IJNRD.ORG ISSN : 2456-4184
INTERNATIONAL JOURNAL OF NOVEL RESEARCH AND DEVELOPMENT (IJNRD) | IJNRD.ORG
An International Open Access, Peer-reviewed, Refereed Journal

FORMULATION AND EVALUATION OF PROPRANOLOL HYDROCHLORIDE TRANSDERMAL PATCHES

Name of Authors: Mr Mali M.R. , Ms. Kazi F. I. , Mr Patil K.D. , Mr Satam P. A.

College Name: Shree Saraswati Institute of Pharmacy

Corresponding author: Mr Kedar Tukaram K.

ABSTRACT :

Since propranolol hydrochloride has a high first-pass metabolism and a low oral bioavailability, various matrix-type transdermal patches containing the drug were developed with the goal of examining the impact of the polymer on transdermal release. The polymers chosen to maintain the drug's release. HPMC, et cetera, were the polymers chosen to maintain the drug's release. Methanol and polymer were used to create the patches. For patients who are unable to take their medication orally, this is one of the greatest pharmaceutical dose forms available. When transdermal patches are applied, TDDS has established itself as a crucial component of innovative drug delivery systems since the medication's distribution through the dermis has a systemic effect. An expensive substitute for traditional formulation is TDDS. Using solvent evaporation techniques, a matrix-type transdermal patch containing propranolol hydrochloride and a mixture of HPMC was to be developed. In the methanol solvent system, methanol served as a penetration booster. Physical evaluations were conducted to assess the drug content, moisture content, thickness, weight change, and folding endurance of transdermal films. Every compound created showed a high degree of physical stability. In terms of their physical parameters and drug content, all of the films were determined to be stable between 37°C and 45°C.

Keywords: Patch, propranolol hydrochloride ,polymer Trasdermal

2] INTRODUCTION:

Definition: Transdermal drug delivery system is defined as a self-contained discrete dosage form, which when applied to the intact skin, will deliver the drug at a controlled rate to the systemic circulation.

Basic components of TDDS:

The components of transdermal devices include:

1. Polymer matrix or matrices

2. The drug

3. Permeation enhancers

4. Other excipients

1. Polymer Matrix: The drug's release from the device is regulated by the polymer. According to Kydoineus and Berner-Briter, a polymer cannot be used in a transdermal system unless the following requirements are met:.

(i) The polymer's molecular weight, glass transition temperature, and chemical activity should all be such that the targeted medication diffuses and is released in the appropriate way

.(ii) The polymer should be cheap, easily formed into the desired product, stable, and non-reactive with the medication

.iii) The polymer and the byproducts of its breakdown must not be harmful or antagonistic to the host.

(iv) When significant amounts of active agent are added to the polymer, the polymer's mechanical characteristics shouldn't suffer unduly. The following polymers could be helpful for transdermal devices:

Natural polymers include natural rubber, starch, zein, gelatin, shellac, waxes, proteins, and gums and their derivatives.Polybutadiene, Hydrin rubber, Polysiloxane, Silicone rubber, Nitrile, Acrylonitrile, Butyl rubber, Styrene-butadiene rubber, Neoprene, and so on are examples of synthetic elastomers.Synthetic polymers include methylmethacrylate, epoxy, polyvinyl alcohol, polyvinyl chloride, polyethylene, polypropylene, polyacrylate, polyamide, polyurea, and polyvinylpyrrolidone.

2. Medicine: Careful consideration should go into selecting the medicine in order to properly create a transdermal drug delivery system. Some of the desired characteristics of a medication for transdermal distribution include the following (Guy et al., 1987; Flynn & Stewart, 1988)

3. Permeation Enhancers: 3. Permeation Enhancers: According to Kydonicus and Berner (1987), these substances increase skin permeability by changing the skin's function as a barrier to the flow of the intended penetrant. where C is the concentration of the diffusing species, J's xrial coordine solution can be spatially coordinate, and D is the diffusion coefficient, which depends on the size, shape, and flexibility of the diffusing molecule as well as Sutipor combrane resistance. extremely, despite the fact that the fundamental ideas of flow and diffusion coefficient are related. The extremely complicated atient has a thermodynamic genesis. Its size, concentration, and energy needed to create a hole for diffusion are also factors. Therefore, improving flow across membranes comes down to the following factors:

i. Thermodynamics (lattice energies, distibution coefficients).
ii. Molecular size and shape.
iii. Reducing the energy required to make a molecular hole in the membrane

Although the process of changing the barrier energy to hole formation is mostly empirical, the work is being approached from a basic study of the dynamics of extending the structure of lipids (Cooper, 1983) and proteins (Ayres & Hopper, 1978; Bettley, 1965). Using L/*angmuir troughs, for instance, the effects of agents on the compressibility of monolayer film are investigated. A range of spectroscopic methods are used to look at specific molecular interactions. In order to improve skin penetration, permeability enhancers are thought to impact one or more of these layers (Idson, 1975). The potential of several different substances to increase stratum corneum permeability has been studied.

