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Formulation and Evaluation of Transdermal Patch of Rabeprazole Sodium

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ABSTRACT: The current study's objective is to create and assess rabeprazole sodium transdermal patches (RPS). Materials and Procedures The creation of transdermal patches for RPS was accomplished by employing hydroxyl propyl cellulose (HPC-EF), polyvinyl pyrrolidone K-30 (PVP K-30), and polyvinyl pyrrolidone K-90 (PVP K-90) as film formers, polyethylene glycol (PEG-400) as a plasticizer, and Tween-80 and azone as permeation enhancers. The patches were created utilising the solvent casting method with aluminium foil serving as the backing membrane. Along with physicochemical characteristics like thickness, stickiness, moisture content, moisture loss, and folding durability, these patches were examined for compatibility using Fourier transform infrared (FTIR) spectrophotometry and for content using ultraviolet (UV) spectrophotometry. The patches underwent in vitro testing for in vitro release in USP dissolving. The characteristic FTIR spectra of RPS were also evident in the spectra of the patches, indicating drug-excipient compatibility. In vitro drug release indicated that the release of the drug was maximum from patches composed of HPC-EF (60.08±1.04%), which was much higher when compared with patches made of PVP K-30 (47.53±0.40%) and PVP K-90 (42.84±0.74%).

KEY WORDS:HPC-EF, PEG-400, PVP, Rabeprazole sodium, transdermal patch.

I. INTRODUCTION:

Another name for the transdermal drug delivery system (TDDS) is "patches." Traditional dose forms, like tablets or capsules, have drawbacks, such as low bioavailability caused by hepatic first pass metabolism or drug breakdown by enzymatic processes in the gastrointestinal system (GIT). By delaying first pass metabolism and enzymatic or acid-mediated degradation, TDDS can increase bioavailability. (1) Transdermal delivery is an innovative medication delivery method that is intriguing and patient-compliant. It administers the medicine through the epidermis at a controlled rate during the therapeutic window. (2) The sulfonamide derivative rabeprazole sodium (RPS), a powerful proton pump inhibitor, is used to treat peptic ulcers. The GIT's H+K+ATPase enzyme system is inhibited by RPS. The drug's oral bioavailability is dramatically decreased (by about 52%) as a result.(3)

II. MATERIALS AND METHODS:

polyvinyl pyrolidone k30, polyvinyl pyrolidone k90,polyethylene glycol (200),hydroxyl propyl cellulose, tween -80,azone was produced from Global scientific company, Erode, India.
The supplier of rabeprazole sodium was Yarrow Chem Pvt. Ltd. in Mumbai, India.

PREFORMULATION STUDIES

Ultraviolet spectrophotometry drug estimation:

The Indian Pharmacopoeia (IP) was used to generate standard solutions with levels of 10, 20, 30, 40, and 50 g/mL in phosphate-buffered saline (PBS), pH 7.4.(4) Using PBS pH 7.4 as a blank, the absorption of these values was measured at 283 nm using a UV spectrophotometer. In Microsoft Excel, the acquired data were shown in figures and then submitted to linear regression.(5)

ESTIMATION OF THE MELTING POINT:

Thiele's tube equipment was used to detect the drug's melting temperature. A capillaries tube was stuffed with the medication,(6) and a thermometers was used to determine the product's melting range. To ensure reproducibility, the measure was performed three times. at a point of melting.(7)

DETERMINATION OF THE PKa:

N-Octanol and PBS pH 7.4 were combined in an equivalent amount to calculate the partition coefficient. A precisely weighed 10 mg of the medication was added to a mixture of 5 mL of

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PBS pH 7.4 and 5 mL of n-octanol, which was then stirred intermittently in a separating funnel for 24 hours before being kept at room temperature for an additional 24 hours. A UV spectroscopy operating at 283 nm was used to calculate the RPS content after 24 hours. An equation was used to calculate the drug's partition coefficient Pharmaceutical inorganic phase concentrations drug level in the aqueous solution to determine the drug.(6)

INFRA - RED SPECTROSCOPY:

Using only a Fourier series infrared (FTIR) spectrophotometer, the drug's spectra was measured(8). The drug was inserted into the specimen holder employing IR graded KBr powder as a blank, and the distinctive peaks of the substance were identified by scanning between 400 and 4000 cm1.(9)

TRANSDERMAL DELIVERY DEVELOPMENT:

Assess and manage and dissolved in the chosen stock solution were the chosen polymers. Until a resulting solution was achieved, the polymer solution was left to stir.(10) The plasticizer was then added and mixed into the polymeric matrix. To achieve a clear solution, the medication was finally introduced while being constantly stirred.(11) To create the transdermal patches, a polymeric drug solution was cast in an Anumbra petri dish utilising aluminium foil as a foundation membrane. The transdermal drug delivery made using the solvent casting process are made of.(12) The patches were let to dry for 24 hours at room temperature. The dried patch were utilised for additional assessment investigations and kept in a centrifuge tube between 0 and 4°C(13)

EVALUATION OF TDDS PATCHES:

Patches are created for their physical and chemical properties, including their visual appeal, in vitro drug release, ex vivo permeability, adhesiveness, thickness, homogeneity in weight, and adhesiveness.(14)

VISUAL APPEARANCE:

The TDDS was assessed visually for flexibility, colour, transparency, and texture. Additionally, an optical microscope was used to look at the cast patches in order to look for any potential crystallisation.(15)

THICKNESS:

Using a Digimatic calliper, the transdermal patches' thickness was tested at five random locations (Mitutoyo, Japan).(16) Three patches' worth of thickness data were averaged, and mean and SD values were used to describe the data. (17)

WEIGHT UNIFORMITY:

A digital balance was used to weigh each patch randomly chosen from each batch, and the mean value and the root mean square deviation were computed.(18)

TEST FOR ADHESION:

Ball rolling tack examination was employed to determine how sticky transdermal patches were. a 7–16-inch diameter stainless steel ball was released from the 22.5-degree-inclined track that was parallel to the ground. The horizontal surface is created by the transdermal patch, whose adherence needs to be determined. On the patch's upper surface, the ball moved a distance that was measured in centimetres. The transdermal patch's adhesiveness is inversely proportional to how far the ball travels.(19)

FOLDING ENDURANCE:

By measuring the folding endurance, the mechanical strength of the transdermal patches was assessed. the tack was folded repeatedly in the same spot until a crack became apparent, at which point the data were recorded. Folding durability is determined by how many times the patches had to be folded before a visible crack appeared.(20)

DRUG CONTENT:

In order to equilibrate the drug-loaded patch (1 cm2) with PBS, an analytical flask. For 24 hours, a mechanical shaker was used to shake the flasks. The drug concentration of the patch was then determined by diluting 1 mililitre of the filter the solution while the buffer is turned on to 10 millilitre, and measuring the optical density at 283 nanometer.

The measurements were carried out three times, and the mean and standard deviation were used to express the findings.(21)

PERCENTAGE WATER ABSORPTION:

TDDS are mass in content that are stored in a dryer at 25°C for a . The patches were

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collected after a day and exposed in the desiccator at 84% RH are soaked in kcl upto a consistent mass occurs

$$\% \text{ water absorption} = \frac{\text{Finalweight} - \text{Initialweight}}{\text{Initialweight}} \times 100$$

For 24 hours at 25°C, precisely weighed patches were stored in a desiccator filled with fused calcium chloride. 24 hours later, The percentage moisture content of the patches was calculated using equation . (22)

$$\% \text{ Moisture content} = \frac{\text{initial weight} - \text{finalweight}}{\text{finalweight}} \times 100$$

PERCENTAGE MOISTURE CONTENT:

III. RESULTS AND DISCUSSION

DETERMINATION OF PURITY OF DRUG BY FTIR

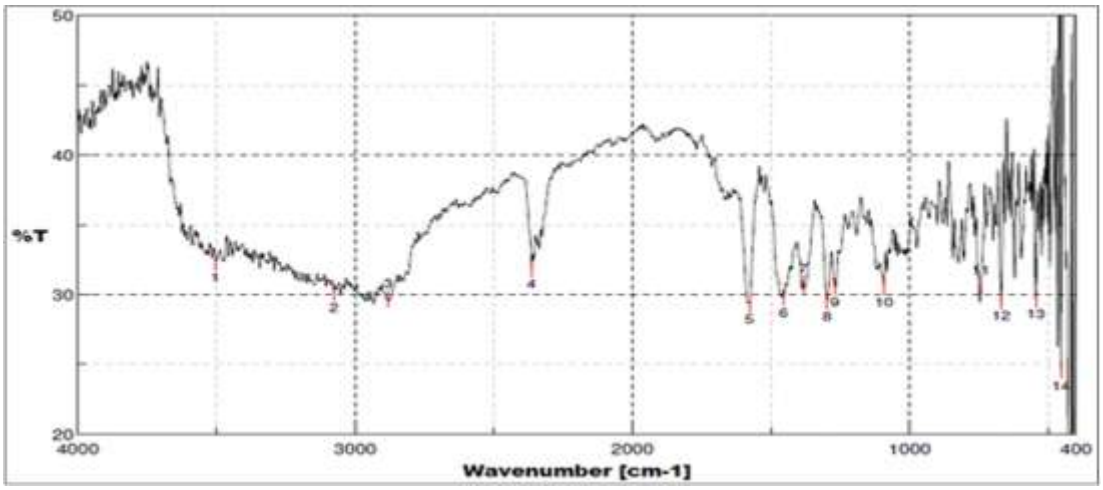

Fig .1 FT-IR analysis of rabeprazole sodium

FTIR ESTIMATION OF DRUGS' PURITY:

It is well known that rabeprazole exhibits its characteristic peaks. at the locations shown in Table 2 due to C-N, S = O,CH3 CH, C = C ,OH stretching, NH stretching, and CH. The distinctive peaks of Spectra of the optimised samples clearly showed the presence of rabeprazole.formula (F8) in roughly identical places(26). The ghostly Observations indicated the drug's compatibility with a number of excipients used to create the rabeprazole transdermal patch The peak of RPS was seen in Figure 1 using FTIR, and Figure 2's improved formulation demonstrated that it was stable.(27) Table 2 shows the spectrum observations, which excludes a potential conflict and demonstrates the RPS's compatibility with the formulations' usage of excipients.(28)

ESTIMATION OF WAVELENGTH:

It was discovered that the absorption maxima in the UV spectra of RPS in PBS (pH 7.4) are at 283 nm(29). The absorption maxima were discovered to be in good agreement with what was written about in the literature. The RPS's typical calibration curve exhibits linearity with the R2 value of 0.998 at a wavelength of pusy 283 nm. incline of the The drug content in most samples was determined using a standard curve.a result of the ex vivo and in vitro samples produced throughout the investigations.(30)

CURVE OF STANDARD CALIBRATIONRABEPRAZOLE SODIUM:

Table 1 standard curve of rabeprazole sodium at 283nm

SNO	CONCENTRATION(µg/ml)	ABSORBANCE (nm)
1.	0	0
2.	10	0.1
3.	20	0.2
4.	30	0.283
5.	40	0.37

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6.	50	0.46
y = 0.009x + 0.007 R^2 = 0.998		

