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FORMULATION AND EVALUATION AND PILOT PRODUCTION OF TRANSDERMAL DRUG DELIVERY SYSTEM

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Abstract

Thiocolchicoside is used for the controlling the painful muscle spasm in the cervical spondylitis and arthritis. Thiocolchicoside was found to be compatible with Eudragit L100 and HPMC and they were used in the formulation. The flux of the Thiococolchicoside was found to be 30µgm/cm^2/hr and calculated dose in the patch was about 16.36mg per patch for providing the release over 48hrs. Ginger oil along with DMSO, oleic acid and ginger oil was investigated for the permeation enhancement. Ginger oil at 4% provided the highest flux of 41µgm/cm/hr over 24hrs on 1% solution of drug. The effect of adhesive on the permeation of the drug was also investigated and Dura Tak-87-6908 was selected & used as the adhesive in the formulation. The bioadhesivity evaluation apparatus was developed and force transducers. The formulation was optimized with full factorial design and the final batch was formulated and tested for all quality control parameters. The final formulation was casted on the pilot scale lab coater developed in the studies. The prepared batch was also tested for the skin irritation and sensitization. The final preparation was tested for stability at 40°C±5°C and RH 75% and it was found to be stable in the stability studies.

Key words: Thiocolchicoside, Transdermal Patch, Bioadhesivity, optimization, permeation enhancers.

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INTRODUCTION

To overcome the cons of oral , intravenous and other drug delivery methods, the Transdermal drug delivery system provide the most efficient system for drug delivery system. The stratum corneum, however, acts as a strong inhibition barrier of foreign substances examples include in case of drugs, hormones, peptides and proteins. The activation of the barrier in the stratum corneum and the biological characteristics of drug molecules such as cellsize and polarity impede their ability to improve drug transport (2). Several ideas have been developed to overcome this disadvantage and improve the permeability of the stratum corneum. These strategies are based on active or passive methods Passive systems depend on factors such as diffusion, solubility and or mobility gradient, where the active pathways involve external agents in penetration such as iontophoresis, sonophoresis etc. Atpresent many, new methods have been shown to bypass or modify the skin barrier function to allow easy passage of drugs into the dermal circulation (4). Transdermal drug delivery has been designed with a promising research interest since the launch of the first Transdermal product.

Advantages

i) They bypass through complex drug reactions such as altered stomach pH, enzymatic activityand drug interactions.

ii) Oral administration may be replaced by TDDS when the route is less favorable in the event ofvomiting and diarrhea.

iii) .

1.1.2. Disadvantages

i) Contact dermatitis in some cases on applying the Transdermal drug delivery system.

ii) Very selected drugs can be formulated in the Transdermal drug delivery system .

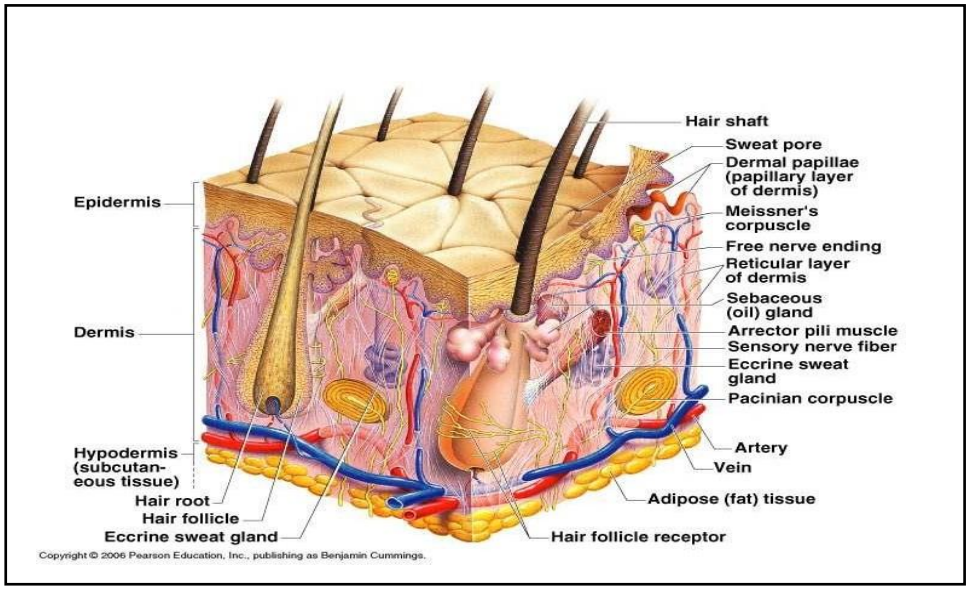


Figure 1: Structure of skin

Physicochemical factors

Hydration of skin

Hydration of the skin increases the skin permeability. Skin cells swells on contact with the water and increased hydration increases the permeability (18).

1.3.2.2.Temperature and pH of the skin Skin elasticity decreases with the decrease in the temperature and permeation rate also varies with it. Thus,

adequate fabrics on the skin prevent the fluctuations in the temperature and thus improve the permeation. On the other hand the unionized particles pass through the skin.

Polymer matrix/drug reservoir

Polymers are the used in the Transdermal drug delivery system to regulate the release of the drug from the polymer system . The drug is added into the drug polymer system and drug is slowly released from the polymer matrix.

Membrane

Membranes are mounted on the surface of the drug reservoir and they are used to study the permeation and the drug diffusion characteristics.. Concentration gradient pushes the drug across the membrane. Examples are ethylene vinyl acetate, rubber silicone, poly urethane, etc

Drugs

Drug candidates are selected very carefully for the Transdermal drug delivery systems . Usually, drugs with low molecular weight and potent in dose are selected for the Transdermal drug delivery system. The drugs need to have short half-life life along with narrow therapeutic window.

Prodrug

The use of prodrug may enhance the re-delivery of drugs with an unfavorable partition coefficient or solubility nal groups into the pro-moiety will increase not only lipid but also water solubility (35).