4. Solvents: These substances may improve penetration by fluidizing lipids and/or enlarging the polar route (Wurster & Kramer, 1961; Chandrashekharan et al., 1977). Examples include laurocapram (Azone), propylene glycol, glycerol, silicone fluids, isopropyl palmitate, alkyl methyl sulfoxides, dimethyl sulfoxide,

alkyl homologs of methyl sulfoxide, dimethyl acetamide, and dimethyl formamide; pyrrolidones, 2-pyrrolidone, N-methyl, 2-pyrrolidone; and water alcohols, methanol and ethanol.

TYPES OF TRANSDERMAL PATCHES:

a) Single layer drug in adhesive:

This kind has the medication embedded in the sticky layer. The medicine is released into the skin via the adhesive layer, which also acts as a glue to hold the other layers together. There is a backer and a temporary liner all around the adhesive layer.

Fig no. 1

b) Multi-layer drug in adhesive:

This kind is comparable to the single-layer kind as well, but in addition to the adhesive layer, it has two additional layers: one for controlled release and the other for immediate medication release. The medicine is released due to the action of the sticky layer. This patch also features a permanent backing and a transient liner layer.

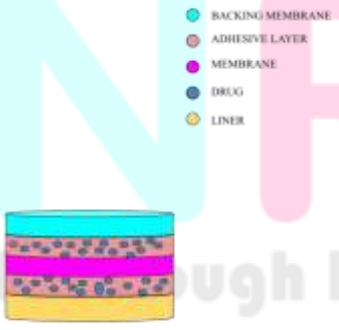


Fig no. 2

c) Vapour patch:

In this type of patch the role of adhesive layer not only serves to adhere the various layers together but also serves as release vapor. The vapor patches are new to the market.

d) Reservoir system:

The drug reservoir is embedded in this system between an impermeable backing layer and a rate-controlling membrane. The drug can only be released through the rate-regulating membrane, which may or may not be microporous. The drug may be distributed across a solid polymer matrix in the drug reservoir compartment, or it may take the form of a gel, suspension, solution, or other combination. One possible use is a hypoallergenic, sticky polymeric membrane with an outside surface that is drug-compatible.

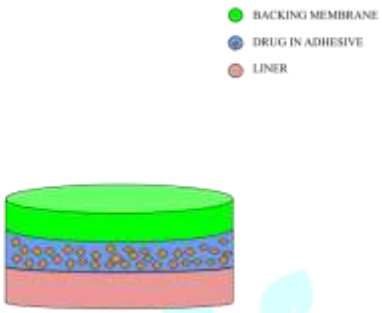


Fig no.3

e) Matrix type patch:

Transdermal matrix patches use an adhesive polymer matrix to gradually administer the medication to the skin. Unlike reservoir patches, which have a rate-controlling membrane, this patch's drug delivery rate is dictated by the drug formulation and polymer matrix.

Fig no.4

PROPRANOLOL HCL:

Molecular Formula:

- $C_{16}H_{22}ClNO_2$

Synonyms:

- Propranolol hydrochloride
- Propranolol Hcl

Molecular weight:

295.80 g/mol

Description:

Propranolol hydrochloride is a synthetic beta-adrenergic receptor blocker that has antihypertensive, antianginal, and antiarrhythmic properties. Propranolol reduces the negative chronotropic and inotropic effects of beta-adrenergic responses, including vasodilation, by competitively opposing beta-adrenergic receptors.

METHODS:

(i) Take all necessary ingredients, including glycerine for plasticizers, methanol as a solvent, HPMC as a polymer, and propranolol HCl as the medication.

(ii) Fill a beaker with 20 ml of methanol.

(iii) Next, dissolve the medication (20 mg) in a beaker filled with solvent while stirring constantly.

(iv) After the medication has completely dissolved in the methanol, add the HPMC.

(v) After the HPMC has fully dissolved in the entire solution, add 1 millilitre of glycerine to it.

(vi) Constantly stirred to obtain a uniform mixture.

(vii) At this point, a thin layer of this solution is placed on a petri dish.

(viii) Use a funnel to cover a petri dish to stop it from drying out too much.

(ix) A day later, we observed that the patch had fully formed.

