JETIR.ORG ISSN: 2349-5162 | ESTD Year : 2014 | Monthly Issue
JOURNAL OF EMERGING TECHNOLOGIES AND INNOVATIVE RESEARCH (JETIR)
An International Scholarly Open Access, Peer-reviewed, Refereed Journal

FORMULATION AND EVALUATION OF NAPROXEN SODIUM TRANSDERMAL PATCHES

K.Srinu[1*], M. Gayatri Devi[2], D. Pavitra[3]

Assistant Professor[1], Associate Professor[2], Assistant Professor[3]
Pharmaceutical Technology,
Visvanadha Institute of Pharmaceutical Technology, Visakhapatnam, India.

Abstract:

Significant improvements in medication safety, toxicity reduction, and patient compliance through long-lasting therapeutic effects are all made possible by controlled drug delivery systems, or CDDS. These methods include site-targeting, feedback-regulated, activation-modulated, and rate-pre-programmed techniques; transdermal patches are especially successful in this regard. Transdermal patches are a useful substitute for traditional dosage forms because they avoid first-pass metabolism, administer medications consistently, and stop dose dumping. Nonsteroidal anti-inflammatory drugs (NSAIDs) and other medications with gastrointestinal (GI) adverse effects benefit greatly from this delivery strategy. When taken orally, naproxen, a popular NSAID for treating pain and inflammation in ailments like arthritis, headaches, and muscular aches, frequently results in gastrointestinal problems such peptic ulcers and bleeding. The purpose of this project is to create and assess transdermal naproxen patches in order to reduce the negative side effects of oral administration. The patches work to administer the medication through the skin, avoiding the gastrointestinal tract and possibly reducing the risk of bleeding and ulcers while keeping the bloodstream at steady therapeutic levels. With an emphasis on formulation optimization and in vitro testing to confirm the therapeutic potential of transdermal naproxen patches, this strategy may greatly improve patient safety, compliance, and overall therapy efficacy

Keywords - Naproxen sodium, Osteoarthritis, HPMC, Transdermal Patches, Casting solution

INTRODUCTION

A. Controlled Drug Delivery:

Controlled drug delivery systems are one of the fastest-growing areas of research where chemists and chemical engineers are improving human health care. Such delivery techniques offer several advantages over traditional dose forms, including better patient care, reduced toxicity, enhanced efficacy, and convenience.

The following are some possible classifications for controlled drug delivery systems (CDDS) [2], [3]:

1. Drug delivery devices that are rate-preprogrammed
2. Drug delivery systems with activation modulation
3. Drug delivery systems with feedback regulation

4. Drug delivery methods that target certain sites

Although oral pharmaceutical delivery is the most well-known method, it has a number of drawbacks, such as first-pass digestion, drug degradation, and other issues in the gastrointestinal tract due to chemicals, pH, and other factors. Chien (1992), Banker (1990), and Guy (1996) developed a sophisticated pharmaceutical transportation architecture to overcome these problems. It was either a transdermal conveyance framework or transdermal patches. Sedated cement patches are used in this framework, which, when applied to the skin, deliver a potent restorative dose of drug[4], [5]

Compared to controlled release oral systems or traditional dosage forms, transdermal patches have numerous advantages. Transdermal patches provide stable blood levels, prevent dose dumping, avoid first-pass metabolism, and increase patient consistency [6], [7]

A nonsteroidal anti-inflammatory medication called naproxen reduces pain and swelling. It is used to treat gout, migraines, joint inflammation, tendinitis, tooth pain, muscular aches, spinal problems, and female spasms. This drug functions by blocking the production of prostaglandins by the protein. Reduced prostaglandins help to reduce pain and promote growth. The goal of the current study was to address the negative side effects of naproxen, a non-steroidal anti-inflammatory medicine [NSAID] that, when taken orally, produces significant bleeding in the gastrointestinal tract[9]. The majority of NSAIDS are used orally, which is related to with possible flaws such as gastrointestinal death and peptic ulcers. This serious disadvantage raises the possibility that NSAIDS transdermal patches will need to be developed.

B. Anatomy of the Skin

The largest organ in the human body, the skin accounts for about sixteen percent of total body weight. A healthy adult man's skin measures 1.5–2 m² and weighs 6–10 kg. The epidermis, the basic dermis, and the subcutaneous layer are the three main cell layers that make up the skin.

Layers of the skin:

1) Epidermis: The skin's outermost layer, indicated by the presence of distinct squamous division. The cells that make up the epidermis are called keratinocytes. Because it is connective in nature, the epidermis relies on the dermis to remove waste and carry supplements through the cellar film. Although the epidermis is divided into four layers, the area of the body with the thickest skin has five layers. I. Layer Germinativum (Layer Basal). Ii. The prickle cell layer, or layer spinosum. Iii. Granulosum layer. Layer Lucidum, Iv. V. Corneum layer.

2) Dermis: This layer is located beneath the epidermis and is significantly thicker than the epidermal layer, which is only 1–5 mm thick. The dermis plays a crucial role in supporting and preserving the epidermis. The tissues that link the Collagen strands and a small amount of elastin make up the dermis. Some specific cells, such as fibroblasts and pole cells, as well as structures like veins, lymphatic, sweat organs, and nerves, call it home. The two main layers of connective tissues comprise the dermal layer.

• Papillary layer: This thin, externally exposed layer contains free connective tissues.

• The reticular layer is a deeper, thicker layer with fewer cells that contains thick collagen filaments and connective tissue.

3) Hypodermis: Also known as the Panniculus layer or the subcutaneous layer/fat. The layer that connects the skin to the fundamental belt (stringy tissue) of the bones and muscles is located underneath the dermis. The hypodermis is made up of free, areolar, and highly vascularized Connective tissues and fat tissues serve as a store of energy, shield the body from heat-related harm, and serve as a cushion to protect fundamental structures from harm. It has the largest capacity for fat in the body and is connected to veins and nerves [23]–[27].

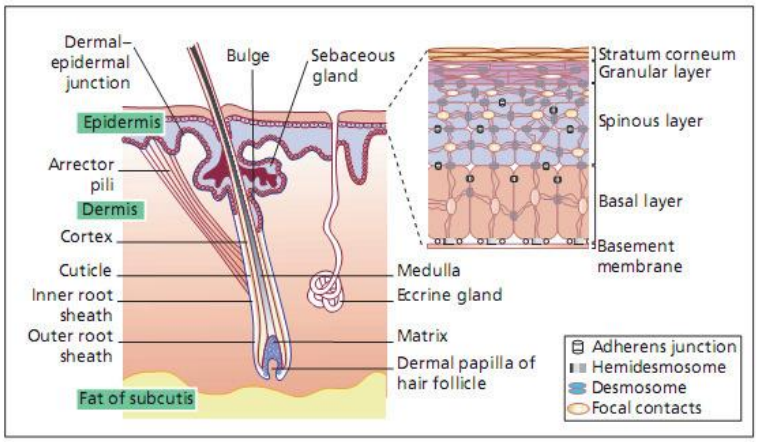

Figure 1: Skin's anatomical and physiological makeup

TRANSDERMAL DRUG DELIVERY SYSTEMS' SKIN PATHWAYS:

There are several ways for medications to penetrate and pass through the skin when they are administered to its surface. Drugs can enter the body through the appendages (transappendageal) or the stratum corneum (transepidermal) (Figure:1). There are two distinct pathways for penetration through the stratum corneum: Penetration via the transcellular route, which alternates between the lipid lamellae and corneocytes, and ii) Penetration via the lipid lamellae's convoluted conduit.