MATERIALSANDMETHODS

Thiocolchicoside (TH; M/s Mega Chem Pvt. LTD. India), As a Gift Sample, Eudragit-E 100 (RanbaxyFine Chemical Limited, New Delhi.) and Carbopol 940 (LobaChemie Pvt., Mumbai-400002,India), Carbopol 934, HPMC (Hydroxypropyl methyl cellulose) (Himedia Laboratories Pvt.Ltd. Mumbai, India). All other ingredients used invarious studies were of analytical grade and were employed as such as procured. Double distilled water was used duringthe experiment.

Identification of Drug

Physical Appearance

Drug was tested for the organoleptic properties like taste, odor and color

Determination of melting point of Thiocolchicoside

A small amount of Thiocolchicoside was taken on watch glass. Next a capillary was taken and its one end was fused on flame. A small amount of drug was pushed into capillary through open end and further capillary was tapped slightly sealed end pointing towards the ground.

Determination of saturation solubility in water and other solvents

Saturation solubility was determined by flask shaking method. Excess amount of drug was added to 25 ml of distilled water in 250 ml conical flask placed in orbital shaker at 37^{0}C for 72 hrs . Determination of λmaxA minimum amount of drug was dissolved in the phosphate buffer pH7.4. This wasscanned in the range of 200-400 nm over the U.V spectrophotometer

Conformation of structure by Infra-red spectroscopy

The structures of drug and polymer were confirmed by the IR spectroscopy

Compatibility Studies

Drug and its physical mixtures were prepared and placed in petri plates. Afterwards these were stored over for a period of 1 month . Then after 1 month physical mixtures were visualized and IR and DSC were carried out to find any interaction.

Calibration Curve

Preparation of stock Solution in phosphate buffer pH 7.4

100 mg of drug was dissolved in phosphate buffer pH7.4 to prepare 1mg/ml solution thatis of concentration of 1000µg . Then 10 ml of this solution was taken and volume wasmade up to 100 ml again with phosphate buffer pH 7.4 having concentration 100µg/ml. This was taken as stock solution.

Construction of calibration curve

A UV-Visible spectrophotometer was employed in the absorbance determination of samples concentration ranging from1-10 µ gm/ml. Further different test samples were analyzed at wavelength 259.5nm.

The permeation and flux rate through the skin was determined on the modified Franz diffusion cell. Pig ears were obtained from the local slaughter house . Ears were collected immediately after scarifying the animals and transported to laboratory within one to two hrs in ice cooled normal saline to prevent any loss of the tissue

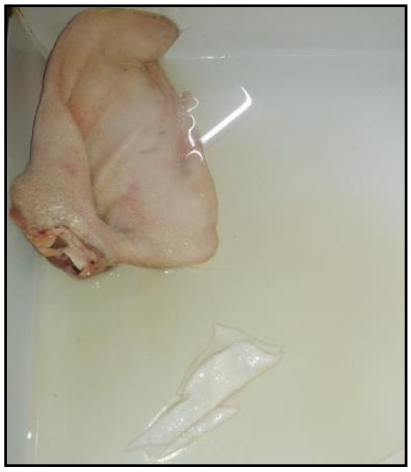


Figure 13: Pig ear

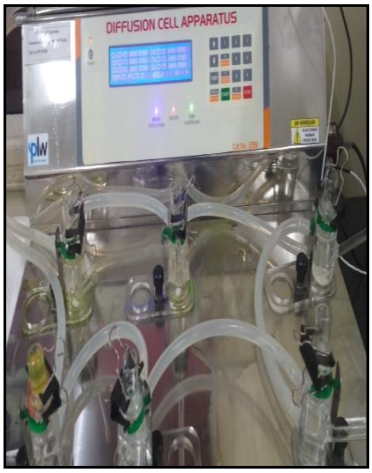


Figure 14: Franz diffusion cell

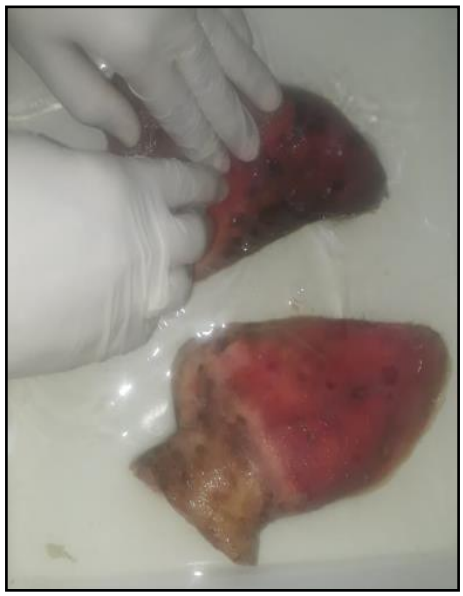


Figure 15: Shaved Pig ear

Figure 16: Permeation studythrough Franz diffusion cell

Determination of the effect of the adhesives on the permeation of the drug :

The different concentrations of the adhesive ranging from 0.5%, 1.0%, 1.5%.....up to 4% was used to study the effect of the adhesives on the permeation of the Thiocolchicoside across the pig ear skin.

Study the effect of permeation enhancers on the permeation of drug through the Pig Ear Skin

Ginger Oil, DMSO, Lemon Grass Oil, and Eugenol, and Oleic Acid were investigated for their effect on permeation of drug across the pig ear skin. Permeation enhancers were used in the concentration from 1%, 2%, 2.5% , 3% and 4% respectively. The permeation of the drug across the pig ear skin was calculated.

Formulation of Transdermal Patch:

The suitability of the polymers and solvent system for casting as film was determined by employing the drug polymer compatibility study. The polymer which was compatible with the Thiocolchicoside were subjected to the placebo patch making with desired solvents. The composition of various solvents and polymers used in the study are given in Table 5.3 and 5.4.

