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Formulation and Evaluation of Transdermal Patch of Nifedipine

Km Pragati Chaturvedi[1]*,Priyakanaujiya[2],DrNidhi Tyagi[3], Dr.Prashant Kumar katiyar[4]

[1*]Research Scholar, Kanpur Institute of Technology and Pharmacy, Kanpur, UP
[2]Assistant Professor, Kanpur Institute of Technology and Pharmacy, Kanpur, UP
[3,4]Professor&Director,KanpurInstituteofTechnologyandPharmacy,Kanpur,UP

Correspondingauthor: Km Pragati Chaturvedi
[1*]ResearchScholar,KanpurInstituteofTechnologyandPharmacy,Kanpur,UP

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ABSTRACT:

At present, the most common form of delivery of drugs is the oral route. While this has the notable advantage of easy administration. Nifedipine (NF) is a yellow crystalline substance, practically insoluble in water but soluble in ethanol. NF is a selective calcium-channel blocker and a peripheral arterial vasodilator which acts directly on vascular smooth muscle. The present research was based on the Formulation and evaluation of transdermal patch of Nifedipine. Preformulation studies was performed for the drug Nifedipine. After it was identified for appearance, solubility, melting point etc. and drug-excipients compatibility study. Preparation of transdermal patches using different polymers and their combinations was done. The developed transdermal patches were evaluated for the weight uniformity, thickness, tensile strength, folding endurance, swelling index, water vapour transmission, percentage moisture content and flatness. In results, Formulation EF1 to EF4 were designed by taking combination of EC and Eudragit S-100 as film forming polymer along with PEG-400 as plasticizer and DMSO as permeation enhancer. All the formulation were easily peeled off and had smooth surface, uniform texture and transparent. The all films were evaluated and results were reported. Based on film characteristics Ethyl cellulose and Eudragit S-100 film were selected. The ex- vivo permeation was studied which revealed that formulation EF2, EF3 and EF4 showed 33.2±0.20%, 35.4±0.24% and 40.1±0.25% drug release respectively. The formulation EF4 was selected as finally optimized formulation as it showed 40.1±0.25% drug release. Further it followed zero order kinetics and can be used as once a day transdermal patch. In conclusion, we optimize the ratio and weight of polymer required to achieve proper thickness, elegance and other transdermal patch characteristics for Nifedipine transdermal patch.

Keywords: Nifedipine, transdermal patches, preformulation study, in-vitro, polymers.

1. INTRODUCTION

At present, the most common form of delivery of drugs is the oral route. While this has thenotable advantage of easy administration [1], it also has significant drawbacks namely poorbioavailability due to hepatic metabolism (first pass) and the tendency to produce rapid bloodlevel spikes (both high and low), leading to a need for high and/or frequent dosing, which canbebothcostprohibitiveandinconvenient[2].Toovercomethesedifficultiesthereisaneedforthe development of transdermal drug delivery system; which will improve the therapeuticefficacy and safety of drugs by controlling the release of drug and avoiding the first passmetabolism,therebyreducingboththesizeandnumberofdoses.[3]Nifidipine(NF)isayellowcrystalline substance, practically insoluble in water but soluble in ethanol. NF is a selectivecalcium-channel blocker and a peripheral arterial vasodilator which acts directly on vascularsmooth muscle. [4] NF is widely used in the treatment of angina pectoris and systemichypertension.Itisapoorlysolubledruganditsabsorptionfromgastrointestinaltractislimitedbydissolutionrate.Ithasashortbiologicalhalf-life(4hrs.).AbsorptionofNFispoorfollowingadministrationorallyviaimmediatereleasedosageforms.[5]Itexhibits45-65%oralbioavaibility due to hepatic first pass metabolism. Immediate release formulations of NFclearly show fluctuation in drug plasma concentration results in specific side effects likeincreasein heartrate [6][7].

Transdermaldeliverynotonlyprovidescontrolled,constantadministrationofthedrug,butalsoallows continuous input of drugs with short biological half-lives and eliminates pulsed entryinto systemic circulation, which often causes undesirable side effects [8]. Thus various formsof Novel drug delivery system such as Transdermal drug delivery systems, Controlled releasesystems,Trans mucosaldelivery systemsetc. emerged [9].

Transdermal drug delivery systems are adhesive drug containing devices of defined surfaceareathatdeliverapredeterminedamountofdrugtothesurfaceofintactskinataprogrammedrate. These systems provide drug systematically at a predictable rate and maintain the rate forextended period of time thus eliminating numerous problems associated with oral dosingincludingproductstability,bioavailabilityandthepeaksandtroughsofpulsedosing [10].

2. MATERIALSANDMETHODS

ListofChemical

Tableno.4.1Listofchemical

Chemical	Suppliers
Nifedipine	Hi-media
Hydroxylpropylmethylcellulosek-15	YARROWCHEM
Hydroxypropylcellulose	YARROWCHEM
EudragitRs-100	YARROWCHEM
Eudragits-100	YARROWCHEM
Polyethyleglycol-400	SDFCL
Isopropylalcohol	RANKEM
Ethylcellulose	CDH
Dichloromethane	RANKEM
Polyvinylpyrolidonek-30	YARROWCHEM

ListofInstruments/Equipment's

Table2.ListofInstruments/Equipment's

Instruments/equipment's	Manufacturer/supplier
UV-visspectrophotometer	Shimadzu
ElectronicWeighingBalance	Shimadzu
StablilityChamber	Lab ControlEquipmentCo.Mumbai
Magneticstirrer	REMI
Ultrasonicbathsonicater	PCI,Mumbai
HumidityChamber	LabControlEquipmentCo.Mumbai

TableNo.4.2ListofInstruments

PreformulationStudies

Preformulation testing is an investigation of physical and chemical properties of drug subjectaloneandwhencombinedwithexcipients.Itisthefirststepintheformulationdevelopment.The overall objective of preformulation testing is to generate information usefulto the formulator in developing stable and bioavailable dosage form obviously thetype ofinformationneededwilldependonthedosageformtobedeveloped.Athoroughunderstandingof these properties may ultimately provide a rationale for formulation designor support formolecular modification. Preformulation investigation may merely confirm that there is nosignificantbarrier to thecompound development

IdentificationofNifedipine

APhysicalappearanceThedrugwasyellowodourlessandnon-crystallinepowderdrugwasreceivedfromHi-media.

B Melting point The melting point of the compound is the temperature at which it changesfrom solid to liquid this is physical property often used to identify compound melting of thecompoundwas determined by using capillary melt method.

Ultravoiletspectroscopy:100mgofNifedipinewasweighedaccuratelyanddissolvedinmethanol. Thevolumeofsolutionwasmadeupto100ml.Thesolutionwasmarkedasstocksolution-I,the10mlofstockonewastakenandvolumeofsolutionwasmadeupto100ml(stock-II). After that 20ml of stock II was taken and volume was made up to 100ml (stock-III)From stock-III, dilution having concentration 1µg/ml, 2µg/ml, 4µg/ml, 6µg/ml, 8µg/ml,10µg/ml,12µg/ml, 14µg/ml,16µg/ml, 18µg/ml and20µg/ml werepreprepared.

Above prepared solution were observed in double beam UV- Spectrophotometer (Shimadzu,Model No.1700) to measure the absorbance, in increasing order of concentration taken wavelength 235nm.

I.R.spectroscopy

Infrared spectrum of any compound or drug gives information about the groups present inparticular compound an spectrophotometer for recording the spectra in the infra-red regionconsists of an optical system capable of providing in the monochromatic light in the region of4000 to 400cm^{-1}.1mg of the sample and 300mg of KBr were taken in mortar and triturated. Asmall amount of triturated sample was taken into a pellet maker and compressed at 10kg/cm^2.The pellet was kept onto the sample holder and scanned from 4000$cm^{-1}$to 400cm^{-1}. Theinfraredspectrum of drugsamplewas obtained usingFTIR-8400S shimmadzu.