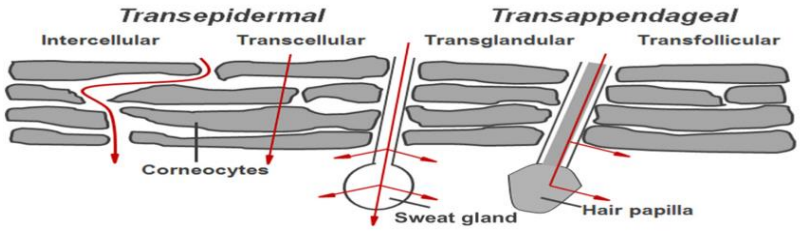

Figure 2: potential routes for medication penetration across skin barriers

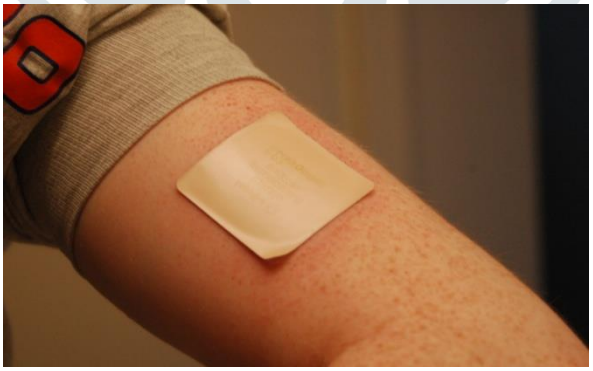

Figure 3: Transdermal bandage

Transdermal medication delivery benefits include:

1. The gastrointestinal ph, enzymatic activity, and drug interaction with food, drink, and other oral administration drugs can all be avoided by using TDDS to prevent gastrointestinal drug absorption issues.

2. Increases the therapeutic effectiveness of many medications by preventing certain issues with the medicine, such as gastrointestinal irritation, poor absorption, hepatic "first-pass" effect-induced breakdown, the production of metabolites that result in adverse effects, short half-life requiring frequent dosage, etc.

3. A longer duration of effect means fewer doses are needed.

4. Prevents parenteral therapy's inconvenience.

5. It is feasible to administer oneself.

6. Preserves the powerful drug's plasma concentration.

7. Offers prolonged treatment with just one application.

8. In the event of toxicity, drug delivery can be easily stopped.

Disadvantages*:*

1. Drugs having a high or extremely low partition coefficient are unable to enter the bloodstream.

2. Due to the limitations of drug absorption into the skin, transdermal patches are only appropriate for powerful medications.

3. Age, individual differences, and the same person may all have an impact on the skin's barrier function.

4. Transdermal delivery will be extremely challenging if the daily dose of the medicine needed for therapeutic benefit exceeds 10 mg.

DRUG PROFILE

NAPROXEN SODIUM

A non-steroidal anti-inflammatory medication that reduces pain and swelling, naproxen is a member of the BCS system's class 2. It is used to treat gout, arthritis, headaches, backaches, muscle aches, tendinitis, tooth pain, and menstrual cramps. This medication functions by inhibiting the prostaglandin-producing enzyme. Pain and edema can be lessened by lowering prostaglandins. The goal of the current study was to address the negative side effects of naproxen, a non-steroidal anti-inflammatory medicine [NSAID] that, when taken orally, produces severe bleeding in the gastrointestinal tract[1,2] (RESEARCH GATE)

Chemical structure

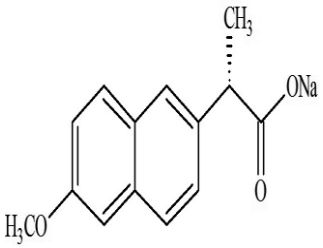

Figure 4: Naproxen sodium's chemical structure

IUPAC NAME:

[propionic acid d-2-(6-metoxy-2naphthyl)].
Formula for molecules: C14H14O3
Weight in molecules: 230.25 g/mol.
Melting temperature range: 1540–1590°C.
Point of boiling: 403.90C.

The density is 1.064 g/cm².

Cmax: Naproxen sodium is a white to creamy crystalline powder that has no smell. 375 mg, 500 mg, and 750 mg of naproxen and 37.5, 50 mg, and 75 mg of sodium, respectively, are contained in NAPRELAN® Tablets in amounts of 412.5 mg, 550 mg, or 825 mg of naproxen sodium.

Duration of action: Up to two hours after application, the medication may be released.

pH stability: 7.4.

It is soluble in both water and methanol.

Contraindications: Heart issues or stroke, such as breathing difficulties, limb swelling, slurred speech, weakness in one or both sides of the body, or chest pain[11].

APPLICATIONS:

- ❖ Used to treat osteoarthritis (arthritis brought on by a breakdown of the joint lining).
- ❖ Rheumatoid arthritis (arthritis brought on by swelling of the joint lining).
- ❖ juvenile arthritis (a type of joint disease in children) by reducing pain, tenderness, swelling, and stiffness.

EXCIPIENTS:

1. GELATIN

Collagen, a structural protein present in animal connective tissues, is the source of the protein gelatin.

Gelatin's biological source:

Collagen, which is isolated from animal tissues such skin, bones, and connective tissues, is the main biological source of gelatin.

Physical characteristics:

Look: Gelatin usually takes the form of granules or powder that is colorless or pale yellow.

Gelatin is liquid in hot water, but when it cools, it solidifies into a gel-like substance.

Chemical Structure

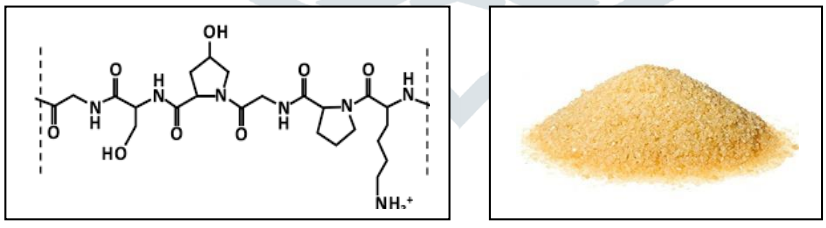

Figure 8: Gelatine's chemical structure

Uses:

1. Gelatin is utilized in the pharmaceutical industry to make capsules, tablet coatings, and drug delivery systems..

2.HYDROXYL PROPYL METHYL CELLULOSE K_{100}

Synonym: Hypromellose is a synthetic polymer derived from cellulose.

