

3.7 Drug content

The outcome demonstrates that the technique used to plan patches was equipped for creating patches with practically uniform medication dissemination. The rates of medication appropriation was found in the middle of 71 to 100%

3.8 The water vapor transmission rate

Water vapor evaporation through the distinctive patch formulations was arranged by HPMC and Eudragit RL 100 in various proportions. The water vapor transmission rate was found in range of 0.0616 to 2.75gm/cm^2, and this is higher worth.

3.9 Tensile strength

Tensile strength ranging from 2.3 to 6.0 dynes/cm^2,as the polymer concentration increase slightly increase in tensile strength.

3.10 Drug release of medicated films

Normal aggregate present discharge from (F1,F2,F3,F4, F5,F6,F7,F8) containing mg polymer focus was not the same as one another. They give 73.85%,86.96%, 77.93%, 94.23%, 92.19%, 88.35%, 68.54% and 93.99% release. Figure 1 and Table 2

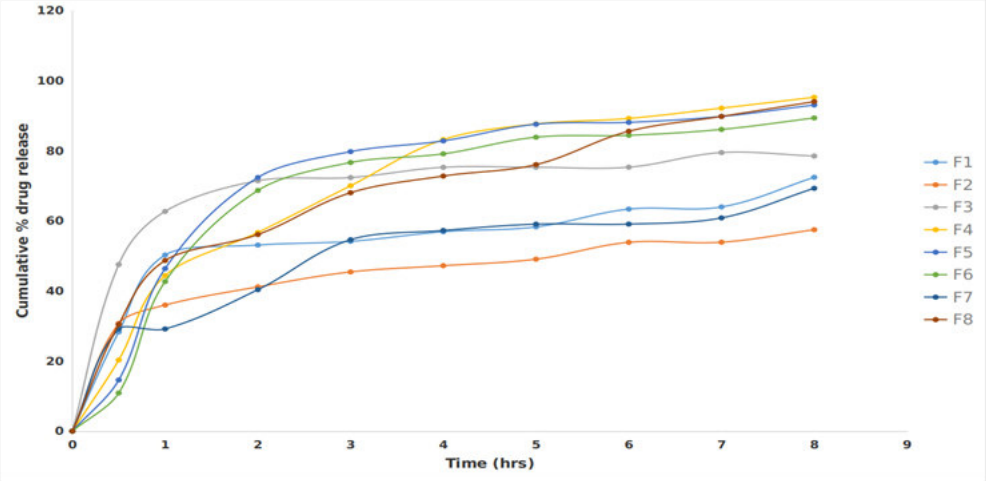

Fig 1. Average cumulative present release from (F1, F2, F3, F4, F5, F6, F7, F8)

Table 2.Evaluation of drug loaded patch Evaluation of drug loaded patch [Thickness, Folding Endurance, Water vapour transmission rate, Tensile strength]

FC	Thickness	Folding endurance	Weight variation(mg)	Water vapour transmission rate (gm/cm2)	Tensile strength (dynes/cm2)	% Drug release
F1	0.07mm	435	60.2	0.138	3.5	73.85%
F2	0.12mm	480	45.7	0.142	4.5	86.96%
F3	0.12mm	390	47.9	0.114	2.4	77.93%
F4	0.12mm	487	47.4	0.197	3.4	94.23%
F5	0.16mm	388	49.1	0.201	3.8	92.19%
F6	0.16mm	470	48.3	0.132	3.4	88.35%
F7	0.08mm	370	72.6	1.140	3.9	68.54%
F8	0.13mm	388	64.5	0.112	4.5	93.99%

3.11 Stability study

Stability studies were performed on film of formulation F4 and F8 for 2 months at different storages conditions as per ICH guidelines. From the result , it was found that no major changes in values of drug content and drug diffusion was found. This shows that the formulations are stable at different temperature

4. DISCUSSION

It can be noted that as the concentration of polymer increases the thickness of patch, weight uniformity, folding endurance increases. All the films were evaluated similar to kharia et al 16 for their physical parameters (weight, thickness, folding endurance), and they were found to be flexible, uniform, smooth, and transparent. All the formulations were uniform in their weight, thickness, folding endurance. The thickness of the patches varied from 0.07mm to 0.16 mm. Film thickness measurements ensured uniformity of the patches which further indicated the reproducibility of the procedure followed for the preparation of the patches. Folding endurance values varied between 388 and 487. Thus, no amount of constriction was observed which indicated that all patches had a smooth flat surface which would be maintained when the patches are applied to the skin. Combination of HPMC E30 & Eudragit RL 100 grade polymers shows better drug release than compared with other polymers [16]

5. CONCLUSION

Edivoxetine HCl was successfully formulated as transdermal patch. Drug excipient compatibility concluded that the drug and excipient were compatible with each other. Transdermal patches were set up using polymers like HPMC E 50, HPMC K 15M HPMC K 100,HPMC E 15, chitosanand different blends of HPMC E 50, Polyox 303,Eudragit RL 100. Considering the solubility of drug and polymer, the solvent mix of water: ethanol was selected. Polyethylene glycol 400(PEG 400) was used as a plasticizer. Every formulation of the patches were assessed for physical and mechanical properties like thickness, weight variety, dampness take-up, elasticity, and assessments like medication content, weight variation and in vitro medication release and the results were found to be within the acceptable limits. The F4 containing HPMC E30 and Eudragit showed a good mechanical However Pharmacokinetic studies are needed to be performed to affirm the consequences of this investigation.

6. AUTHORS CONTRIBUTION STATEMENT

Ramakrishna Reddy Voggu formulated the transdermal patch , computational system , investigated the experiments,the primary theoretical thoughts and results Ramakrishna Reddy Voggu and Ravi Teja.Tumburu performed the numerical calculations for the suggested experiment. Both authors discussed the results and commented on the manuscript. Ramakrishna Reddy Vogguand RaviTeja.Tumburu drafted the manuscript.

7. CONFLICT OF INTEREST

Conflict of interest declared none.

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