MicroscopyoftheDrug

MicroscopyoftheDrugWasPerformedByTwoMethods

DirectmethodAsmallquantityofthepowderwasspreadontotheslideuniformlyandviewedunderthelight microscope.

Smear method Small quantity of powder was placed on to the slide and wet it with 1 or 2dropsof10%water,thesuspensionwasspreaduniformlybyusinganotherslideat45^{0}angles.After that it was observed under the light microscope.

Loss on Drying The test was performed by placing 1.0 gm of Nifedipine in the oven at 600Cforthefourhouranditwasweighedagain.The%lossondryingwascalculatedbytheformula.

SolubilityStudies

Quantitativesolubilityanalysis

Excess amount of drug was dissolved in 10 ml of water and it was shaken properly and it waskept for 48-72 hour for complete hydration. After 72 hours the solution was again shakenproperly and filtered. The filtrate was analyzed by UV double beam spectrophotometer bytaking absorbanceat wavelength 340nm.

Partitioncoefficient

Partition coefficient provides a means of characterizing lipophilic/hydrophilic nature of thedrugwhichaffectttherateandextentofdrugabsorptionpartitioncoefficientismeasureofdruglipo philicity and an indication of its ability to cross cell membrane. 25ml n-octanol and 25mlof aqueous solution of 0.5% sodium lauryl sulphate (SLS) and 100mg drug were taken in aseparating funnel and shaken well for about 15 minute. Then allowed to separate both layerandaqueous layer was filteredand theabsorbance was taken at 340nm

QuantitativeEstimationofDrug

Preparationofcalibrationcurveofnifedipineinmethanol

100 mg of Nifedipine was weighed accurately and dissolved in methanol. The volume ofsolutionwasmadeupto100ml.Thesolutionwasmarkedasstocksolution-I,the10mlofstockone was taken and volume of solution was made up to 100ml (stock-II). After that 20ml ofstockII was taken and volumewas madeup to 100ml (stock-III).

- Fromstock-III,dilutionhavingconcentration1µg/ml,2µg/ml,4µg/ml,6µg/ml,8µg/ml,10µg/ml,12µg/ml,14µg/ml,16µg/ml,18µg/mland20µg/mlwereprepared.
- Above prepared solution were observed in double beam UV- Spectrophotometer (Shimadzu,ModelNo.1700)tomeasuretheabsorbance,inincreasingorderofconcentrationtakenwavelengthAt 235nm.

CalibrationCurveofNifedipineinDistilledWaterContaining0.5%SlS

The dilutions having concentration 1µg/ml, 2µg/ml, 4µg/ml, 6µg/ml, 8µg/ml, 10µg/ml, 12µg/ml 14µg/ml, 16µg/ml, 18µg/ml and 20µg/ml were prepared in distilled water containing0.5%SLSabovepreparedilutionswereobservedindoublebeamSpectrophotometer(shimadzu,model) no. 1700) to measure the absorbance in increasing order of concentrationtakenwavelength at 235nm

DrugExcipientInteraction

The drug and excipient were taken in 1:1 ratio and mixed properly using a polybag. Now themixtures were transferred into the glass vials and samples were placed in stability chamber at40^0Cfor21days.Glassvialsfilledwithplanedrugandpolymerswerealsoplacedinthesameway.

TableNo.4.3Drugexcipientinteraction

Excipient	Quantity
Drug	100mg
EC	100mg
PVPK-30	100mg
EudragitRS-100	100mg
EudragitS-100	100mg
DRUG+EC+PVP-K-30	100mg+100mg+100mg
DRUG+EC+EUDRAGITRS-100	100mg+100mg+100mg
DRUG+EC+EUDRAGITS-100	100mg+100mg+100mg

FORMULATIONDEVELOPMENT

CompositionofNifedipineTransdermalPatchFormulationTrialFormulation(1)

TableNo.4.4TrialFormulation1

Ingredient	Quantity
Drug	**100mg**
EthylCellulose	**200mg**
PvpK-30	**800mg**
DibutylPhthalate	**300mg**
IPA	**4ML**
DCM	**6ML**

TrialFormulation(2)

TableNo.4.5TrialFormulation2

Ingredient	Quantity
Drug	100mg
EthylCellulose	200mg
PvpK-30	100mg
PEG-400	55mg
DCM	4ml
IPA	1ml

TrialFormulation(A)

TableNo.4.6TrialFormulationA

Formulation	AF1	AF2	AF3	AF4
Drug	**100mg**	**100mg**	**100mg**	**100mg**
EthylCellulose	**50mg**	**100mg**	**150mg**	**200mg**
PVPK-30	**25mg**	**50mg**	**75mg**	**100mg**
PEG-400	**55mg**	**55mg**	**55mg**	**55mg**
IPA	**1ml**	**1ml**	**1ml**	**1ml**
DCM	**4ml**	**4ml**	**4ml**	**4ml**

TrialFormulation(B)

TableNo.4.7TrialFormulationB

Formulation	BF1	BF2	BF3	BF4
Drug	**100mg**	**100mg**	**100mg**	**100mg**
EthylCellulose	**50mg**	**100mg**	**150mg**	**200mg**
H.P.C.	**25mg**	**50mg**	**75mg**	**100mg**
PEG-400	**55mg**	**55mg**	**55mg**	**55mg**
IPA	**1ml**	**1ml**	**1ml**	**1ml**
DCM	**4ml**	**4ml**	**4ml**	**4ml**

TrialFormulation(C)

TableNo.4.8TrialFormulationC

Formulation	CF1	CF2	CF3	CF4
Drug	**100mg**	**100mg**	**100mg**	**100mg**
EthylCellulose	**50mg**	**100mg**	**150mg**	**200mg**
H.P.M.C.K-15	**25mg**	**50mg**	**75mg**	**100mg**
PEG-400	**55mg**	**55mg**	**55mg**	**55mg**

IPA	**1ml**	**1ml**	**1ml**	**1ml**
DCM	**4ml**	**4ml**	**4ml**	**4ml**

TrialFormulation(D)

TableNo.4.9TrialFormulationD

FORMULATION	**DF1**	**DF2**	**DF3**	**DF4**
DRUG	**100mg**	**100mg**	**100mg**	**100mg**
ETHYLCELLULOSE	**50mg**	**100mg**	**150mg**	**200mg**
EUDRAGITRS-100	**25mg**	**50mg**	**75mg**	**100mg**
PEG-400	**75mg**	**75mg**	**75mg**	**75mg**
IPA	**1ml**	**1ml**	**1ml**	**1ml**
DCM	**4ml**	**4ml**	**4ml**	**4ml**

TrialFormulation(E)

TableNo.4.10TrialFormulationE

Formulation	**EF1**	**EF2**	**EF3**	**EF4**
Drug	**100mg**	**100mg**	**100mg**	**100mg**
EthylCellulose	**50mg**	**100mg**	**150mg**	**200mg**
EudragitS-100	**25mg**	**50mg**	**75mg**	**100mg**
PEG-400	**75mg**	**75mg**	**75mg**	**75mg**
IPA	**1ml**	**1ml**	**1ml**	**1ml**
DCM	**4ml**	**4ml**	**4ml**	**4ml**