(x) And now cut into specific size and shape.

EVALUATION TEST:

PHYSICAL APPEARANCE TEST

THICKNESS

CALIBRATION CURVE

MOISTURE CONTENT

FOLDING ENDURANCE

WEIGHT VARIATION

SWELLABLITY

SURFACE PH

DISSOLUTION TEST

(I) Physical appearance:

The patches form were smooth and transparent in appearance.

(II) Thickness:

The thickness of patch was determined by using VERNIAR CALIPER recording mean of 6 determination.

(III) Calibration curve:

1. Preparation of phosphate buffer solution (PH-7.4) :

To prepare the phosphate buffer solution (PH-7.4), fill a 200 ml volumetric flask halfway with 50 ml of 0.2 M sodium phosphate, add 39.1 ml of 0.2 M sodium hydroxide, and top up the volume with 200 ml of distilled water. A pH meter was used to calibrate the solution, which came out to be 7.4.

2. Preparation of primary stock solution :

100 mg of propranolol Hcl was added in 100 ml phosphate buffer(7.4). Solution conc. Was 1000 micro gm.

3. Preparation of secondary stock solution :

10ml primary stock sol was made up to 100ml with phosphate buffer pH =7.4 conc. of 100 micro gm.

4.Sample solution:

1, 2, 3, 5, 6, 7, 8, 9, and 10 ml of the secondary stock solution were pipetted out, and 10 ml of phosphate butter pH 7.4 was used as the volume. The absorbance was measured at 290 nm using phosphate buffer pH 7.4 as a reference.

(IV) MOISTURE CONTENT:

There was a desiccator with a fused CACL2. First, the patches to be examined were weighed and placed in a desiccator for a whole day. reweighed after a 24-hour period, and the moisture content was computed by deducting the final weight from the initial weight.

(V) FOLDING ENDURANCE:

The test for folding durability involved folding the patch multiple times at the same time and location until the patch broke. The value of folding endurance is determined by the number at which a patch folds without breaking.

(VI) WEIGHT VARIATION:

Although weight variation between patches in the same batch should be minimised or eliminated, it is always possible; therefore, this test provides an idea of whether weight variation exists in any of the patches. Essentially, five patches are precisely weighed after being chosen at random. A mean calculation was made. We can get a sense of weight fluctuation from the patches' varying weights.

(VII) SWELLABLITY:

The prepared patches were weighed (w1) and individually incubated in an agar gel (2%) plate at 37 + 0.5 °C. The patches were carefully taken from the petri dish at regular intervals of 15 minutes to an hour, and any extra water was carefully wiped out using filter paper. Weighing the enlarged areas again (w2).

Swelling index = $\frac{w2 - w1}{W1} \times 100$

(VIII) SURFACE PH :

The patch is left in 0.5 millilitres of water and let it swell for an hour. By placing a combination glass electrode close to the patch's surface and letting it equilibrate for an hour, the surface PH can be determined.

(IX) DISSOLUTION TEST:

Using a paddle apparatus (50 rpm) with the addition of a modified disc assembly in acetate buffer with PH 4.5 and a temperature of 32 °C + 0.5 °C, the patch was placed at the bottom of the apparatus,, filled with buffer solution, and allowed to rotate at a specific rpm and temperature for 1 hour. the desired 5 ml of solution removed at each 15-min interval for 1 hour, and absorbance checked by UV spectroscopy at 228 nm. At a same time each 5ml of buffer sol inserted in beaker during removal of solution from beaker. The graph was a plot of absorbance vs. time.

RESULT AND DISCUSSION:

1. Physical Appearance:

Colour – Whitish

Texture – Smooth

Trasparency - Clear

2. SWELLABLITY:

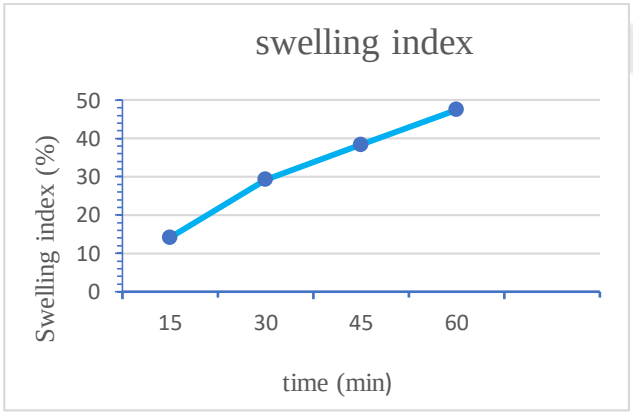
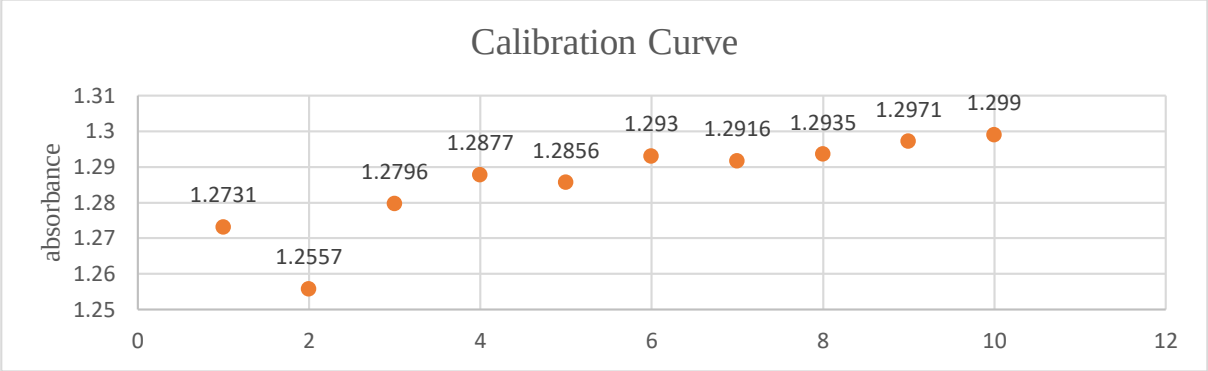


Fig. No. 5

3. CALIBRATION CURVE:



4. WEIGHT VARIATION:

PATCH NO	WEIGHT (mg)
1	71
2	68
3	69
4	55

Fig no. 6

Fig no. 7

Fig no. 8

Fig no 9

5.THICKNESS TEST:

PATCH NO	THICKNESS (mm)
1.	0.200
2.	0.230
3.	0.280
4.	0.220

Fig no. 10

6.SURFACE PH :

The surface pH of propranolol Hydrochloride is found to be 6.01 .

Fig no. 11

7. MOISTURE CONTENT :

Initial weight: 55 mg

Final weight : 60 mg

$$MC = \frac{DW - Ww}{Ww} * 100$$

$$= \frac{60 - 55}{55} * 100$$

= 9.090 %

Fig no. 12

Fig no. 13

8. DISSOLUTION TEST :

Table of Standard readings

Sample name	228.0nm	Abs(eff)	min
Standard-1	1.5401	1.5401	0.0000
Standard-2	1.5398	1.5398	0.0000
Standard-3	0.2251	0.2251	0.0000
Standard-4	0.2860	0.2860	0.0000
Standard-5	0.3197	0.3197	0.0000

Table of Sample readings

Sample name	228.0nm	Abs(eff)	min
Sample-1	0.0022	0.0022	0.0022
Sample-2	0.1435	0.1435	0.1435
Sample-3	1.5208	1.5208	1.5208
Sample-4	1.5240	1.5240	1.5240
Sample-5	1.5142	1.5142	1.5142

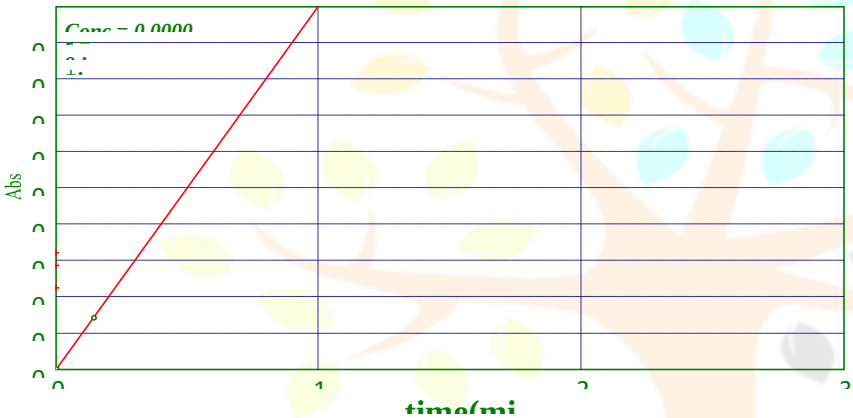


Fig No.14

9. FOLDING ENDURANCE:

PATCH NO	FOLDING ENDURANCE (TIMES)
1.	230
2.	235
3.	232
4.	240

CONCLUSION :

The goal of the current work is to create and develop a solvent evaporation method for HPMC-induced propranolol hcl patches. The drug is the hypertension treatment that has undergone the most extensive research. The effectively designed reference transdermal patch uses skin propranolol HCl as a continuous permeation, which reduces the need for frequent administration and promotes strong pattern compliance. The chosen medication satisfies the required physicochemical requirements. A subsequent assessment of the patches was conducted, taking into account variables like moisture content, medicine content, thickness, and endurance. Each of these parameters was not in line. Mernod's anti-executive formulation is employed. It is clear from these reliable and uncomplicated observations that the formulation evaluation of propranolol HCl patches.