Table 5.3: Formulation Trials- Set 1

Formulationcode	Polymer	Qty	Polymer	Qty	Solvent system (ml)	Plasticizer (ml)	Cross linking agent(ml)
T1	Eudragit E100	750mg	Nil	0 mg	20 ml	5 ml	2ml
T2	Eudragit E100	500mg	PVP K30	250mg	20 ml	5 ml	2ml
T3	HPMC	750mg	Nil	0 mg	20 ml	5 ml	2ml
T4	HPMC	500mg	PVP K30	250mg	20 ml	5 ml	2ml
T5	Eudragit L100	750mg	Nil	0mg	20 ml	5 ml	2ml
T6	Eudragit L100	500mg	PVP K30	250mg	20 ml	5 ml	2ml
T7	Ethyl Cellulose	750mg	Nil	0 mg	20 ml	5 ml	2ml
T8	Ethyl Cellulose	500mg	PVP K30	250mg	20 ml	5 ml	2ml
T9	Eudragit RLPO	750mg	Nil	0 mg	20 ml	5 ml	2ml
T10	Eudragit RLPO	500mg	PVP K30	250mg	20 ml	5 ml	2ml”

Table 5.4.: Formulation Trials -Set 2

Formulation Code	Polymer	Qty	Polymer	Qty	Solvent system	Plasticizer (ml)	Crosslinking agent(ml)
ST1	Eudragit E100	750mg	Nil	0 mg	20 ml	5 ml	2ml
ST2	Eudragit E100	375mg	PVP K30	375 mg	20 ml	5 ml	2ml
ST3	HPMC	750mg	Nil	0 mg	20 ml	5 ml	2ml
ST4	HPMC	375mg	PVP K30	375 mg	20 ml	5 ml	2ml
ST5	Eudragit L100	750mg	Nil	0mg	20 ml	5 ml	2ml
ST6	Eudragit L100	375mg	PVPK30	375 mg	20 ml	5 ml	2ml
ST7	Ethyl Cellulose	750mg	Nil	0 mg	20 ml	5 ml	2ml
ST8	Ethyl Cellulose	375mg	PVPK30	375 mg	20 ml	5 ml	2ml
ST9	Eudragit RLPO	750mg	Nil	0 mg	20 ml	5 ml	2ml
ST10	Eudragit RLPO	375mg	PVP K30	375 mg	20 ml	5 ml	2ml

Evaluation

Visual Inspection: Visual inspection of the patches was done in order to determine their shape ,morphology and

appearance.

Weight variation and thickness:

Individual patches were weighed on the electronic balance and next the mean weight and standard deviation was measured. Thickness of the patch was measured from three points with screw gauze. (168).

Drug content Drug content uniformity of Thiocolchicoside:

Transdermal patch was taken and dissolved in the 100 ml of the phosphate buffer (PBS

7.40. The content was stirred well on the homogenizer. the mixture was filtered through the Whatman filter paper 0.45 µm and then it was assessed over the UV spectrophotometerat 259.5nm(169).

Folding endurance test:

In this test, the patch was folded repeatedly at the same place for several times until it broke down. The number was counted. This test is done in order to check the efficiency of the plasticizer and crosslinking agent (170).

Moisture Uptake

The accurately weighed films were kept in the desiccator at the RH of 75%. (171) Change in the weight of the patches after 24 hrs was measured by the formula

% Moisture Uptake = (Final Weight – Initial Weight) /Initial Weight × 100

In vitro Drug Release Studies

In vitro drug release studies were performed by using a Franz diffusion cell . The capacity of the donor and receptor compartment was determined. Volume of the donor compartment was found to be 3.319 cm^3 and the area was found to be 1.3263 cm^2. Pig ear skin was used in the study. PBS 7.4 was used as the receptor medium and the temperature was maintained at 37.5℃ during the studies. The sample of the drug permeated was taken at different intervals and analyzed at 259.5nm(174).

Skin irritation test(20)(21)(22)

All animal experiments were carried out in accordance with the guidelines of CPCSEA and the protocol was approved by the Institutional Animal Ethical Committee, (Registeration No:2068/PO/ReRc/S/20/CPCSEA) University Institute of Pharma Science, Nagpur University. An optimized patch was used for the skin irritation studies on the rabbit.

- Dermal irritation is the production of reversible damage of the skin following the application of a test chemical for up to 4 hours .
- Dermal corrosion is the production of irreversible damage of the skin; namely, visible necrosis through the epidermis and into the dermis, following the application of a test chemical for up to four hours .

The erythema scale was as: 0 - None; 1 - Slight; 2 - Well defined; 3 - Moderate; and 4 - Scare formation.

The edema scale was: 0 - None; 1 - Slight; 2 - Well defined; 3 - Moderate; and 4 –Severe .

Skin Sensitization test

Skin sensitization was tested for the optimized patches. Guinea pig was used in the study.

- Skin sensitization studies was carried out on the Guinea Pig. Test was carried out in three groups comprising positive, negative and placebo groups having two animals each.
- 6 healthy guinea pigs were assigned to three groups and study was carried out.
- A positive control group that received 0.1% w/v 1-chloro-2,4-dinitrobenzene (CDNB) in 10% propylene glycol as a standard skin sensitizing agent.

RESULTS AND DISCUSSION

Pre-formulation Studies of the Thiocolchicoside with polymers:

Drug identification and various Pre-formulation test were carried out for the drug and

polymers used in the formulation development.

Identification of the Drug:

Physical appearance: Faint yellow to dark yellow powder

Determination of the Melting Point: Melting point of the Thiocolchicoside was determined experimentally by capillary fusion method on melting point apparatus and it was found in range 190-198 ℃ (Table-6.1).

Table 6.1.: Melting point of Thiocolchicoside

Drug	**Melting Point**			**Mean /Range**
	Trial 1	**Trial 2**	**Trial 3**	
Thiocolchicoside	198 ℃	194 ℃	198 ℃	194-198 ℃.

Solubility of the Thiocolchicoside:(53)

Thiocolchicoside was tested for solubility in 0.1N HCl, water, pH 4.5 Acetate buffer, pH 6.8 andpH 7.4 Phosphate buffers. It showed good solubility of 0.2958±0.0065 µg/ml in 0.1N HCl and 0.2019±0.0024µg/ml in water.