EVALUATIONOFTRANSDERMALPATCHESOFNIFEDIPINE

- **Physical Appearance**: All the prepared patches were visually inspected for color, Clarity,flexibilityand smoothness.
- **ThicknessUniformity**:Thethicknessoftheformulatedfilmwasmeasuredat3differentpointsusing adigitalcaliperandaveragethicknessofthreereadingwascalculated.
- **FoldingEndurance:** ThefoldingendurancewasmeasuredAstripoffilm (3×3cm)wascutandrepeatedlyfoldedatthesameplacetillitbroke.Thenumberoftimesthefilmcould befoldedatthesameplacewithoutbreakinggave thevalueoffoldingendurance.
- **PercentageMoisture Absorption:** Thefilmswereweighedaccuratelyandplacedinthedesiccatorscontaining100mlofsaturated solutionofpotassiumchloride, whichmaintain80-90% RH After 3 days, the films were taken out and weighed. The study was performedatroom temperature.
  %ofmoistureabsorption=finalweight–initialweight/initialweight×100
- **PercentageMoistureLoss**:Thefilmswereweighedaccuratelyandkeptindesiccatorsanhydrousso diumsulphateafter3daysthefilmsweretakenoutandweighed.
  %ofmoistureabsorption=initialweight–finalweight/ initialweight×100
- **WaterVapourTransmissionRate:**Glassvialsof5mlcapacitywerewashedthoroughlyand dried to a constant weight in an oven. About 1 g of fused calcium chloride was takenin the vials and the polymer films of 2.25cm^2 were fixed over the brim with the help of anadhesive tape. Then the vials were weighed and stored in a humidity chamber of 80-90 %RH condition for a period of 24 h The vials were removed and weighed at 24 h timeintervalsto note downtheweight gain
  %oftransmissionrate=initialweight –finalweight/time×area×100
- **Drug Content Uniformity of Films:** The patches added to a beaker containing 100ml ofmethanol.Thecontentwerefilteredusingwhatmannfilterpaperandfiltratewasexaminedfor the drug content against the reference solution consisting of placebo films at

235nmspectrophotometrytheexperiment was repeatedto validatethe result

- **Ex vivo Drug Release Studies:** In vitro skin permeation studies were performed by usinga modified Franz diffusion cell with a receptor compartment capacity of 60.1 ml. The goatskin was mounted between the donor and receptor compartment of the diffusion cell.formulated patches were cut into size of 1cm^2 and placed over the drug release membraneand the receptor compartment ofthe diffusion cell was filled with phosphate buffer pH7.4.Thewholeassemblywasfixedonmagneticstirrer,andthesolutionin thereceptorcompartmen twasstirredconstantly.

3. RESULTANDDISCUSSIONPREFORMULATIONSTUDIES

IdentificationofNifedipine

PhysicalAppearanceThedrugwasyellowincolour,odourlessandnoncrystlline

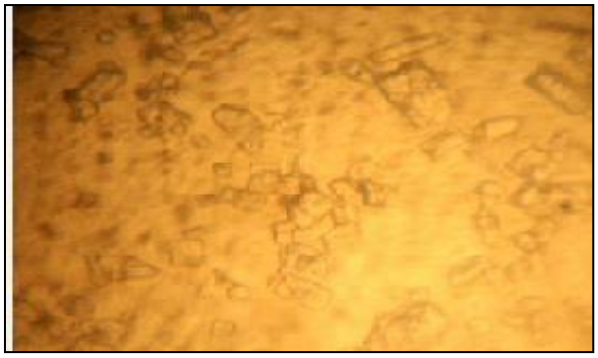
MeltingPointDetermination

Observedmeltingpoint=172±1.52^{o}c(n=3)

MeltingpointoftheDrug			veragevalue	StandardDeviation
Trial I	TrialII	TrialIII		
172	171	174	172	1.52

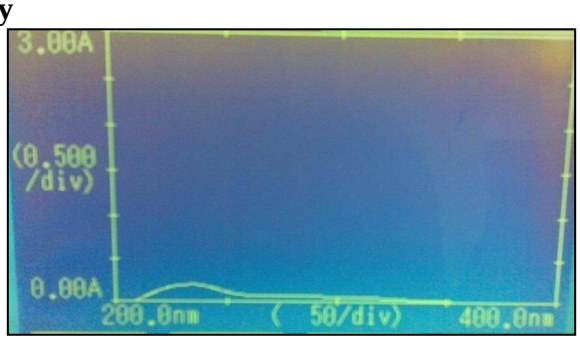
Tableno.5.1MeltingpointoftheDrug

Microscopyofdrug



FigureNo.5.1Microscopyofdrug

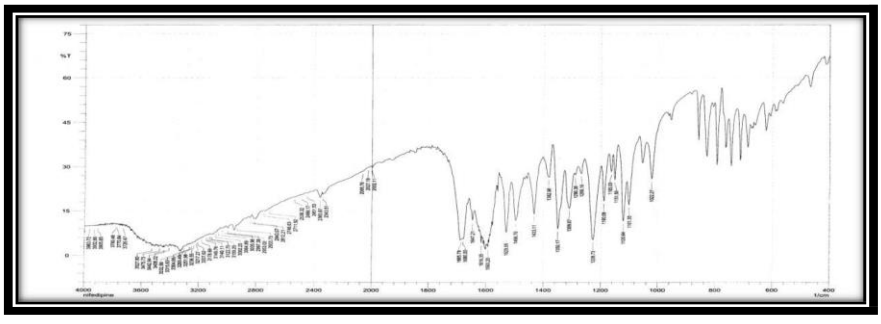
U.V.Spectrophotometry



FigureNo.5.2U.V.SpectroscopyofDrug

Infra-Redspectrum

Nifedipine

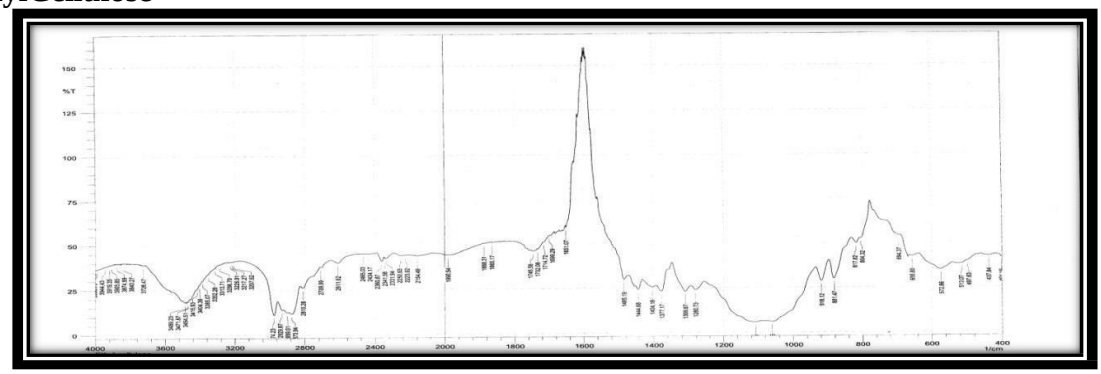


FigureNo.5.3I.R.ofnifedipine

TableNo.5.2I.R.OfDrug

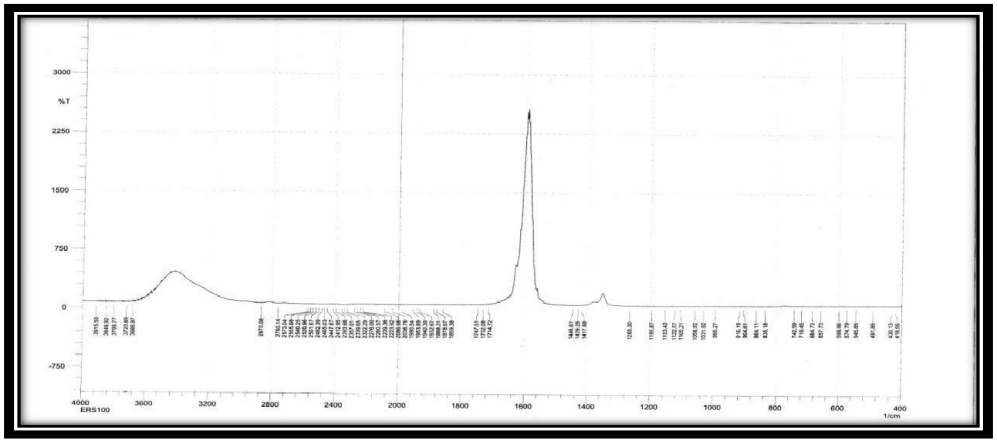
Regionincm^{-1}andintensity	Typeofvibration
1680	**C=0str**
1685	**C=0str**
1616.35	**C=0str**
1593.20	**N-HDiffrection**
1309	**N=0Str**
1350	**N=0Str**
1150	**C-0Str**