Molecular formula : $C_{56}H_{108}O_{30}$

Melting point : 225-230^{0}c

Boiling point:1101.5^{0}c

Density: 1.326g/cm^3

PHYSICAL PROPERTIES:

Appearance: HPMC is commonly available as a white to off-white powder or granules.

Solubility: HPMC is soluble in cold water, forming clear, colorless solutions.

pH Stability: 3-11

USES:

It serves as a binder, disintegrant and controlled-release agent in formulations.

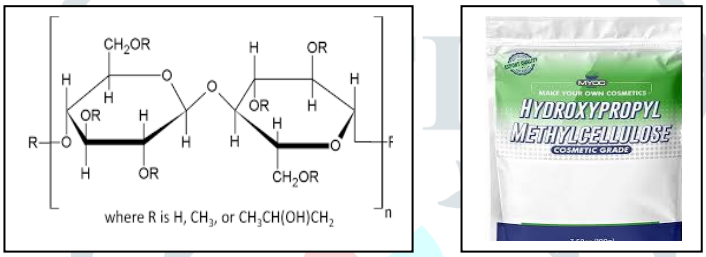

Figure 9: Chemical structure of HPMC

3. HYDROXYL ETHYL CELLULOSE

Synonym: HEC cellulose or hydroxyethyl cellulose ether.

Biological Source: Ethylene oxide and cellulose combine chemically in an etherification reaction using an alkaline catalyst to change cellulose.Structure:

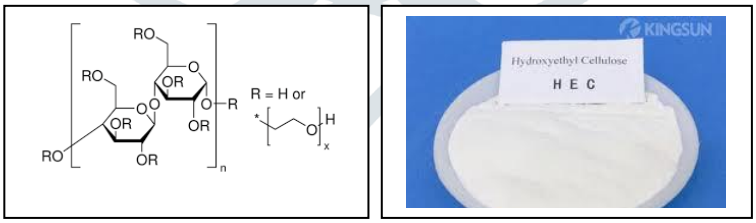

Figure 10: chemical structure of HEC

Uses:

Its capacity to modify drug release kinetics makes it suitable for usage in pharmaceuticals' controlled-release formulations.

4. EUDRAGIT S$_{100}$:

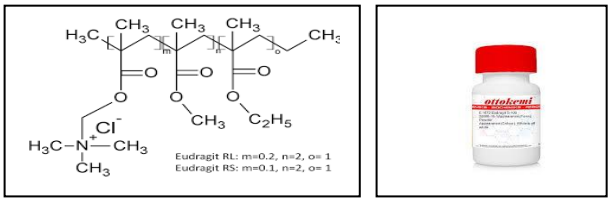

Figure 11:chemical structure of Eudragit S$_{100}$

5. CORSPOVIDONE:

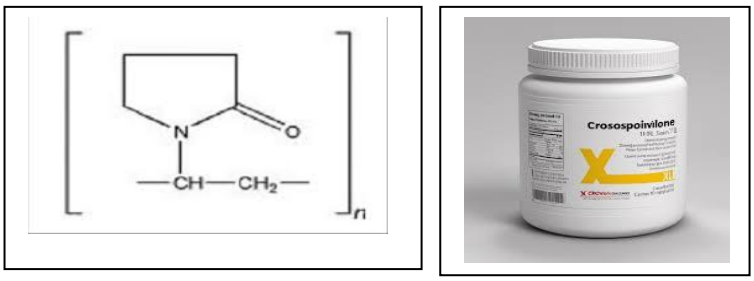

Figure 12: Chemical structure of crosprovidone

6. GLYCERINE:

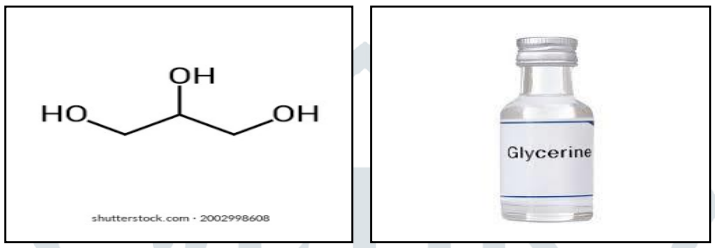

Figure 13: chemical structure of glycerine

Uses: It improves penetration.

As a result, the transdermal patch is more effective since it helps improve the drug's absorption into the bloodstream.

MAGNETIC STIRRER:

Figure 14: Magnetic Stirrer

TABLE 1: Ingredients used in naproxen sodium transdermal patches

S.NO	INGREDIENTS AND REAGENTS	MANUFACTURER/ SUPPLIERS
1	Naproxen sodium	Laurus laboratory
2	HPMC k_{100}	Oxford laboratory
3	HEC	Oxford laboratory
4	Gelatin	Oxford laboratory
5	Eudragit s_{100}	Oxford laboratory
6	Crosprovidone	Oxford laboratory

PREFORMULATION STUDIES:

Preformulation testing examines the chemical and physical characteristics of medicinal ingredients both by themselves and in combination with pharmaceutical excipients. It is the initial phase of the dosage form's logical development[15].

Studies of compatibility [Infrared spectroscopy investigations using Fourier transform]

Compatibility is one of the requirements for choosing appropriate excipients or carriers for pharmaceutical formulation. Thus, in the current work, an investigation was conducted utilizing an FT-IR spectrophotometer to determine whether naproxen sodium may potentially interact chemically with various grades of HPMC K100, HEC, and GELATINE POLYMERS.

PROCEDURE:

Solid admixtures were made by combining naproxen sodium with each polymer individually in a 1:1 ratio. The admixtures were then kept in airtight containers at 30±20c/65%rh to investigate the compatibility of different polymers with naproxen sodium. The Fourier transform infrared spectroscopy [FT-IR] was used to characterize the solid admixtures.

Using spectrometry, the absorption maxima of naproxen sodium can be calculated at 270 nm.Depending on the kind of electronic transition occurring, organic molecules in solutions absorb light of a specific wavelength when exposed to visible or ultraviolet light. In a standard cuvette, the extract solution (5, 10, 15, 20, 25 µg/ml) in distilled water was scanned between 200 and 400 nm using a UV spectrophotometer.

Reagents Preparation:

Standard medication solution preparation

A stock solution

Phosphate buffer pH 7.4 and methanol were used to create the drug's stock solution, which was then further diluted with the same pH 7.4 buffer. The UV double beam spectrophotometer was used to measure the drug absorption at 30 nm. It was discovered that the absorbance's linearity ranged from 5 to 25 µg/ml.

Phosphate buffer 7.4pH preparation

Fill a 1000 ml volumetric flask with 6.8 g of potassium dihydrogen phosphate, 0.9 g of sodium hydroxide, and water to fill the remaining volume.