Table 6.2.: Solubility of Thiocolchicoside

Drug	**Solubility in water**	**Solubility in 0.1N HCl**	**Solubility in pH 4.5 acetate buffer**	**Solubility in pH 6.8 PBS**	**Solubility in pH 7.4 PBS**
Thiocolchicoside	0.2019±0.0024 µg/ml	0.2958±0.0065 µg/ml	0.2698±0.0095 µg/ml	0.1054±0.0024 µg/ml	0.1924±0.0058 µg/ml

Partition Coefficient Of Thiocolchicoside :

The partition coefficients of Thiocolchicoside in different molar ratio were determined between pH-7.4 phosphate buffer and n-octanol.. The compounds were dissolved in aqueous phase (5 mg/ml). The buffer/octanol solutions were shaken for 8 hr at room temperature. After separation of the samples, into two phases. Thiocolchicoside was analyzed spectrophotometric ally at λ max 259.50 nm.

Determination of λ max and plotting the standard curve:

A stock solution of Thiocolchicoside in phosphate buffer pH 7.4 was prepared and serial dilutions ranging from 1 µl,2 µl…….to 10 µl were made. Spectrum analysis of the drug was done and peaks were recorded (Table-6.4)

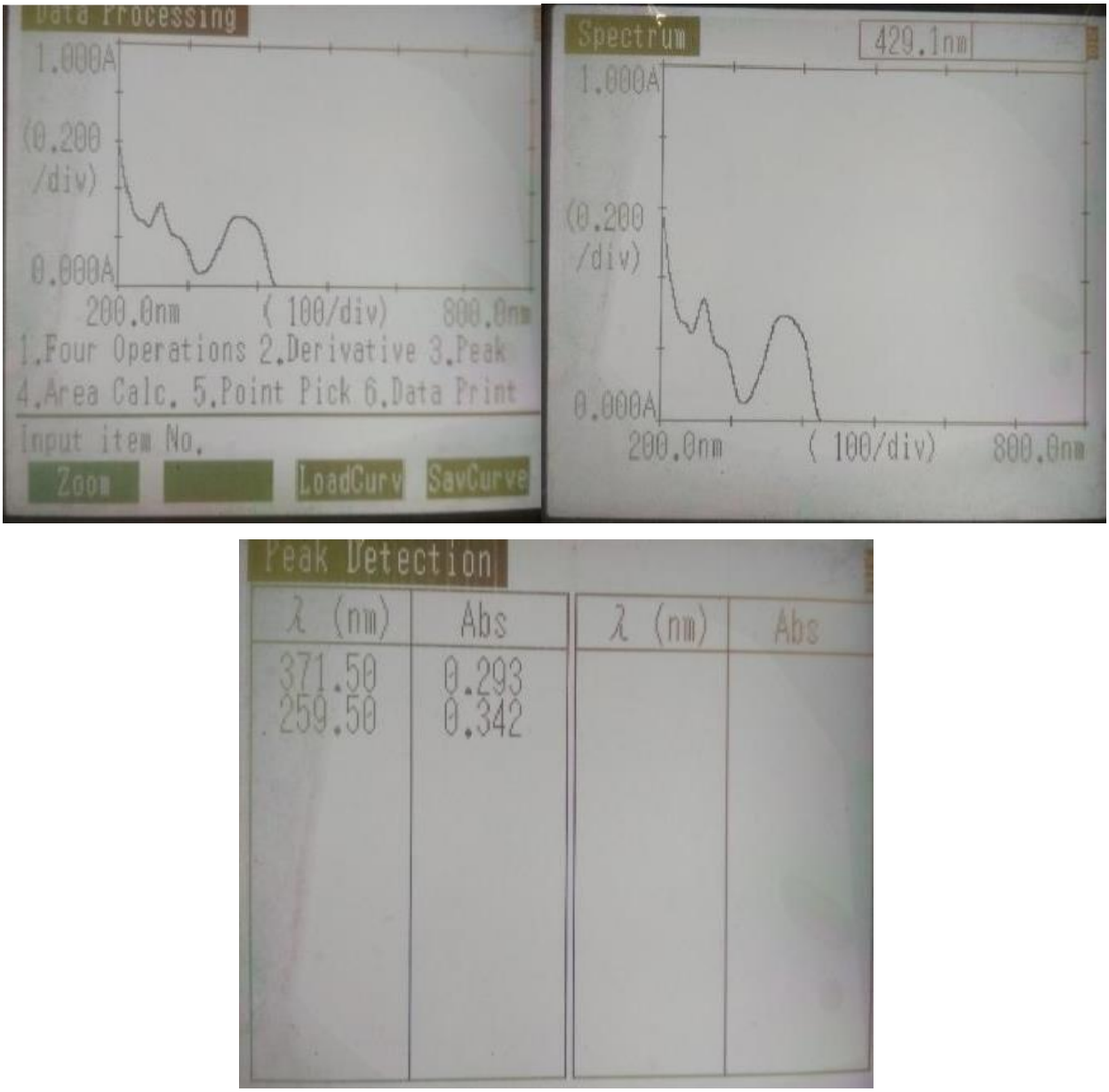


Figure 19: UV spectra of Thiocolchicoside and determination of the λ max

Table 6.4.: UV spectra of drug and determination of the λmax

S.No.	Wavelength(nm)	Absorbance
1	259.5	0.342*
2	371.5	0.293*

Dilutions of the Thiocolchicoside solutions ranging from 1 to5 µg/ml were prepared and scanned at 259.5nm. The experiment was replicated three times and standard deviation was calculated. Table 6.5 depicts the Absorbance for thiocolchicoside in phosphate buffer 7.4 at various concentrations.