EthylCellulose



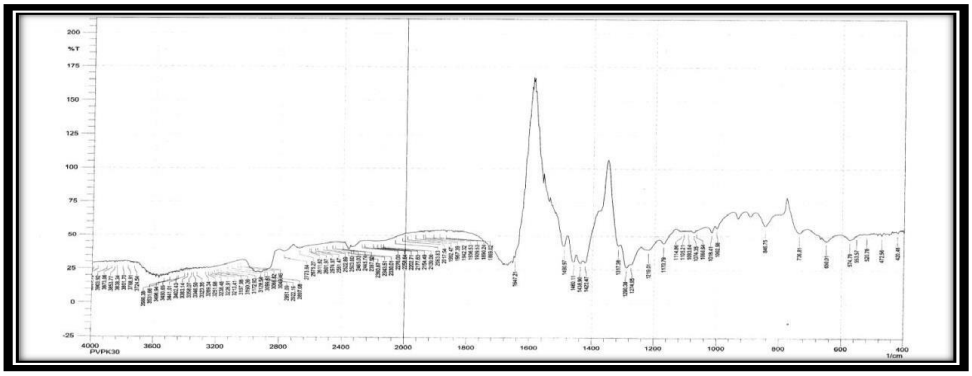
Figureno.5.3I.R.ofEthylcellulose

RS-100

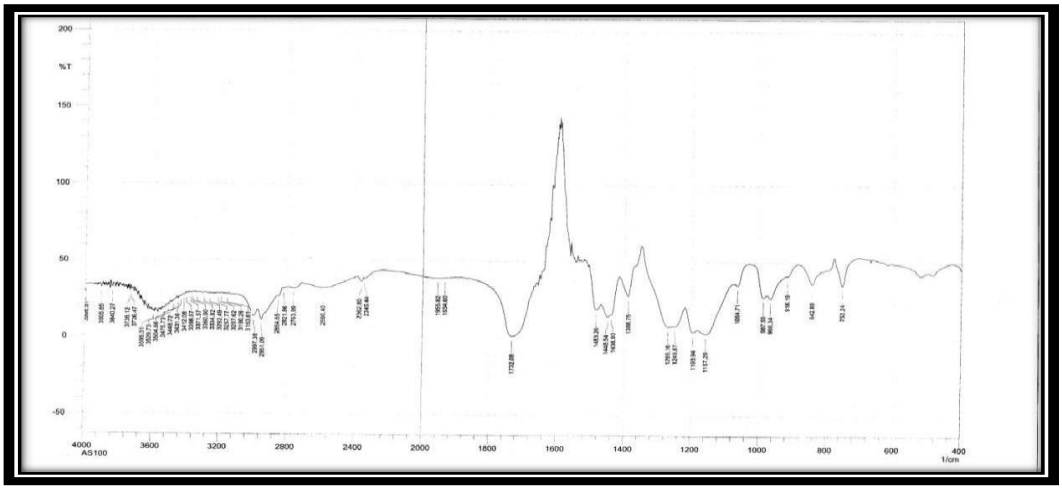


FigureNo.5.5I.R.ofEudragitRS-100

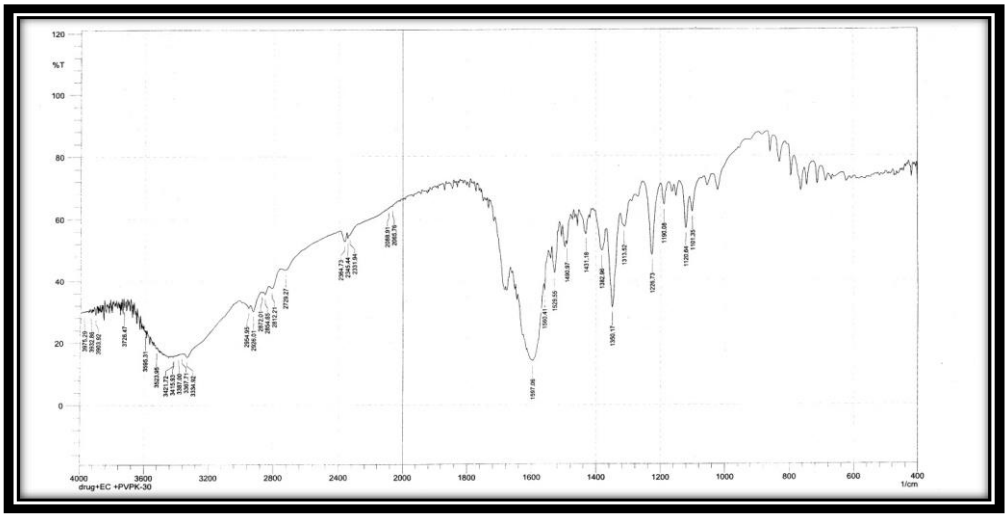
PVPK-30



S-100

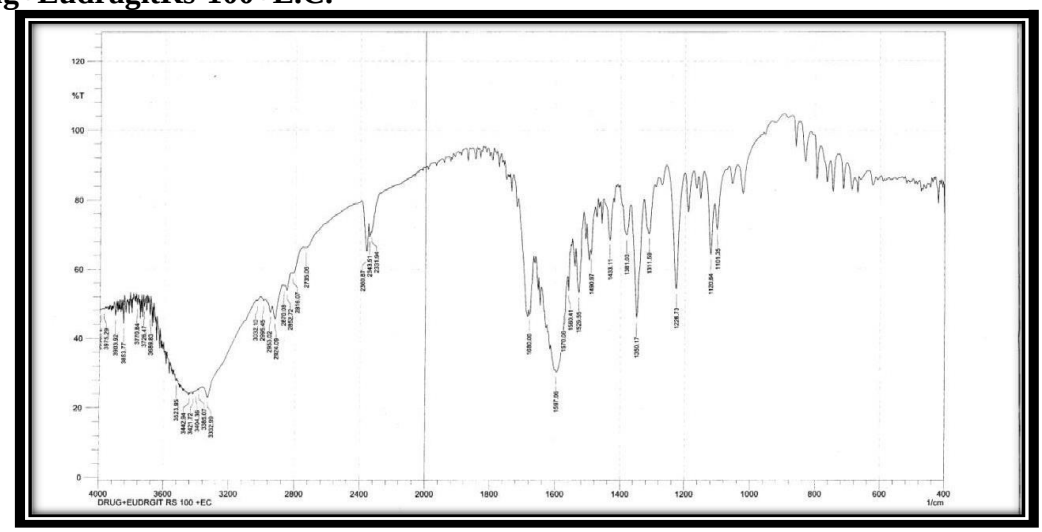


FigureNo.5.6I.R.ofEudragitS-1006:DRUG+E.C.+PVPK-30

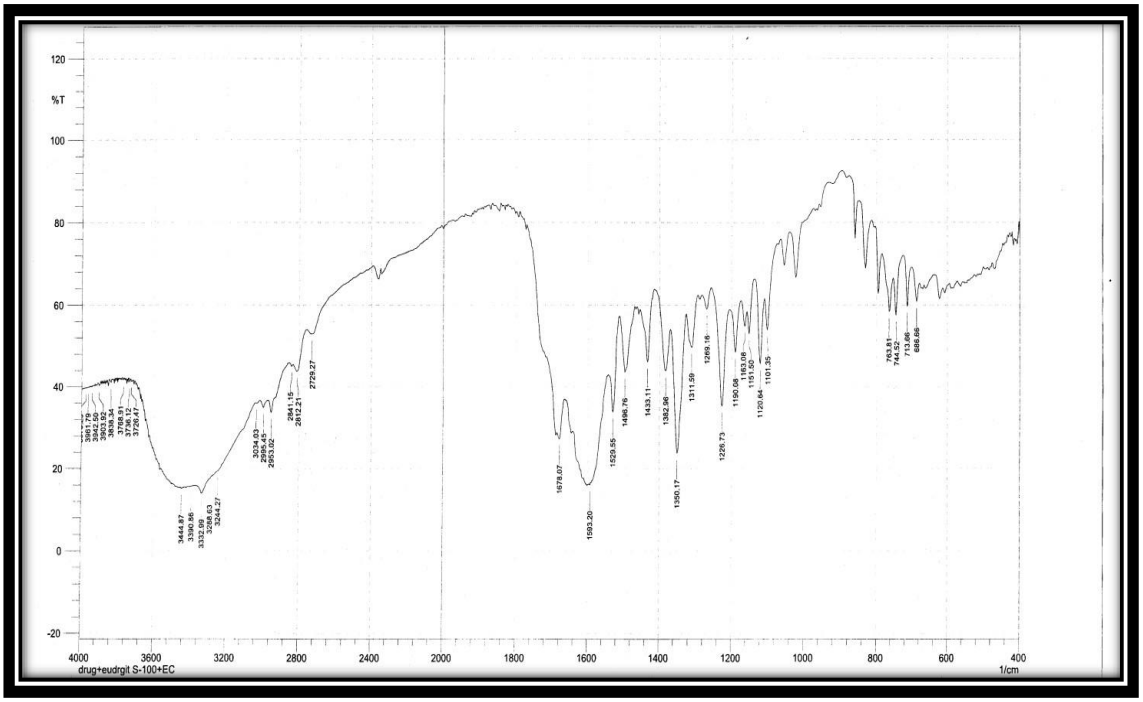


FigureNo.5.7I.R.ofDrug+E.C.+pvpk-30

Drug+EudragitRs-100+E.C.



FigureNo.5.8I.R.ofDrug+EudragitRS-100+E.C.Drug+EudragitS-100+E.C.



FigureNo.5.9I.R.ofDrug+EudragitS-100+E.C.

The drug and excipient compatibility study was performed by placing the samples as perprotocol. The physical mixture drug and excipient were evaluated for physical abservation i.e.liquefaction, colour change odour generation and finally by comparision of their I.R. spectra.The no. observation of any new peak of drug was found in all of physical mixture of drug andexcipients and all characteristic peaks of drug were found in physical mixture which revealedcompatibilityof drug with allof the excipient andpolymerselected.

LossonDrying

S.NO	InitialWeight(gm.)	Finalweight(gm.)	%LOD
1	**1.0**	**0.9982**	**0.18**
2	**1.0**	**0.9986**	**0.14**
3	**1.0**	**0.9978**	**0.22**
Average(%lossondrying)			**0.18±0.04**