Making a typical medication solution

A stock solution

A 1000µg/ml concentration was obtained by dissolving 100 mg of naproxen sodium in 100 ml of pH7.4 phosphate buffer (stock 1).

The standard method

I took 10 milliliters of the aforesaid stock, put it in a 100 milliliter volumetric flask, and added buffer to bring it up to par.

NAPROXEN SODIUM PATCH FORMULATION

Weighed and formed were the necessary amounts of dung and excipients as shown in the formulation table.

Table 1: composition of 5mg of naproxen sodium trandermal patches.

S.NO.	INGREDIENTS	F1	F2	F3	F4
1	Naproxen sodium	0.5g	0.5g	0.5g	0.5g
2	HPMC $_{100}$	1	1	-	-
3	HEC	-	-	1	-
4	Gelatin	1	-	-	-
5	Eudragit	-	-	-	1
6	Crospovidone	-	-	1	-
7	DMSO	qs	qs	qs	qs

METHODOLOGY:

Transdermal Patch Preparation:

1. Casting solution preparation

• Weigh the necessary quantity of HPMC 100 and gelatin, then add it to 10 milliliters of distilled water in an appropriate container. Give the polymer mixture fifteen minutes to hydrate.

• To the polymer solution, add the measured quantity of glycerine.

• Bring the mixture to 60°C until all of the gelatin has dissolved.

2. Drug incorporation:

• Mix the polymer glycerine solution with the weighed amount of naproxen sodium.

• To guarantee that the medication is distributed evenly, stir the mixture well.

3. Transfer to mold:

- After the medication solution has been distributed uniformly, move it to the glass mold.
- Verify that the mold is the right size for the intended patch measurements, which in this case are 25 cm2.

4. Controlled solvent evaporation:

- To prevent quick drying, which may result in an uneven medication distribution and formulation flaws, place an inverted funnel over the mold to regulate the pace of solvent evaporation.

5. Drying and solidification:

- Depending on the patch's thickness and ambient circumstances, let the solvent slowly evaporate under carefully monitored settings until the gelatine solution hardens. This process could take several hours.

6. Cutting and removing the patch:

- After the patch has hardened, carefully take it out of the mold. With the appropriate cutting tool, cut the patch to the appropriate size and form.

Figure 15 : formulated transdermal patch

EVALUATION TESTS :

Weight Uniformity:

Before the test was conducted, the prearranged patches were dried for four hours at 60 degrees Celsius. A specific piece of a clear aspect was cut from various parts of the fix and placed on a computerized balance. After that, the standard deviation and typical weight values were calculated [33], [34].

Patch Thickness:

The normal was determined by measuring the thickness of each patch at five different points along the fix using a screw gauge[35].

Percentage Moisture:

Each medicine patch was weighed separately and kept in a desiccator with blended calcium chloride for a full day at room temperature. After 24 hours, we inspect the patches and use the following equation to calculate the rate dampness content: The proportion of moisture content is [Final weight - Initial weight] x 100[36], [37].

Folding Endurance:

After being cut fairly, a section of explicit aspect repeatedly collapsed at the same location until it braked. The value of folding endurance is determined by the number of times the film was folded at the same location without breaking. [40]–[42]

Drug Content:

Using an appropriate dissolver, a predetermined patch area must be dissolved in a volumetric flask. A sensible technique (UV) is used to analyze the arrangement after it has been split by a filter medium[3,33,and43].

Permeation experiments:

The ex vivo permeation studies were conducted using a modified Franz diffusion cell system. On a Franz Call diffusion system, clipped chicken skin of the proper size was placed so that the dermis confronts the recipient cell and the stratum corneum faces the donor compartment. Ethanolic phosphate buffer pH 7.4 was added to the receptor compartment of the Franz cell, while 6 grams of patch were poured into the donor compartment. Magnetic beads were positioned within the receiver compartment to guarantee continuous stirring.

Three hours were spent on drug permeability investigations. A constant temperature of 37±0.050C was maintained. At regular intervals, the samples were extracted from the receptor cell.

Stability Studies:

For three months, the TDDS patches are kept at 40±0.5°C and 75±5% relative humidity. The specimens at 0, 30, 60, and 75 days, were taken out.

RESULTS

Several grades of polymers, including HPMC K100, HEC, gelatine, crospovidone, and eudragit, were used to create transdermal patches in matrix form using naproxen sodium for menstrual pain and pain management management.

Table 2 : Linearity range of Naproxen sodium in ph7.4 phosphate buffer.

S.NO	CONCENTRATION[µg/ml]	ABSORBANCE
1	25	0.08
2	50	0.168
3	75	0.254
4	100	0.341
5	125	0.431

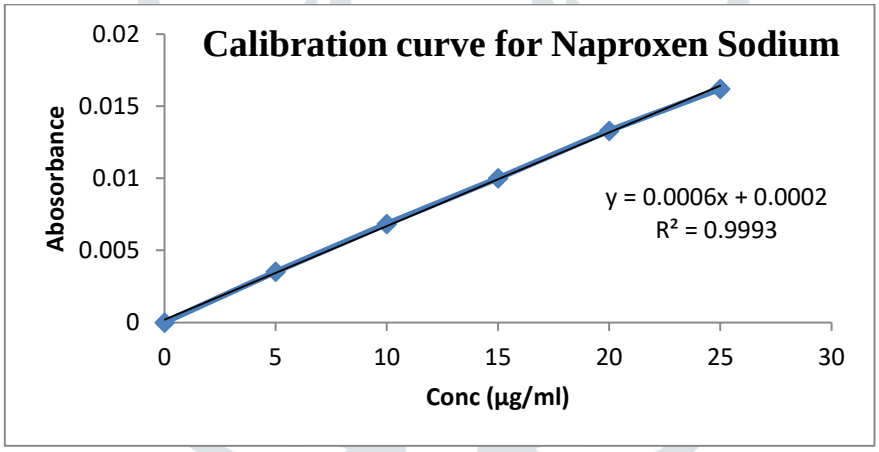

Figure 16: standard curve of naproxen sodium

DRUG POLYMER INTERACTON

File name: E:\SVU-SUCHARITHA\N.ispd
Spectrum Name: N
Sample Name: Aamb
IR Range: MID
Light Source: Infrared
Detector: standard
No.of Scans: 10
Resolution: 4 [cm-1]