REFERENCES :

1. Borkar, K., Channawar, M., Chandekar, S., Nandgaye, D. C., & Moon, P. (2023). *" FORMULATION AND EVALUATION OF TRANSDERMAL PATCHES ". July*.
2. Chander Jhawat, V., Saini, V., Kamboj, S., & Maggon, N. (2013). Transdermal drug delivery systems: Approaches and advancements in drug absorption through skin. *International Journal of Pharmaceutical Sciences Review and Research*, *20*(1), 47–56.
3. Delivery, N. D. (n.d.). *Controlled and Novel Drug Delivery Controlled and Novel Drug Delivery*.
4. Edition, E., Waugh, A., & Grant, A. (n.d.). *Ross and Wilson ANATOMY and PHYSIOLOGY in Health and Illness*.
5. Kandavilli, S., Nair, V., & Panchagnula, R. (2002). Polymers in Transdermal. *Pharmaceutical Technology*, *May*, 62–80.
6. Kumar, K. L. S., Gokulan, P. D., Vasanthan, A., Venkateswaran, S., & Santhosh, H. (2022). *Preparation and evaluation of matrix type of transdermal patches containing anti – diabetic drug*. *9*(1), 29–34.
7. Borkar, K., Channawar, M., Chandekar, S., Nandgaye, D. C., & Moon, P. (2023). *" FORMULATION AND EVALUATION OF TRANSDERMAL PATCHES ". July*.
8. Chander Jhawat, V., Saini, V., Kamboj, S., & Maggon, N. (2013). Transdermal drug delivery systems: Approaches and advancements in drug absorption through skin. *International Journal of Pharmaceutical Sciences Review and Research*, *20*(1), 47–56.
9. Delivery, N. D. (n.d.). *Controlled and Novel Drug Delivery Controlled and Novel Drug Delivery*.
10. Edition, E., Waugh, A., & Grant, A. (n.d.). *Ross and Wilson ANATOMY and PHYSIOLOGY in Health and Illness*.
11. Kandavilli, S., Nair, V., & Panchagnula, R. (2002). Polymers in Transdermal. *Pharmaceutical Technology*, *May*, 62–80.

12. Kumar, K. L. S., Gokulan, P. D., Vasanthan, A., Venkateswaran, S., & Santhosh, H. (2022). *Preparation and evaluation of matrix type of transdermal patches containing anti – diabetic drug*. *9*(1), 29–34.

13. Kumar, K., Sissodia, N., Rai, A. K., Prajapati, S. K., & Bhardwaz, P. (2008). Development and evaluation of matrix type transdermal patches of aspirin. *Oriental Journal of Chemistry*, *24*(2), 485–494.

14. Kumar, S. S., Behury, B., & Sachinkumar, P. (n.d.). *Formulation and Evaluation of Transdermal Patch of Stavudine*.

15. *NDDS by nirali Prakashan.pdf*. (n.d.).

16. O.G., B. (2017). Formulation and Evaluation of Oral Fast Dissolving Film of Glipizide. *World Journal of Pharmaceutical Research*, *6*(2), 1279– 1297. https://doi.org/10.20959/wjpr20177-8835

17. Renu. s, B. P. (2012). International Journal of Biomedical and Advance Research 770. *International Journal of Biomedical and Advance Research*, *3*(2), 770–774.

18. Sheth, N. S., & Mistry, R. B. (2011). *Formulation and evaluation of transdermal patches and to study permeation enhancement effect of*

eugenol. *01*(03), 96–101.

19. Sirisha, V. N. L. (2012). Formulation and Evaluation of Transdermal Patches of Propranolol Hydrochloride. *IOSR Journal of Pharmacy (IOSRPHR)*, *2*(5), 31–37. https://doi.org/10.9790/3013-25603137

20. Specifications, D., Oral, F. O. R., & Forms, D. (2008). *European Pharmacopeia 8.8. (2.9.4. Dissolution Test for Transdermal Patches)*. *1*, 275–277.

21. Swarbrick, J., & Rubin, A. A. (n.d.). *Novel Drug Delivery Systems*.