TableNo.5.3lossondryingPartitionCoefficient:PartitioncoefficientofNifedipine(logp)was1.80 found to be1.80

SolubilityStudies

SolubilityStudyofDruginDifferentSolvents

S.No.	Solvents	Solubility
1	DistilledWater	Practicallyinsoluble
2	Ethanol	Practicallysoluble
3	Chloroform	Practicallysoluble
4	ACETONE	Practicallysoluble
5	IPA	Freelysoluble
6	Di-chloroMethane	Soluble
7	Methanol	Practicallysoluble

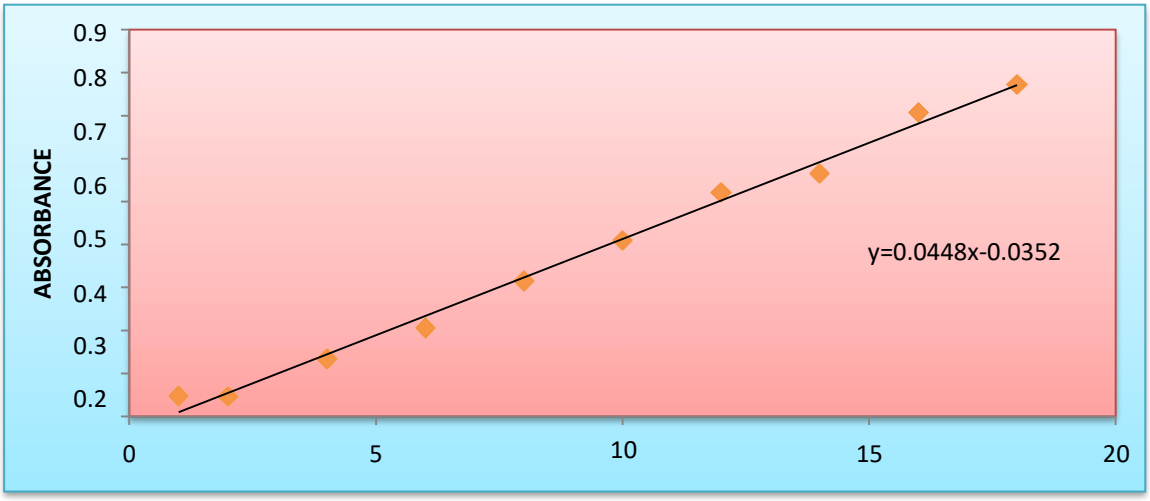
TableNo.5.4Solubilitystudyofdrugindifferentsolvents

QuantitativeSolubilityAnalysisAbsorbanceatwavelength340nm. Absorbance of solution= 0.499AqueousSolubilityofNifedipinewas foundto be=3.556 µg/ml

QuantitativeEstimationofDrug
Preparationofcalibrationcurveofnifedipineinmethanol

S.no.	Concentration(µg/ml)	Absorbance(λ235)
1	1	0.048
2	2	0.046
3	4	0.134
4	6	0.206
5	8	0.315
6	10	0.410
7	12	0.521
8	14	0.566
9	16	0.707
10	18	0.772

TableNo.5.5calibrationcurveofNifedipineinmethanol

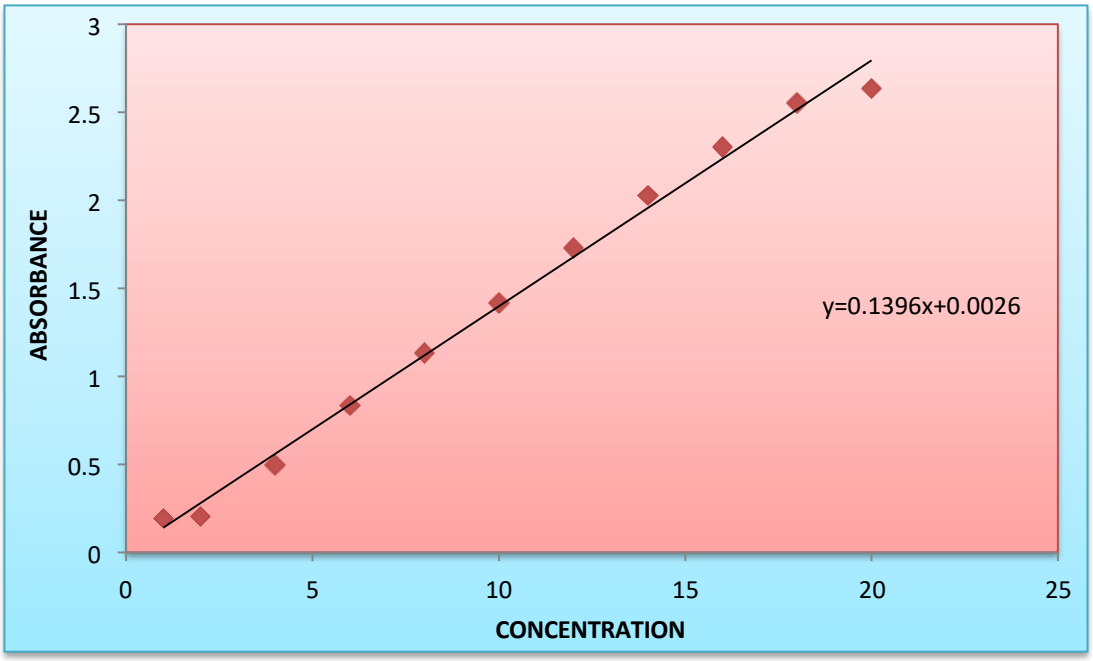


FigureNo.5.10CalibrationcurveofNifedipineinmethanol

CalibrationCurveofNifedipineInDistilledWaterContaining0.5%SlS

S.no.	Concentration(µg/ml)	Absorbance(λ340)
1	1	0.193
2	2	0.205
3	4	0.497
4	6	0.834
5	8	1.134
6	10	1.418
7	12	1.729
8	14	2.027
9	16	2.301
10	18	2.552
11	20	2.635