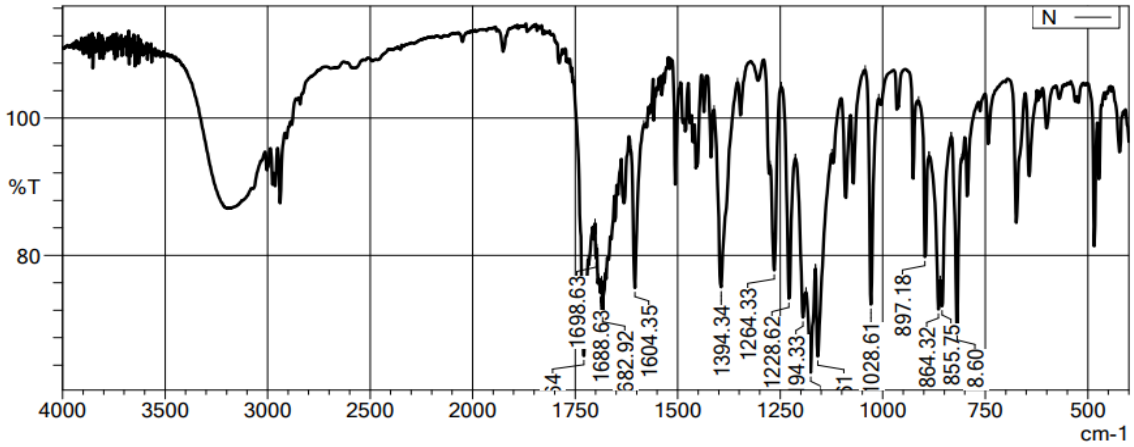

Figure 17: FT-IR Spectrum of NAPROXEN SODIUM

File name: E:\SVU-SUCHARITHA\M.ispd
Spectrum Name: M
Sample Name: Aamb
IR Range: MID
Light Source: Infrared
Detector: standard
No.of Scans: 10
Resolution: 4 [cm-1]

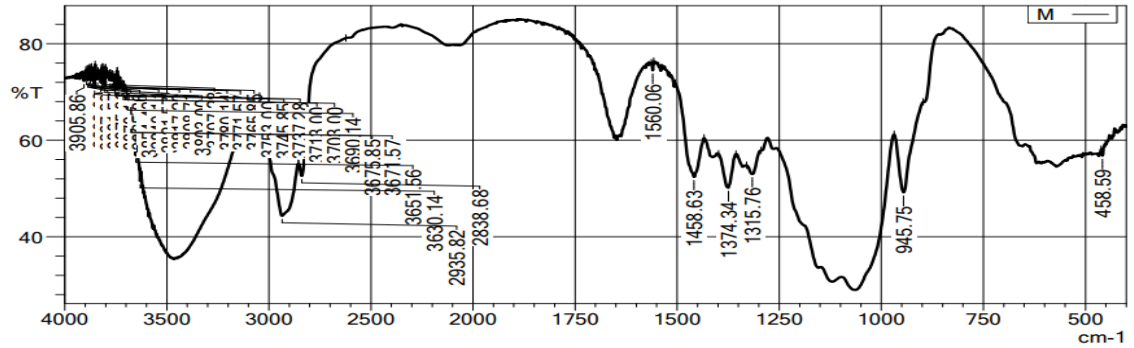

Figure 18: FT-IR Spectrum of GELATIN

File name: E:\SVU-SUCHARITHA\H.ispd
Spectrum Name: H
Sample Name: Aamb
IR Range: MID
Light Source: Infrared
Detector: standard
No.of Scans: 10
Resolution: 4 [cm-1]

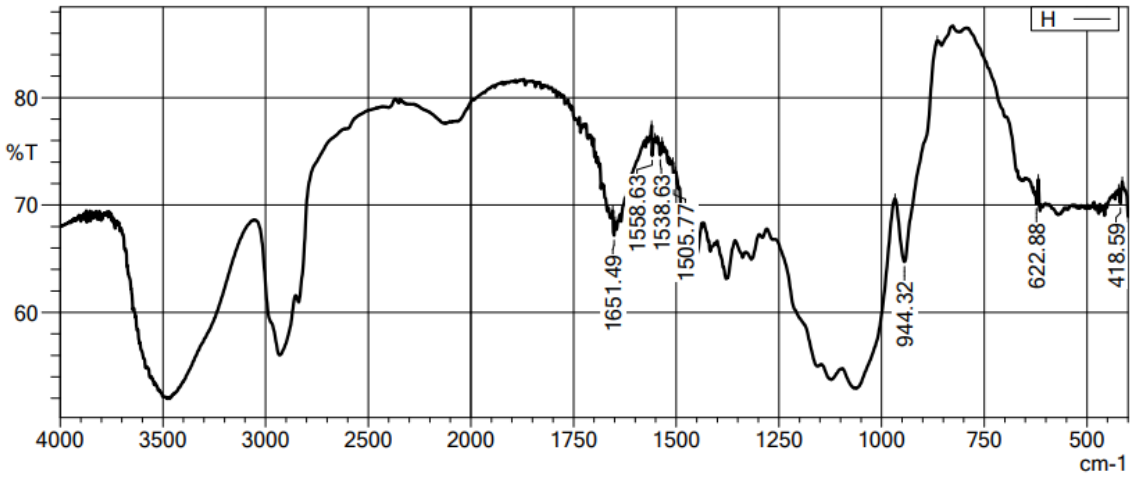

Figure 19: FT-IR Spectrum of HPMC K_{100}

File name: E:\SVU-SUCHARITHA\HM.ispd
Spectrum Name: HM
Sample Name: Aamb
IR Range: MID
Light Source: Infrared
Detector: standard
No.of Scans: 10
Resolution: 4 [cm-1]

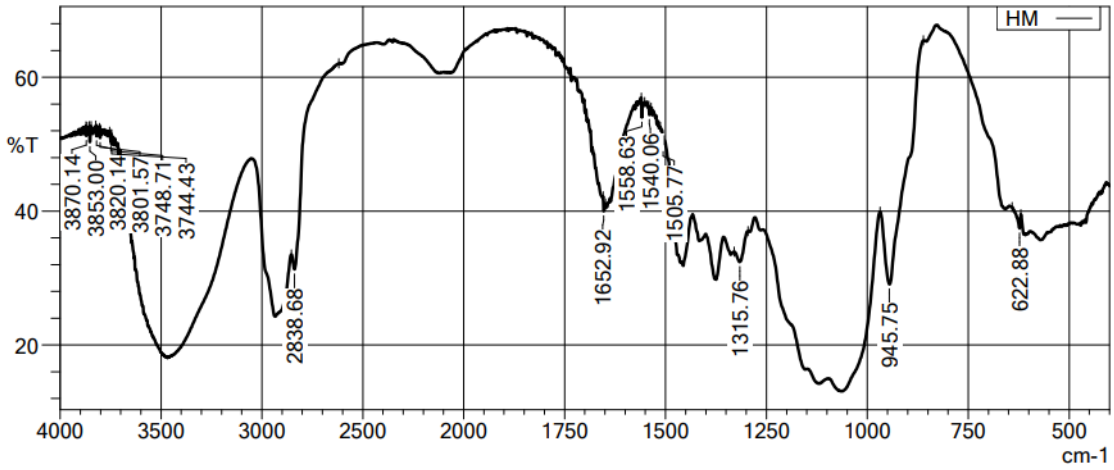

Figure 20: FT-IR Spectrum of HPMC K_{100}+GELATIN

File name: E:\SVU-SUCHARITHA\T.1spd
Spectrum Name: T
Sample Name: Aamb
IR Range: MID
Light Source: Infrared
Detector: standard
No.of Scans: 10
Resolution: 4 [cm-1]