Table 6.5.: Calibration curve of Thiocolchicoside

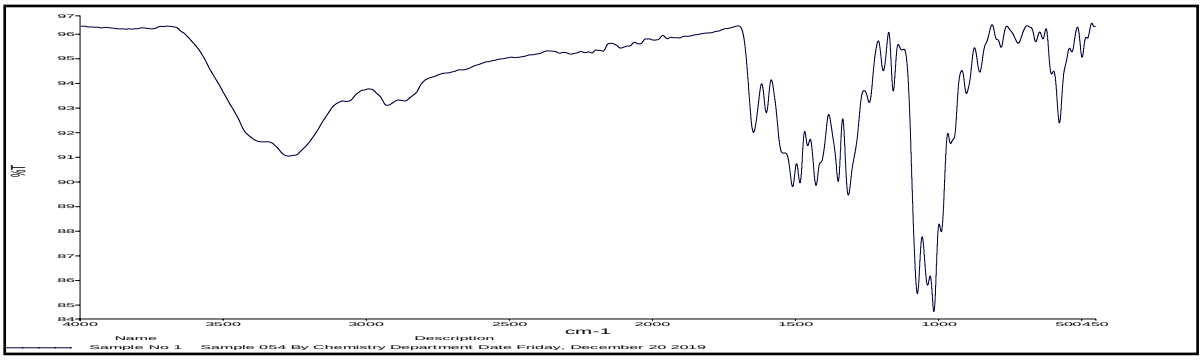
Conc(µg/ml)	**Absorbance(±S.D)**
1 µg/ml	0.034(±0.0005)
2 µg/ml	0.066(±0.0020)
3 µg/ml	0.098(±0.001)
4 µg/ml	0.126(±0.002)
5 µg/ml	0.159(±0.003)

Graph 6.1.: Concentration vs Absorbance plot for Thiocolchicoside in PBS 7.4 pH

The validation parameters for the Thiocolchicoside in PBS 7.4 are given in Table 6.6. The LOD for Thiocolchicoside was calculated as 0.048µg/ml. its limit for quantification was calculated as 0.161µg/ml. The accuracy of the analytical procedure was found to be 98.25±0.98 and precession was calculated as 96.89±1.45.

Drug Polymer Identification

IR spectrophotometry was used in order to identify the Thiocolchicoside and polymers and theirelaboration is given as under:



Determination of flux of the Thiocolchicoside across pig ear skin:

The permeation and flux rate through the skin was determined on the modified Franz diffusion cell. Pig ears were obtained from the local slaughter house. Pig ears were collected immediately after the sacrifice of the animals and transported to laboratory within one to two hrs in ice coolednormal saline to prevent any loss of

the tissue. A uniform thickness 1mm skin portion was taken and mounted on the diffusion cell. The volume of the receptor compartment and donor compartment was determined. Volume of the donor compartment was found to be 3.319 cm^3 and the area was found to be 1.3263 cm^2. PBS 7.4 was used as the receptor medium and the temperature was maintained at 37.5 ℃ during the studies. The λ max of the drug was found to be 259.5nm. Completely saturated solution of the Thiocolchicoside was prepared and placed in the donor compartment. 1 ml samples were withdrawn at 0, 1, 2, 3, 4, 6, 8, and 24 hrs. Each withdrawn aliquot was replaced with an equal volume of receptor phase. Subsequently Thiocolchicoside solution of 50 %, 40%, 30%, 20% and 10% concentration, were prepared and studied on the Franz diffusion cell. The flux of the drug was calculated from the data.

Figure 36: Permeation studies of Thiocolchicoside across pig ear skin on Franz Diffusioncell

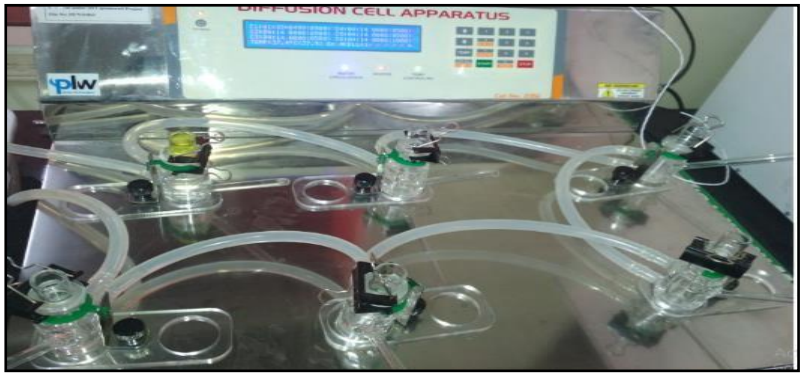


Figure 37: Thiocolchicoside Diffusion studies

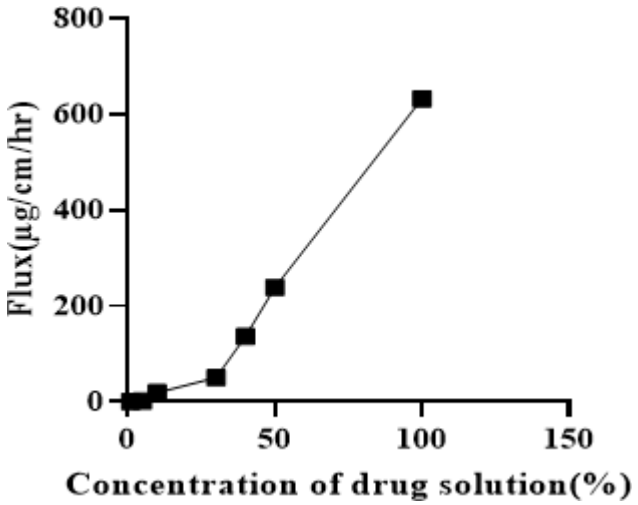
After the UV Spectrophotometric evaluation, the flux of the drug was found out to be 30 µg/cm^2

/hr. The linear part of the curve was used for the determination of the steady state flux (J) and the permeability coefficient (P), by means of Fick's equation for steady state membrane transport:

Flux of the Thiocolchicoside:

Table 6.15: Flux of Thiocolchicoside at Different Concentration of Thiococlchicoside Solution

Concentration of Thiocolchicoside solution	**Slope**	**Permeabilitycoefficient**	**Flux(µg/cm^2/hr)**
100%	2.515	6.323	632.370
50%	1.898	4.772	238.616
40%	1.356	3.409	136.380
30%	0.665	1.672	50.162
10%	0.747	1.878	18.782
5%	0.234	0.588	1.950
1%	0.142	0.105	0.350



Effect of Permeation Enhancer and Adhesive on the Permeation of Thiocolchicoside solution :

The permeation of the Thiocolchicoside along with the adhesives was also calculated in the study.It was calculated in order to determine the best adhesive which could provide sufficient support, tackiness and release of the drug from the transdermal drug delivery system. Table 6.17 representsthe flux of Thiocolchicoside solution along with various concentration of adhesives across the pigear skin.