TableNo.5.6calibrationcurveofNifedipineindistilledwatercontaining0.5%SLS



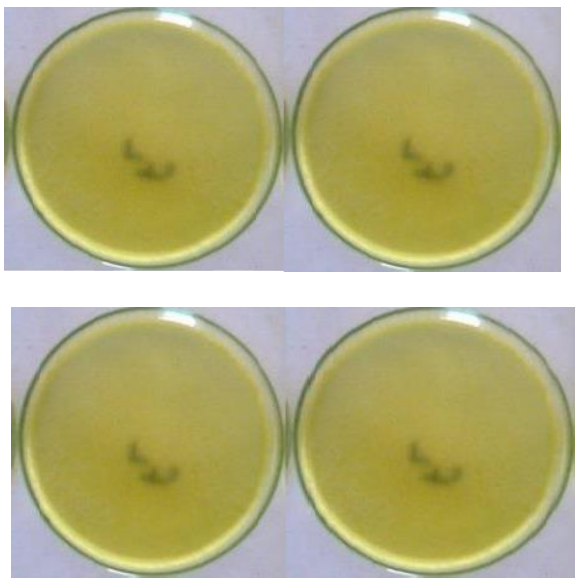
FigureNo.5.11calibrationcurveofNifedipineindistilledwatercontaining0.5%SLS

SELECTEDNIFEDIPINETRANSDERMALPATCHFORMULATION

TrialFormulation(A)

Formulation	AF1	AF2	AF3	AF4
Drug	**100mg**	**100mg**	**100mg**	**100mg**
EthylCellulose	**50mg**	**100mg**	**150mg**	**200mg**
PVPK-30	**25mg**	**50mg**	**75mg**	**100mg**
PEG-400	**55mg**	**55mg**	**55mg**	**55mg**
IPA	**1ml**	**1ml**	**1ml**	**1ml**
DCM	**4ml**	**4ml**	**4ml**	**4ml**

Tableno.5.7TrialformulationA

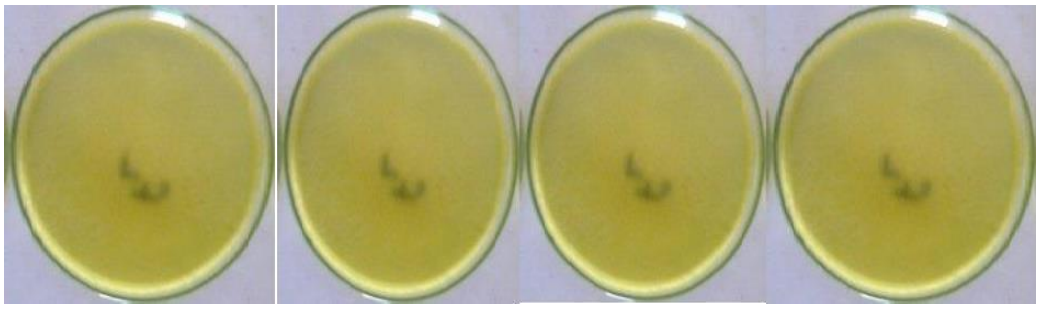


Figureno.5.12TrialformulationA

TrialFormulation(D)

Tableno.5.8TrialformulationD

Formulation	DF1	DF2	DF3	DF4
Drug	**100mg**	**100mg**	**100mg**	**100mg**
EthylCellulose	**50mg**	**100mg**	**150mg**	**200mg**
EudragitRs-100	**25mg**	**50mg**	**75mg**	**100mg**
PEG-400	**75mg**	**75mg**	**75mg**	**75mg**
IPA	**1ml**	**1ml**	**1ml**	**1ml**
DCM	**4ml**	**4ml**	**4ml**	**4ml**

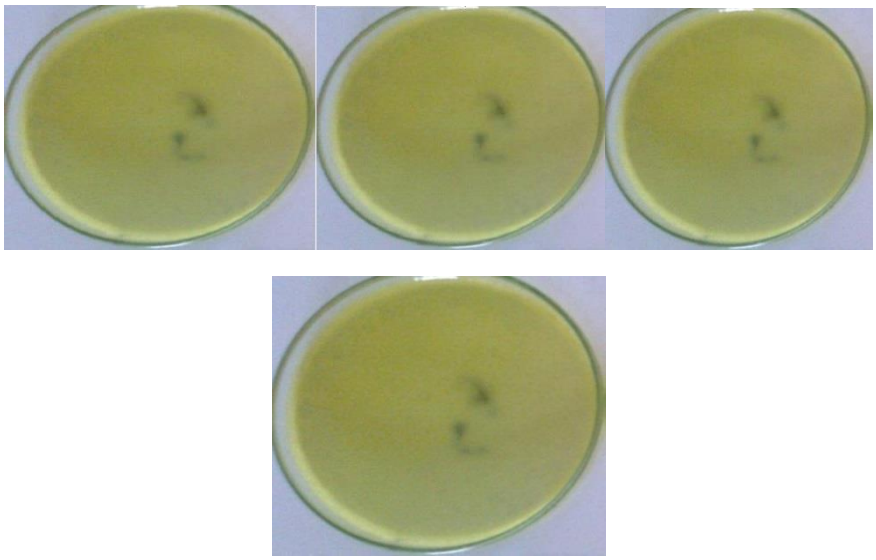


Figureno.5.13TrialformulationD

TrialFormulation(E)

Tableno.5.9TrialformulationE

Formulation	**EF1**	**EF2**	**EF3**	**EF4**
Drug	**100mg**	**100mg**	**100mg**	**100mg**
EthylCellulose	**50mg**	**100mg**	**150mg**	**200mg**
EudragitS-100	**25mg**	**50mg**	**75mg**	**100mg**
PEG-400	**75mg**	**75mg**	**75mg**	**75mg**
IPA	**1ml**	**1ml**	**1ml**	**1ml**
DCM	**4ml**	**4ml**	**4ml**	**4ml**
DMSO	**55mg**	**55mg**	**55mg**	**55mg**



FigureNo.5.14TrialFormulationE

EVALUATIONOFTRANSDERMALPATCHESOFNIFEDIPINE

FormulationA(AF1)

Formulation	AF1(f1)	AF1(f2)	AF1(f3)	Mean±S.D.
Thicknessuniformity	0.11	0.12	0.13	0.12±0.01
Weightuniformity	0.315	0.326	0.365	0.335±0.03
Foldingendurance	32	34	35	33±1.52
Percentagemoistureabsorption	29.330	30.314	30.614	30.086±0.67
Percentagemoistureloss	1.220	1.560	2.210	1.66±0.50
rvapourtransmissionrate	0.0032	0.0034	0.0035	0.0033±0.0001
contentuniformityoffilms	0.293	0.295	0.296	0.294±0.0015

TableNo.5.10EvaluationoftransdermalpatchesformulationAF1

FormulationA(AF2)

TableNo.5.11Evaluationoftransdermalpatchesformulation(AF2)

Formulation	AF2(f1)	AF2(f2)	AF2(f3)	Mean±S.D.
Thicknessuniformity	0.12	0.13	0.14	0.13±0.01
Weightuniformity	0.331	0.352	0.432	0.371±0.05
Foldingendurance	45	46	48	46±1.52
Percentagemoistureabsorption	28.115	29.512	29.612	29.079±0.83
Percentagemoistureloss	1.220	2.310	2.432	1.98±0.66
Water vapourtransmissionrate	0.0038	0.0040	0.0041	0.0039±0.0001
Drugcontentuniformityoffilms	0.312	0.314	0.315	0.313±0.0015