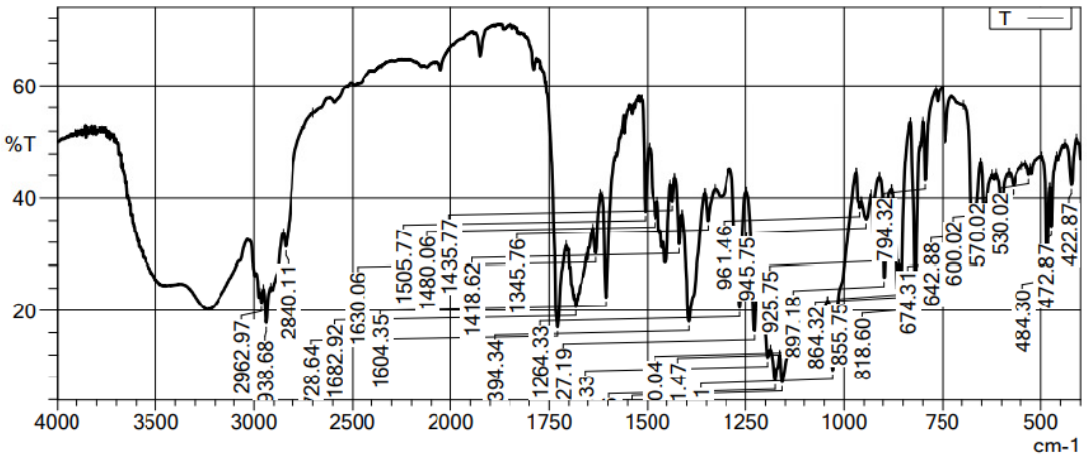

Figure 21: FT-IRSpectrumofNAPROXEN+HPMCK$_{100}$+GELATIN

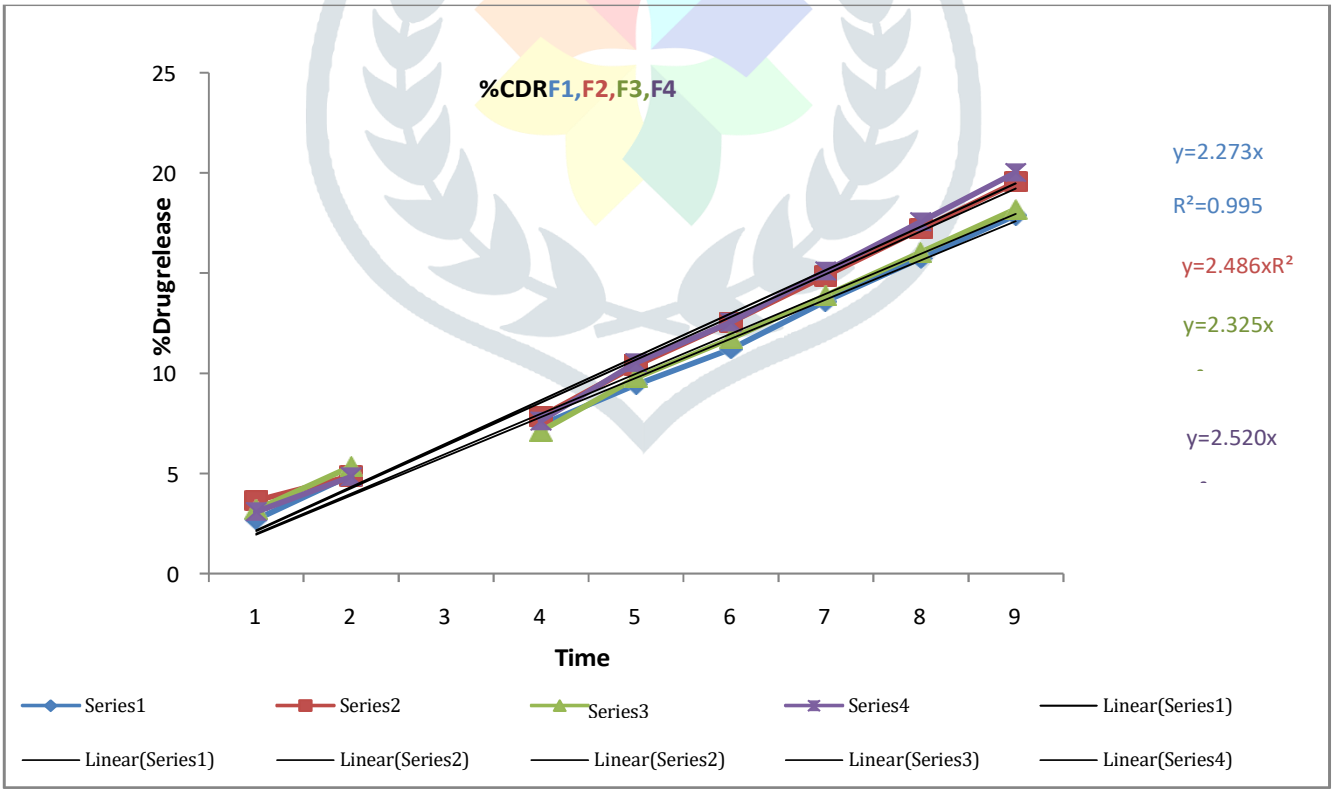

Figure 22:Cumulative drug release

Table 3: Table for %Cumulative drug release

Sno:	Time	F1	F2	F3	F4
1	90	7.432381	7.826667	7.127619	7.617143
2	120	9.438095	10.41714	9.780952	10.52762
3	150	11.21714	12.55714	11.73905	12.54
4	180	13.60019	14.86952	13.89162	15.10152
5	210	15.75124	17.204	16.04191	17.56172
6	240	17.90228	19.53847	18.19219	20.02191

Table 4: Test results are shown below

Formulation	Weight variation(mg)	Thickness (mm)	Folding endurance
F1	59±0.32	0.72±0.2	66
F2	60±0.18	0.73±0.2	64
F3	62±1.12	0.75±0.2	60
F4	61±1.17	0.80±0.2	69
F5	-	-	-

Table 5: Drug-related percentages for various formulations

Formulation	%Moisture absorbed	%Moisture Content	Drug contains (mg/cm2)
F1	13.026±1.12	6.31±0.52	39
F2	12.28±1.32	8.12±0.36	42
F3	12.58±1.62	8.64±0.23	40
F4	11.18±1.44	9.11±0.49	42
F5	12.44±1.22	9.85±0.26	44