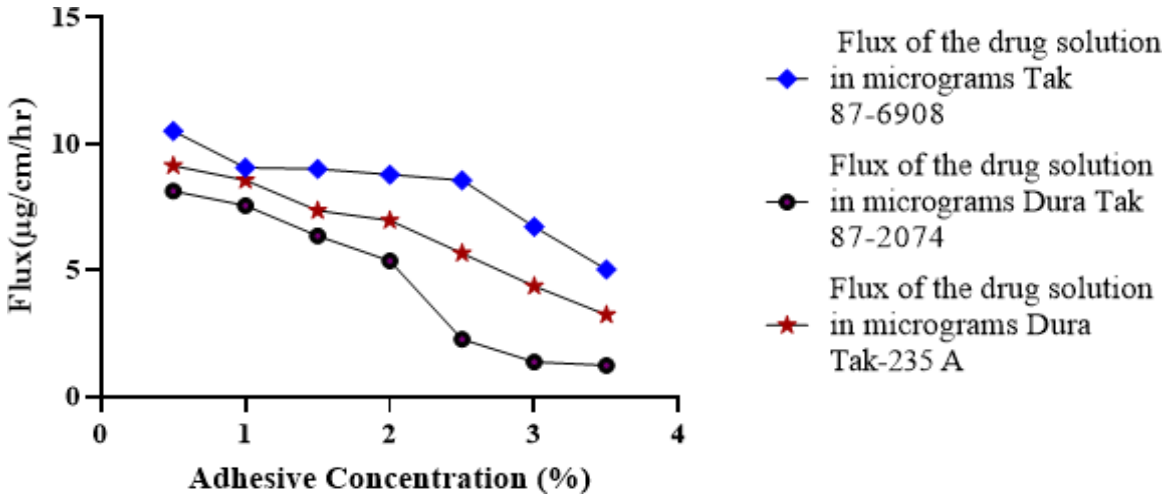


Figure 40.: Graph between flux of the Thiocolchicoside and Adhesive concentration

The flux of the Thiocolchicoside across the pig ear skin was calculated which was found to be 30 µg/cm^2 /hr. The additional factors in the formulation like adhesive concentration tend to decrease the release from the transdermal drug delivery system. The penetration enhancers are used to improve the penetration from the formulation across the skin. Therefore, natural volatile oils and surfactants were examined for their effect on the permeation of the Thiocolchicoside from the system. The effect of penetration enhancers on the permeation of the Thiocolchicoside is given inthe table 6.18.

Table 6.18.: Effect of permeation enhancers on the permeation of the drug:

Conc. of permeation enhancer	**Flux (µg/cm^2 /hr) DMSO**	**Flux (µg/cm^2/hr)Ginger oil**	**Flux (µg/cm^2/hr) Lemon grass oil**	**Flux (µg/cm^2/hr) Eugenol**	**Flux (µg/cm^2/hr)oleic acid**
1%	24.54	22.56	22.1	22.17	23.67
2%	27.45	23.81	25.13	23.81	26.81
2.5%	30.56	27.75	28.46	27.45	30.45
3%	34.15	35.43	32.82	32.43	34.56
4%	39.89	41.97	37.93	35.9	38.97

Different concentrations of the penetration enhancers ranging from 1 % to 4% were used in the experiment. When 4 % ginger oil was used, it provided the highest permeation of the Thiocolchicoside i.e. 41.97 µg/cm^2/hr, followed by the DMSO i.e., 39.89 µg/cm^2/hr and oleic acid

i.e. 38.97 µg/cm^2/hr respectivly. This increase in the permeation of the drug is due to the free

isoprene units causing the disruption of the ceramide heads in the protein of skin which are there in the volatile oils of the natural origin.

Table 6.19.: Transdermal patch formation Results for Set-1 Trials

Formulation code	**General appearance**	**Folding Endurance**	**Tensile Strength (Kg/cm^2)**	**Remarks**
T1	Transparent film observed, but didn't dried	0	0	No Patch formed
T2	Transparent film observed	0	0	No Patch formed
T3	Transparent film appeared, showed slight insoluble material	4	0	Patch formed
T4	Transparent film appeared, showed slight insoluble material	5	0	Patch formed but sticky innature
T5	Transparent patch formed	56	5	Ok
T6	Transparent patch formed, sticky in nature	40	3	Ok
T7	Solid white film formed	0	0	A solid opaque film formed but brittle and noplasticity
T8	Solid white brittle film formed , hard to remove from the petri plate	0	0	No patch formed
T9	Clear film formed but no sign of bridging and interlocking	3	0	No Patch formed
T10	Clear film formed but no sign of bridging, sticky in nature	4	0	No Patch formed

Table 6.19 represents the data for solvent polymer screening .On the basis of the literature review and compatibility studies, different polymers were screened for their suitability as formulating agents in transdermal drug delivery system. The

formulation was screened on the basis of the three responses namely folding endurance, tensile strength and general appearance. The formulation coded T5 and T6 gave satisfactory results in terms of high count for the folding endurance and tensile strength. The patches formed had the transparent appearance and T6 was slightly sticky in the nature. Rest of the combinations except T5 and T6 didn't produced satisfactory results for Folding endurance and Tensile strength.