FormulationA(AF3)

TableNo.5.12Evaluationof transdermalpatchesformulationA(AF3)

Formulation	AF3(f1)	AF3(f2)	AF3(f3)	Mean±S.D.
Thicknessuniformity	0.13	0.14	0.15	0.14±0.01
Weightuniformity	0.358	0.398	0.460	0.405±0.05
Foldingendurance	56	58	57	57±1
Percentagemoistureabsorption	28.425	27.215	28.715	28.12±0.79
Percentagemoistureloss	1.430	2.530	2.690	2.21±0.68
Water vapourtransmissionrate	0.0046	0.0045	0.0043	0.0044±0.0001
entuniformityoffilms	0.353	0.354	0.356	0.354±0.0015

FormulationA(AF4)

TableNo.5.13EvaluationoftransdermalpatchesformulationA(AF4)

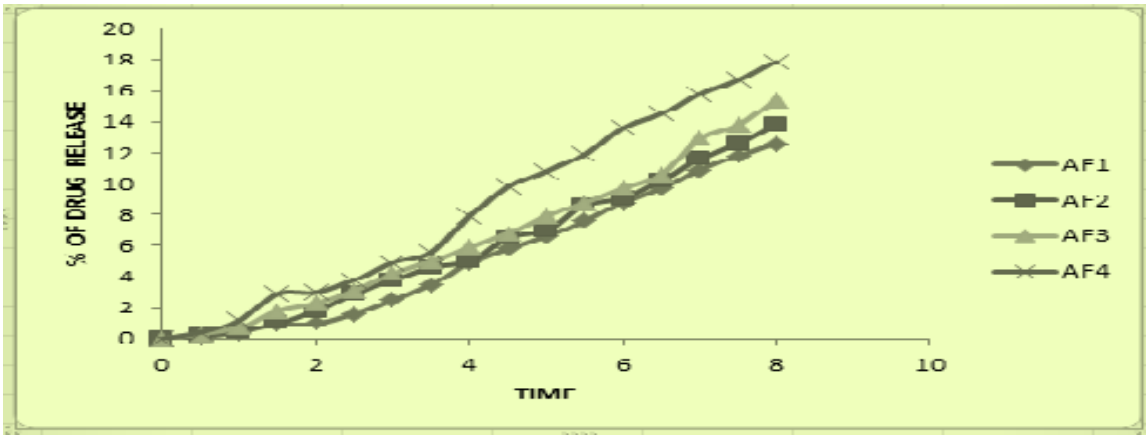
Formulation	Af4(f1)	Af4(f2)	Af4(f3)	Mean±S.D.
Thicknessuniformity	0.16	0.14	0.15	0.15±0.01
Weightuniformity	0.383	0.432	0.498	0.437±0.05
Foldingendurance	61	60	65	31±2.64
Percentagemoistureabsorption	27.314	28.548	27.438	27.766±0.68
Percentagemoistureloss	1..560	2.680	2.770	2.33±0.67
Watervapourtransmissionrate	0.0047	0.0045	0.0047	0.0046±0.0001
Drugcontentuniformityoffilms	0.421	0.423	0.424	0.422±0.0015

EX-VivoReleasePermeationRateofFormulationA

TableNo.5.14EX-Vivoreleasepermeationrateofdrug FormulationA

TIME	%OFDRUGRELEASE

	AF1	AF2	AF3	AF4
0.5	0.1±0.12	0.2±0.15	0.3±0.19	0.4±0.20
1	0.4±0.14	0.5±0.13	0.7±0.17	1.2±0.15
1.5	0.9±0.13	1±0.16	1.8±0.14	2.9±0.12
2	1±0.16	1.8±0.15	2.3±0.15	3±0.10
2.5	1.6±0.17	2.9±0.18	3.1±0.15	3.8±0.21
3	2.5±0.18	3.8±0.17	4.2±0.16	4.9±0.23
3.5	3.5±0.11	4.6±0.21	5±0.12	5.6±0.21
4	4.9±0.12	5±0.21	5.9±0.17	7.9±0.23
4.5	5.8±0.18	6.5±0.24	6.8±0.15	9.8±0.24
5	6.6±0.21	7±0.23	7.9±0.19	10.8±0.14
5.5	7.6±0.20	8.6±0.24	8.8±0.15	11.9±0.13
6	8.8±0.19	9.1±0.22	9.7±0.18	13.6±0.18
6.5	9.7±0.18	10.2±0.23	10.6±0.18	14.5±0.23
7	10.9±0.17	11.6±0.21	12.9±0.12	15.8±0.21
7.5	11.8±0.18	12.6±0.23	13.8±0.19	16.7±0.19
8	12.6±0.19	13.8±0.25	15.4±0.21	17.9±0.24



FigureNo.5.15EX-VivoreleasepermeationrateofdrugFormulationA

FormulationD(DF1)

TableNo.5.15EvaluationoftransdermalpatchesformulationDFormulationD(DF2)

Formulation	DF1(f1)	DF1(f2)	DF1(f3)	Mean±S.D.
Thicknessuniformity	0.10	0.11	0.12	0.11±0.01
Weightuniformity	0.410	0.485	0.530	0.475±0.06
Foldingendurance	31	32	33	32±1
Percentagemoistureabsorption	17.934	18.324	18.698	18.31±0.38
Percentagemoistureloss	2.450	1.350	1.250	1.68±0.66
Watervapourtransmissionrate	0.0015	0.0017	0.0017	0.0005±0.0001
Drugcontentuniformityoffilms(gm)	0.311	0.312	0.314	0.312±0.0015

TableNo.5.16EvaluationoftransdermalpatchesformulationD

Formulation	DF2(f1)	DF2(f2)	DF2(f3)	Mean±S.D.
Thicknessuniformity(mm)	0.11	0.12	0.13	0.12±0.01
Weightuniformity(mg)	0.460	0.530	0.575	0.526±0.06
Foldingendurance	51	53	52	52±1
Percentagemoistureabsorption	16.321	17.821	17.567	17.23±0.80

Percentagemoistureloss	2.890	1.857	2.759	2.502±0.56
Watervapourtransmissionrate	0.0020	0.0018	0.0019	0.0019±0.0001
Drugcontentuniformityoffilms(gm)	0.354	0.356	0.357	0.355±0.0015

FormulationD(DF3)

TableNo.5.17EvaluationoftransdermalpatchesformulationDFormulationD(DF4)

Formulation	**DF3(f1)**	**DF3(f2)**	**DF3(f3)**	**Mean±S.D.**
Thicknessuniformity(mm)	0.12	0.13	0.14	0.13±1
Weightuniformity(mg)	0.520	0.575	0.640	0.578±0.06
Foldingendurance	60	62	64	52±2
Percentage moistureabsorption	16.224	17.342	16.454	16.67±0.59
Percentagemoistureloss	3.132	2.381	3.105	2.87±0.42
Watervapourtransmissionrate	0.0021	0.0022	0.0023	0.0022±0.0001
Drugcontentuniformityof films(gm)	0.398	0.397	0.395	0.396±0.0015