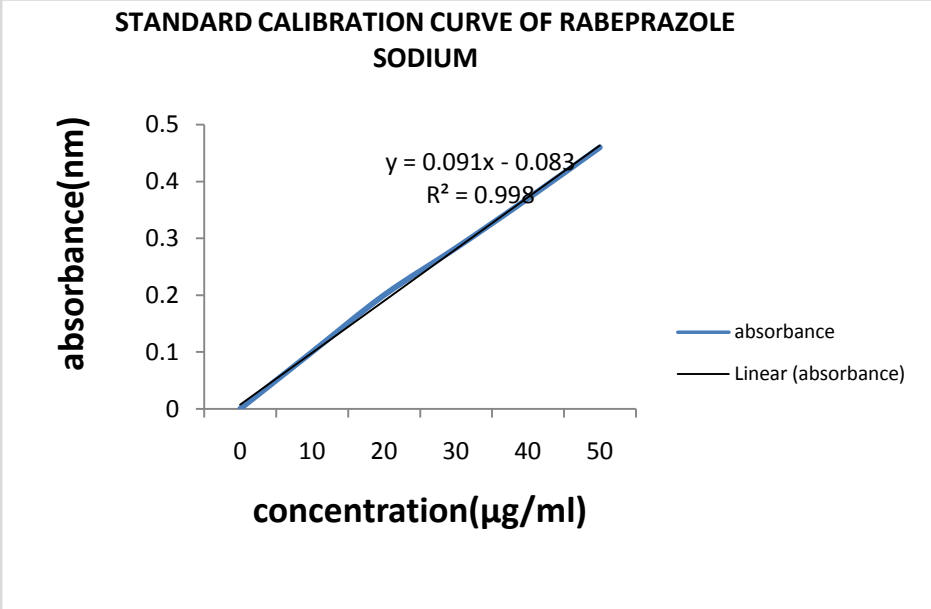

Fig 2 standard calibration curve of rabeparazole sodium

ESTIMATION OF MELTING POINT:

The ease with which a medication may penetrate the skin would depend on its melting point. Drugs with low melting points would penetrate the skin more effectively. as it melts point of RPS was discovered to be 1400.5oC, which according to the reference standard .(25) Moreover, the melting The drug's melting point being less than 200°C suggested its suitability of the medication for the creation of a transdermal patch. Drugs with low melting points are known to infiltrate more effectively and quickly solubilize in the lipid bilayer.

ANALYSIS OF TRANSDERMAL RPS PATCHES

CHARACTERISTIC OF PHYSICOCHEMISTRY:

RPS Transdermal drug delivery have been observed to be transparent, odourless, colourless, and clear. Furthermore, there were no indications of drug precipitation in the patches that were created.When looked at under a microscope. The degree of transdermal patches from various batches was discovered to be consistent and range from 0.24 mm to 0.28 mm, and the patches' thickness is influenced by the amount of the patch contains excipients and polymer. Likewise, The weight of the transdermal drug delivery, which ranged from 0.230 0.02 to 0.2215 0.04, was found to be constant. Additionally, the composition of numerous batches of transdermal drug delivery was found. consistently between 48.02 mg/ml and 49.22 mg/ml cm2

The consistency of the substance, weight, and thickness showed that the solvent casting process was suitable for create rabeprazole transdermal patches. The substance the casting process is still an effective way to make things of patch transdermally. Physicochemical characteristics of it is known that transdermal patches can impact in vitro.(26)

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FORMULATION	FOLDING ENDURANCE (n=3)	THICKNESS (mm ; n=3)	TACK TEST(cm ; n=3)	% MOISTURE CONTENT (n=3)	% MOISTURE UPTAKE (n=3)	FOLDING ENDURANCE (n=3)	DRUG CONTENT (mg; n=3)
F1	89.33±1.53	0.26±0.002	3.97±0.15	6.26±0.76	17.68±1.01	89.33±1.53	48.80±0.54
F2	91.67±1.53	0.24±0.001	2.33±0.15	8.10±0.93	14.09±1.27	91.67±1.53	48.89±0.38
F3	81.69±4.73	0.26±0.002	2.57±0.15	7.69±0.97	11.58±1.95	81.69±4.73	49.22±0.84
F4	85.66±3.51	0.27±0.01	2.60±0.20	7.92±0.70	12.51±1.55	85.66±3.51	49.04±1.36

Table 2 Evaluation of Rabeparazole sodium patches

IN VITRO RELEASE TEST:

The effects of various synthetic polymer patch' release of drug. It was found that formulation F3 had the highest release rate (60.08 ± 1.04%) while F6 had the lowest. This is due to the hydrophilic nature, solubilizing property, and lower molecular weight of HPC-EF.(32) The studies also showed thatas the amount of both the film-forming polymers rises, the medication release declines. Based on these results, formulation F4 was selected for further evaluation. HPC-EF does not prevent drug release from the matrix unlike other high molecular weight polymers such as PVP K-90.(33)