Table 6.20.: Transdermal patch formation results for Set-2 trials

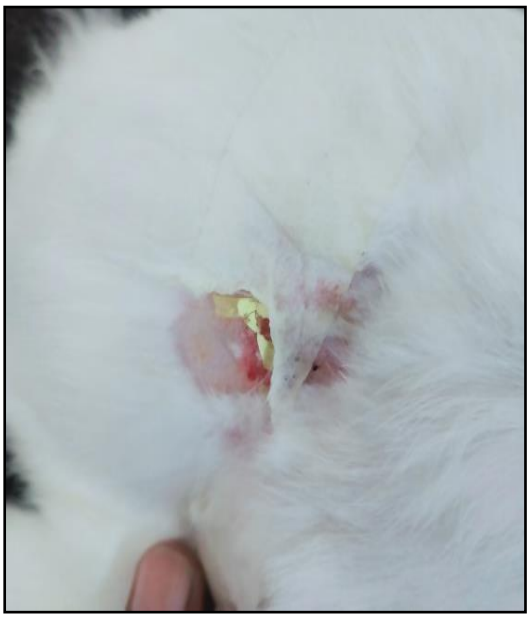
Formulation code	**General appearance**	**Folding Endurance**	**Tensile (Kg/cm^2)**	**Remarks**
ST1	Transparent, clear film observed, but didn't dried	2	0	No patch formed
ST2	Transparent film observed	4	0	Slight consistence observed
ST3	Transparent film appeared, showed slight insoluble material	12	2	Slight consistency observed
ST4	Transparent film appeared, showed slight insoluble material	16	2	Slight consistency observed with stickiness
ST5	Transparent patch formed	35	4	Ok
ST6	Transparent patch formed, sticky in nature	32	4	Ok
ST7	Solid white film formed	5	1	No patch formed
ST8	Solid white brittle film formed, hard to remove from the petri plate	2	0	No patch formed
ST9	Clear film formed but no sign of bridging and interlocking	5	1	No patch but granular mass

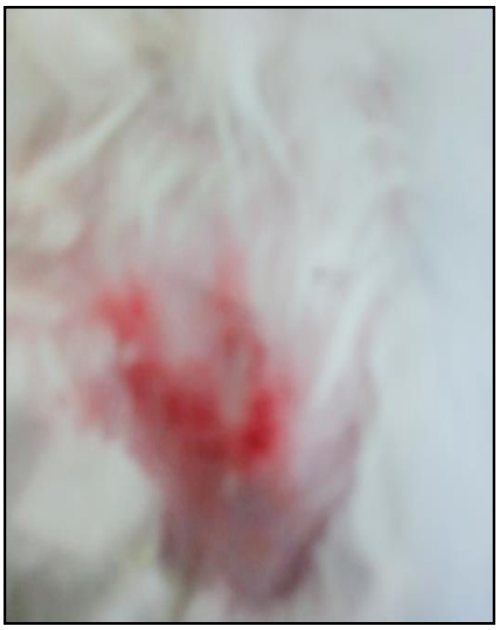
ST10	Clear film formed but no sign of bridging, stickyin nature	4	0	No patch formed

Table 6.31.: Skin Sensitization and Irritation studies

Materials	**Erythema**	**Edema**
I hr after the removal of the patch	0	0
24 hr after the removal of patches	0	0
48 hr after removal of patch	0	0
72 hr after removal of patch	0	0

Positive Controls:





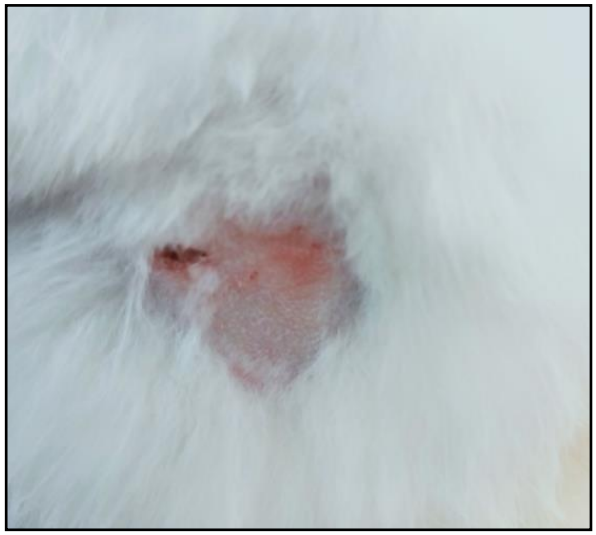
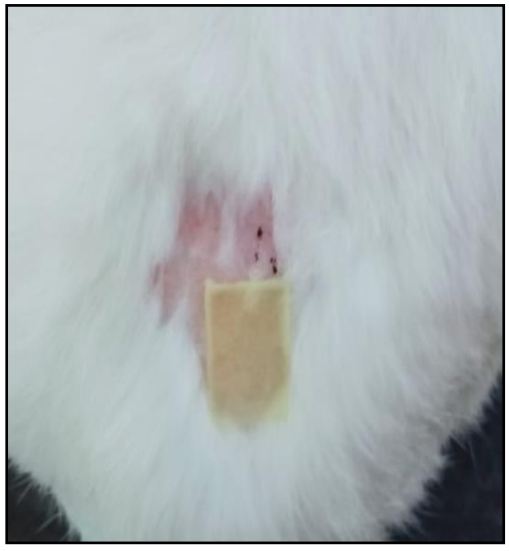


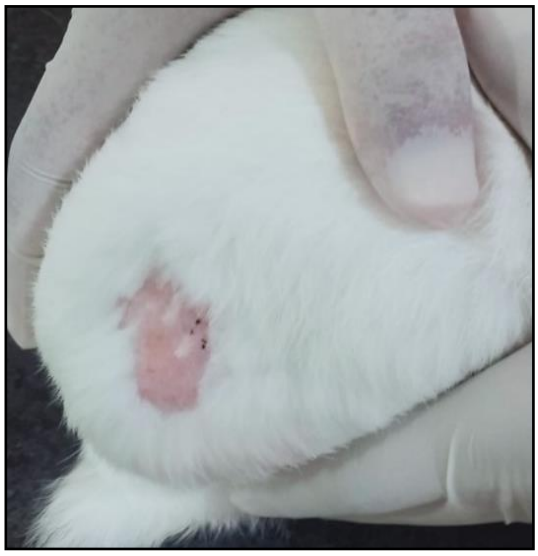
Figure : 52(c)