F1

Figure 23:PatchcontainingNaproxenSodium+HPMCK$_{100}$

F2

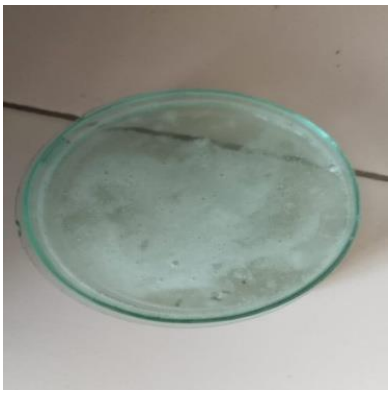

Figure24:Drug+HPMCK$_{100}$+GELATIN

F3

Figure 25: Drug + HEC

F4

Figure 26: Drug + Crospovidone

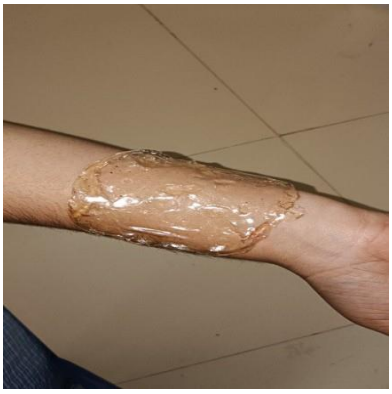

Figure 27: Patch irritancy test

Figure 28: Patch thickness

Figure 29: Diffusion test

DISCUSSION

Naproxen is a non-steroidal anti-inflammatory drug that is used to treat a number of conditions, such as cute gout, ankylosing spondylitis, bursitis, polyarticular juvenile idiopathic arthritis, osteoarthritis, tendonitis, rheumatoid arthritis, pain, and primary dysmenorrhea. Because of its long half-life (12–15 hours) and high metabolic degradation, the drug's dosage should be increased when taken orally; however, this results in a number of side effects. Additionally, naproxen's high protein binding capacity causes protein saturation at high doses, so it should be formulated as a film or patch that can be applied directly to the site of need, allowing for controlled release of the drug for 12–24 hours. After this, we can reduce the amount of drug in comparison to the oral dose of drug by directly targeting the site and minimizing side effects.

This study's primary goal is to develop a control release naproxen transdermal patch for topical use. The two distinct polymers, HPMC K100 and HEC, as regulating agents, DMSO as a permeation enhancer, polyethylene glycol as a plasticizer, and methanol: Dichloromethane (2:1) ratio as a solvent, allow us to regulate the amount of drug release. By varying the amounts of the two polymers, we can create distinct formulations while maintaining the drug's dosage (F1 to F5) and assessing their properties to obtain an optimal formulation with good release.

In-vitro Dissolution Studies:

For in-vitro dissolution studies, which are maintained at 37±0.5 0C, a 60 ml Franz diffusion cell volume and a 7.4 pH buffer are used as media. The egg membrane acts as a barrier to penetration. A 1 cm2 patch should be used for in-vitro studies, and the percentage of drug release should be calculated for each patch that forms (F1 to F5). In vitro drug release studies are necessary to predict the reproducibility of the rate and duration of drug release. High concentrations of HPMC K100 and HEC show altered drug release, while the F5 formulation shows a respectable release pattern when compared to all formulations. The proportion of drug release should vary based on the ratio of polymeric concentrations. because the quantities of methyl cellulose and HPMC K100 varied (1.5:3.5). The controlled release of naproxen was found over a 12-hour period. The best formulation for the current study was F1. As a result, F1 produces a low frequency of doses and adverse side effects by releasing the drug into the applied site or systemic circulation at the recommended rate over a prolonged period of time.

CONCLUSION

The results of naproxen with methyl cellulose and HPMC K100 patches demonstrate distinct release patterns at varying concentrations of polymers.Regarding the release research, the F6 formulation exhibits a good regulated release of the drug over a 12-hour period, whereas all of the formed patches (F1 through F6) show good assessment characteristics. Although there isn't a standard patch for this formulation, we can construct the tablet in a controlled release method, which can have a strong detrimental effect on NSAIDS over an extended length of time.Patch formulations allow us to cut the dosage and release the medicine in a controlled manner, preventing the harmful effects of numerous dosage regimens.

A painless, practical, and possibly efficient method of administering frequent dosages of numerous drugs is transdermal drug administration. Improved medication absorption and a wide variety of drug delivery Easy to use, inexpensive, and with few side effects or difficulties. As an illustration Over a million patients use nicotine patches annually to treat conditions like nitroglycerin for angina, clonidine for hypertension, scopolamine for motion sickness, and estradiol for estrogen deficiency. Ten years ago, the nicotine patch completely changed the way people quit smoking.

A pharmacological product that is currently approved as an oral dose form can be delivered transdermally to bypass first pass metabolism. The most popular method of transdermal medication administration is dermal patches. However, the outer stratum corneum layer's relative impermeability limits the use of transdermal technologies.

Researchers are attempting to use physical and chemical methods to get over this obstacle of low permeability.

REFERENCES:

1. Rita Sachan. Meenakshi Bajpai TRANSDERMAL DRUG DELIVERY SYSTEM: REVIEW International Foumal of Research and Development in Pharmacy and Life Sciences. December kinuary 2013, Vol. 3, No.1, pp 748-765Citation: Afrah addiqueet al. Tippe Haman, 2017, Vol. 11 (1) 162 176, www.ijppr.humanjournals.com
2. Prit Lakhani, Rishabh Bahl. and Piyush Bafsa, heernational journal of pharmaceutical sciences and research a review ces inandermal patches physinchemical I and in-vitro evaluation methods. Vol. 5(5): 1826-36.2014
3. Audumbar Digambar Mali, Ritesh Bathe, and Manojkumar Pazil. An updated review of tomsdermal drag delivery systems Interacional oumal of Advances in Scientific Resmech 2015, 1406) 244-254
4. Hanın Rasheed Shailt, HariBaba R. KhajaMchaddın Md, Viacela J. Transdermal Drug Delivery SystemSimplified Medication Regimen A Review, Research Journal of Pharmaceutical. Biological, and Chemical Sciences, 2011, 2(4): 223-238
5. Dhimus Sonia, Singh Thakur Gurjeet, Rehmi Ashish Kumar. Transdermal Patches: A Recrim Approach to New Daug Delivery System. Int J Pharm Pharm Sci, 2011; 3(5):26-34.
6. Sharma Ajay, Saini Seenu, Rana AC. Transalernal Drag Dehvery System of Researchin Pharmaceutical and Biomedical, 2013, 4(1): 286-292.
7. Saini Nicin, Bajaj Ashal. Review Article Recem Trend in Transdermal Druz Delivery System and Advancemens in Drug Delivery through Skin. Intemational Journal Biosciences, 2014, 4(1): 5-14,
8. Halgral1,GuyR.H.TransdermalDragDelivery2nded.NewYork:MarcelDekker,

i. 35.P.14-16,

9. SandauPremjeeAjayBilaadi,KatanaSahitandMiddhaAkanksha. TRANSDERMAL DRUG DELIVERY SYSTEM (PATCHES), APPLICATIONS IN PRESENT SCENARICI INTERNATIKINAL JOURNAL OF RESEARCH IN PHARMACY AND CHEMISTRY 2011, .
10. Ogundeye O. Bums Overview. Physiopodia. 2021. hitps://www.physio- pedia.com/index.php?title-Burm Overview&oldid-3636-66 Accessed on Nith April 2021.
11. Hettinmatchy S, Deiewuski P. ABC of buree Pathophysiology and Types of Barus, British Medical Journal 2004: 328 1427-1429