Table 3 in vitro drug release in 12 hours

F.CODE	IN VITRO DRUG RELEASE STUDY IN 12 HOURS
F1	26.54 ±2.1
F2	24.3 ±1.1
F3	51.9 ±1.62
F4	81.9 ±2.3

Table:4 in vitro drug release

MINUTES	F1	F2	F3	F4
10	0.74 ±0.2	0.74 ±0.2	6.8 ±0.5	11.7 ±0.5
20	1.94 ±0.1	2.14 ±0.6	10.8 ±1.1	24.4 ±0.8
30	4.34 ±0.3	3.30 ±0.3	15.1 ±1.6	37.7 ±0.9

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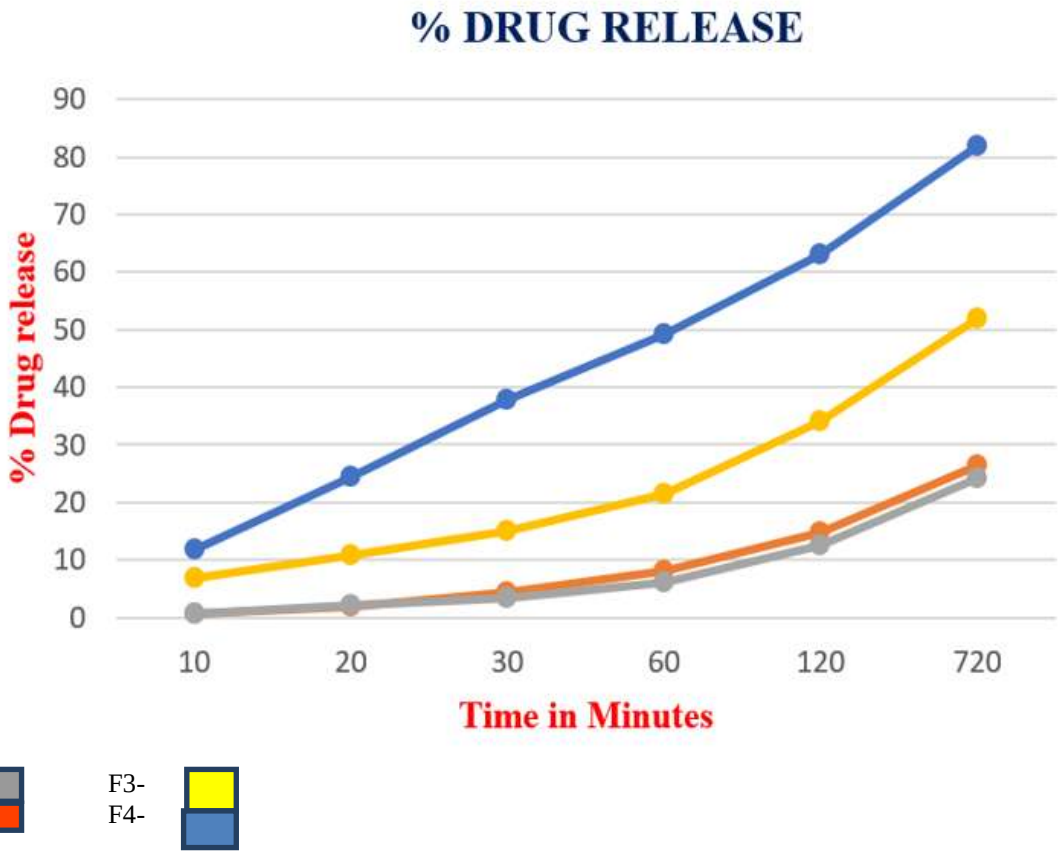
60	8.04 ±1.3	6.01 ±1.1	21.5 ±2.0	49.1 ±1.2
120	14.84 ±1.6	12.6 ±0.6	34 ±1.0	63.0 ±0.7
720	26.54 ±2.1	24.3 ±1.1	51.9 ±1.6	81.9 ±2.3



IV. CONCLUSION:

RPS transdermal patches were made using the solvent casting method with bioadhesive polymers and PEG-400 as a plasticizer. HPC-EF was found to be the best polymer for the patches as it released the most drug. Tween-80 was the best enhancer for drug penetration. The study showed the feasibility of using transdermal patches for RPS delivery, with a 8 cm2 patch likely to deliver a therapeutic dose. The transdermal patch may improve bioavailability and patient compliance by bypassing the first pass metabolism and avoiding gastric degradation.

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