Figure : 52 (d)

Figure 52(c):Skin irritation testing (Positive controls)

Figure 52(d): Skin Sensitization and Skin irritation testing (Positive controls) Patch Treated :





CONCLUSIONS

Transdermal drug delivery systems have tremendous potential in delivering both hydrophilic and hydrophobic drugs across the skin. The foregoing research in transdermal is attempting to improve all the aspects of the drug delivery including the bio adhesion, sustained release and maintaining the steady state concentrations in plasma. In the present investigation transdermal drug delivery system was prepared for thiocolchicoside and following findings were reported

1. Thiococlchcioside is permeable through the animal skin and can be formulated as transdermal drug delivery system.

2. Thiococlchicoside is compatible with HPMC, Eudragit E100,L100 , Sodium CMC, Carbopol-934 and ethyl cellulose.
3. Permeation of thiocolchicoside is highest with ginger oil as compared to DMSO and surfactants.

apparatus was developed and force of adhesion of the adhesive used in the study were calculated..

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REFERENCES

1) Radhakrishnan V, Singirikonda M, Christoper GP, Habibuddin M. Transdermal Drug Delivery Technology - A Prospective Review. Int J Pharm Res Technol [Internet]. 2020;10(2):49–73.
2) Saravanakumar K, Swapna P, Nagaveni P, Vani P, Pujitha K. Transdermal drug delivery system: A review. JGTPS, 2015, Vol. 6(1): 2485 - 2490
3) Shingade Gm. Review On: Recent Trend On Transdermal Drug Delivery System. J Drug Deliv Ther. Volume 2, Issue 1, Jan-Feb 2012;
4) Wokovich AM, Prodduturi S, Doub WH, Hussain AS, Buhse LF. Transdermal drug delivery system (TDDS) adhesion as a critical safety, efficacy and quality attribute. Eur J Pharm Biopharm. 2006;64(1):1–8.
5) Tuan-Mahmood TM, McCrudden MTC, Torrisi BM, McAlister E, Garland MJ, Singh TRR, et al. Microneedles for intradermal and transdermal drug delivery. European Journal of Pharmaceutical Sciences. 2013.
6) Parivesh S, Sumeet D, Abhishek D. Design, Evaluation, Parameters and Marketed Products of transdermal patches: A Review. J Pharm Res. 2010;3(2):235–40.
7) *D. Prabhakar1, J. Sreekanth2 KNJ. Review Article TRANSDERMAL DRUG DELIVERY SYSTEM : A REVIEW. J Drug Deliv Ther. 2013;3(4):213–21.
8) Muzzalupo R, Tavano L. Niosomal drug delivery for transdermal targeting: recent advances. Res Reports Transdermal Drug Deliv. 2015;23.
9) Ranade V V. Drug delivery systems. 6. Transdermal drug delivery. J Clin Pharmacol. 1991;31(5):401–18.
10) Watkinson AC, Kearney MC, Quinn HL, Courtenay AJ, Donnelly RF. Future of the transdermal drug delivery market - Have we barely touched the surface? Expert Opin Drug Deliv. 2016;13(4):523–32.
11) Subedi RK, Oh SY, Chun MK, Choi HK. Recent advances in transdermal drug delivery.
12) . Kumar R, Philip A. Modified Transdermal Technologies: Breaking the Barriers of Drug Permeation via the Skin. Trop J Pharm Res. 2007;6(1).
13) McLafferty E, Hendry C, Alistair F. The integumentary system: anatomy, physiology and function of skin. Nursing standard (Royal College of Nursing (Great Britain) : 1987). 2012.
14) Cooper S. The Biology of the Skin. JRSM. 2002;
15) Nicol NH. Anatomy and physiology of the skin. Dermatol Nurs. 2005;
16) Wysocki AB. Skin anatomy,

physiology, and pathophysiology. The Nursing clinics of North America. 1999.

17) Montagna W. Comparative Anatomy and Physiology of the Skin. Arch Dermatol. 1967;

18) Chandrashekar N, Shobha Rani R. Physicochemical and pharmacokinetic parameters in drug selection and loading for transdermal drug delivery. Indian J Pharm Sci. 2008;

19) Paudel KS, Milewski M, Swadley CL, Brogden NK, Ghosh P, Stinchcomb AL. Challenges and opportunities in dermal/transdermal delivery. Therapeutic Delivery. 2010.

20) Banga AK, Donnelly R, Stinchcomb AL. Transdermal drug delivery. Therapeutic Delivery. 2013.

21) Lopez VC, Hadgraft J, Snowden MJ. The use of colloidal microgels as a (trans)dermal drug delivery system. Int J Pharm. 2005;

22) Alexander A, Dwivedi S, Ajazuddin, Giri TK, Saraf S, Saraf S, et al. Approaches for breaking the barriers of drug permeation through transdermal drug delivery. Journal of Controlled Release. 2012.

23) Rastogi V, Yadav P. Transdermal drug delivery system: An overview. Asian Journal of Pharmaceutics. 2012.

24) Hemanth kumar G. Transdermal drug delivery system: An overview. International Journal of Research in Pharmaceutical Sciences. 2012.

25) Stanekzai A, Sudhakar CK, Zhakfar AM, Karan VS. Recent approaches in transdermal drug delivery system. Research Journal of Pharmacy and Technology. 2019.

26) Samad A, Ullah Z, Alam M, Wais M, Shams M. Transdermal Drug Delivery System: Patent Reviews. Recent Pat Drug Deliv Formul. 2009;3(2):143–52.