12. Yin S. Chemical and Coramon Herns in Children, limeal Pediatrics (Phila). May 2017; 56 (5 Supplic 8 S-125.
13. Gucugnuud PY, Caron H, Bertin-Maghit M. Petit P. Current Advances in the Initial Management of Major Thermal Burm. Crifcal Care Medicine. 2000; 26; 848-856
14. Nguyen CM, Chandler R, Ratunshi I and Logsetty S. In: Jeschke MG. Kamole LP, Sjöberg F and Wolf SE Eds. Handbook of Burns, Vol. Springer. 2020; pp. 529-547,
15. Kirkpatrick If, Enion DS, Burd DA.Hydrefronic Acid Bumse A review Burns 1995 21:483-493.
16. Kalsi R. Vandana KL. Prakash S. Effect of local drug delivery in chronic periodontitis patients:A meta-analysis. J Indian Soc Periodontol. 2011;15:304-9.
17. Indianpharmacopoeia2007,volume-1:477-480.
18. Greenstein G, Polson A. The role of local drug delivery in management of periodontal disease: A comprehensive review. J Periodontol. 1998;69:507-20. [Scholar]
19. Francetti L, Trombelli L, Lombardo G. Guida L, Cafiero C, Roccuzzo M, et al. Evaluation of efficacy of enamel matrix derivative in the treatment of intrabony defects: A 24-month multicenter study. Int J Periodontics Restorative Dent. 2005;25:461-73.
20. Pandita V, Patthi B, Singla A, Singh S, Malhi R, Vashishtha V. Dentistry meetsnature -role of herbs in periodontal care: A systematic review. J Indian Assoc Public Health Dent. 2014;1:148-56
21. Kaur A, Kapoor D, Soni N, Gill S. Phytodentistry-a boon? Arch of Dentand Med 1 2016;2:35-41.
22. Srivastav S, Singh P, Mishra G, Jha KK, Khosa RL. Achyranthes aspera - An important medicinal plant: A review. J Nat Prod Plant Resour. 2011;1:1-14. [Google Scholar]
23. Haffajee AD, Socransky SS. Microbial etiological agents of destructive periodontal diseases. Periodontol 2000. 1994;5:78-111. [PubMed] [Google Scholar]
24. Van Winkelhoff AJ, Rams TE, Slots J. Systemic antibiotic therapy in periodontics. Periodontol 2000. 1996;10:45-78. [PubMed] [Google Scholar]
25. Rams TE, Slots J. Local delivery of antimicrobial agents in the periodontal pocket. Periodontol 2000. 1996;10:139-59. [PubMed] [Google Scholar]
26. Francetti L, Trombelli L, Lombardo G. Guida L, Cafiero C, Roccuzzo M, et al. Evaluation of efficacy of enamel matrix derivative in the treatment of intrabony defects: A 24-month multicenter study. Int J Periodontics Restorative Dent. 2005:25:461.
27. Thombre K., Sharma D., Lanjewar A. Formulation and Evaluation Pharmaceutical Aqueous Gel of Powdered Cordia Dichotoma Leaves With Guava Leaves. Am. J. PharmTech Res. 2018:8:268-277. doi: 10.46624/ajptr.2018.v8.i2.022.
28. Das S., Haldar P., Pramanik G. Formulation and Evaluation of Herbal Gel Containing Clerodendron infortunatum Leaves Extract. Int. J. Pharm. Tech. Res. 2011;1:104-143.
29. Bharathi V., Badrinarayanan V., Gomathi S., Shanmugapriya A., Karpagam T. Antibacterial activity of Tridax procumbens Linn. Int. J. Pharma Sci. Res. 2012;3:364-367.
30. Patel C, Mangukia D. Asija R, Asija S, Kataria S, Patel P. Formulation and evaluationof matrix diffusion controlled transdermal drug delivery.system of Glipizide. Journalof Drug Delivery & Therapeutics 2012; 2: 1-8.
31. Anon. Transdermal delivery systems-general drug release standards. Pharmacopeial Forum 1980; 14 3860-3865.
32. Chirag P and Dhruv M. Transdermal Drug Delivery System (TDDS): Formulation and evaluation of matrix diffusion controlled transdemal
33. Shingade GM, Aamer Q. Sabale PM, Grampurohit ND, Gadhave MV. Jadhav SL, Gaikwad DD. Review On: Recent Trend on Transdermal Drug Delivery System. Journal of Drug Delivery & Therapeuics 2012, 2: 66- 75.
34. SantoshG,DhavalP,ManteshK, Ajay S,Vital V(2009) Formulation and evaluation of matrix type transdermal patches of Glibenclamide. Int J of Pharmaceutical Sciences and Drug Research 1(1), 46-50.
35. Murthy SN, Rani S. Hiremath R (2001) Formulation and evaluation of controlled release transdermal patches of theophylline-

salbutamol sulphate. Indian Jonenal of Pharmaceutical Education and Research 27(2) 1057-1062.

36. Saxena M, Mutalik S, Reddy MS (2005) Formulation and evaluation of transcćermal patches of metoclopramide hydrochloride, indian drugs 43(9): 740-745.
37. Mali AD, Bathe R, Patil M (2015) An updated review on transdermal drug delivery systems. International Journal of Advances in Scientific Research 1(06): 244-254
38. Darwhekar G, Jain DK, Patidar PK (2011) Formulation and evaluation of transcermal drug delivery system of Clopidogrel bisulfate. Asian Journal of Pharmacy and Life Science 1(3): 26
39. Prabhakar P. Shah S. Gundad (2011) Formulation development and investigation of Domperidone transdermal patches Int J of Pharm Investig 1(4): 240-246.
40. Jadhav RT, Kasture PV, Gattani SG, Surana SJ (2009) Formulation and evaluation of transdermal films of diclofenac sodium, Int. J. Pharmtech Res 1(4): 1507-1511.
41. Rhaghuram RK, Muttalik S. Reddy S. Once-daily sustained-release matrix tablets ofnicorandil: formulation and in vitro evaluation. AAPS Pharm Sci Tech 2003;4: 4.
42. Shaila L., Pandey S, Udupa N. Design and evaluation of matrix type membrane controlled Transdermal drug delivery system of nicotin suitable for use in smoking cessation. Indian Journ Pharm Sci 2006; 68: 179-184.