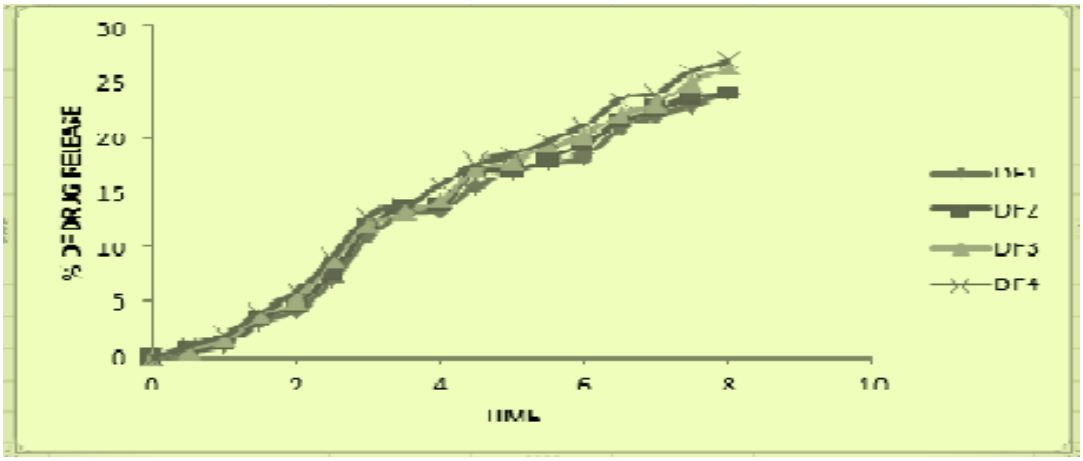
TableNo.5.18EvaluationoftransdermalpatchesformulationD

Formulation	**DF4(f1)**	**DF4(f2)**	**DF4(f3)**	**Mean±S.D.**
Thicknessuniformity(mm)	0.13	0.14	0.15	0.14±1
Weightuniformity(mg).	0.594	0.564	0.690	0.601±0.07
Foldingendurance.	72	73	75	73±1.52
Percentagemoistureabsorption	15.211	16.525	15.225	15.65±0.75
Percentagemoistureloss	3.151	2.685	3.115	2.98±0.24
Watervapourtransmissionrate	0.0021	0.0022	0.0021	0.0022±0.0001
Drugcontentuniformityoffilms(gm)	0.421	0.424	0.423	0.422±0.0015

EX-VivoReleasePermeationRateofDrug

TableNo.5.19EX-VivoreleasepermeationrateofdrugFormulationD

Time	**%OfDrugRelease**			
	DF1	DF2	DF3	DF4
0.5	0.5±0.21	0.6±0.21	0.7±0.19	0.9±0.23
1	1.1±0.15	1.2±0.16	1.5±0.22	1.9±0.18
1.5	3.1±0.16	3.4±0.16	3.8±0.17	4.1±0.15
2	4.1±0.22	4.7±0.17	5.1±0.24	5.9±0.21
2.5	6.9±0.16	7.7±0.18	8.9±0.25	9.2±0.23
3	11±0.17	11.9±0.15	12.1±0.23	12.9±0.17
3.5	13.1±0.18	13.8±0.18	13.1±0.21	13.9±0.21
4	13.5±0.11	13.9±0.12	14.3±0.24	15.7±0.20
4.5	15.6±0.14	16.9±0.16	17.1±0.22	17.8±0.25
5	16.9±0.17	17.1±0.15	17.9±0.23	18.5±0.19
5.5	17.8±0.16	18.1±0.16	19.2±0.25	19.8±0.24
6	18.4±0.17	19.4±0.12	20.3±0.28	21.2±0.24
6.5	20.9±0.15	21.5±0.19	22.1±0.21	23.4±0.25
7	22.1±0.14	22.5±0.11	23.1±0.22	24.1±0.27
7.5	22.9±0.15	23.6±0.16	25.1±0.23	26.1±0.21
8	23.9±0.13	23.9±0.17	26.3±0.25	27.1±0.23



FigureNo.5.16EX-VivoreleasepermeationrateofdrugFormulation D

FormulationE(EF1)

TableNo.5.20EvaluationoftransdermalpatchesformulationEFormulationE(EF2)

Formulation	EF1(f1)	EF1(f2)	EF1(f3)	Mean±S.D.
Thicknessuniformity(mm)	0.12	0.13	0.14	0.13±0.01
Weightuniformity(mg)	0.501	0.622	0.672	0.598±0.08
Foldingendurance	50	55	53	52±2.51
Percentagemoistureabsorption	14.351	15.452	15.512	15.105±0.65
Percentagemoistureloss	2.205	2.182	3.250	2.54±0.61
Watervapourtransmissionrate	0.0018	0.0020	0.0020	0.0019±0.0001
Drugcontentuniformityoffilms(gm)	0.251	0.253	0.254	0.252±0.0015

TableNo.5.21EvaluationoftransdermalpatchesformulationE

Formulation	EF2(f1)	EF2(f2)	EF2(f3)	Mean±S.D.
ThicknessUniformity(Mm)	0.15	0.14	0.13	0.14±0.01
WeightUniformity(Mg)	0.524	0.654	0.698	0.625±0.09
FoldingEndurance	60	65	62	62±2.51
Percentagemoistureabsorption	13.356	14.252	14.298	13.96±0.53
PercentageMoistureLoss	2.151	3.115	3.398	2.88±0.65
WaterVapourTransmissionRate	0.0019	0.0021	0.0021	0.0020±0.0001
DrugContentUniformityOfFilms(Gm)	0.351	0.352	0.354	0.352±0.0015

FormulationE(EF3)

TableNo.5.22EvaluationoftransdermalpatchesformulationFormulationE(EF4)

Formulation	EF3(f1)	EF3(f2)	EF3(f3)	Mean±S.D.
Thicknessuniformity(mm)	0.16	0.15	0.14	0.15±0.01
Weightuniformity(mg)	0.592	0.693	0.705	0.663±0.06
Foldingendurance	70	75	72	72±2.51
Percentagemoistureabsorption	13.254	13.250	12.450	12.98±0.46
Percentagemoistureloss	2.198	3.171	3.468	2.94±0.66
Watervapourtransmissionrate	0.0020	0.0021	0.0022	0.0021±0.0001
Drugcontentuniformityoffilms(gm)	0.391	0.393	0.394	0.392±0.0015

TableNo.5.23EvaluationoftransdermalpatchesformulationE

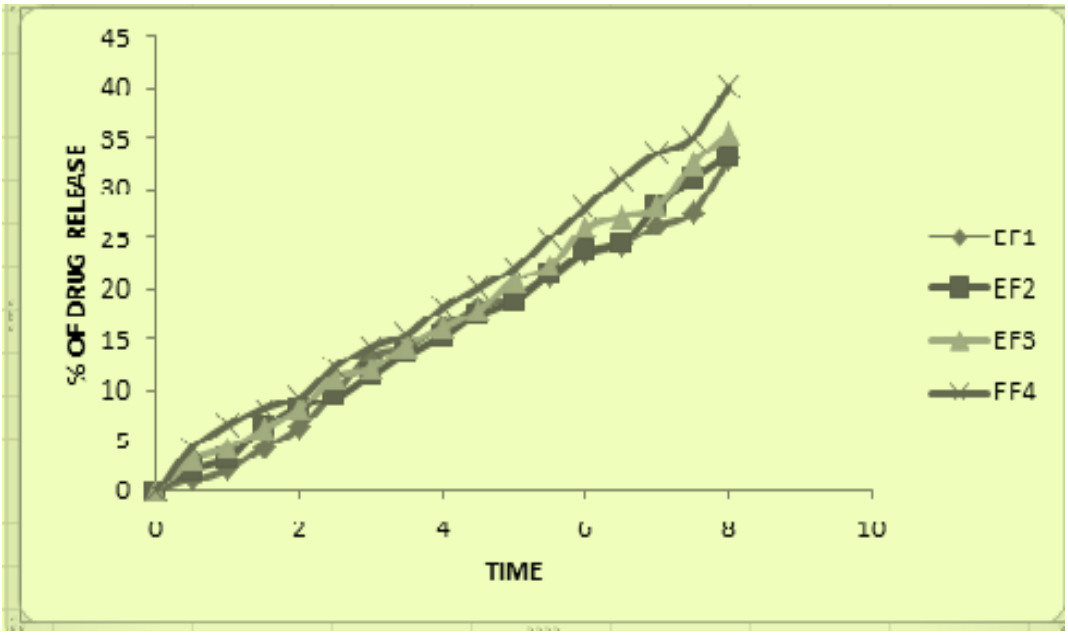
Formulation	EF4(f1)	EF4(f2)	EF4(f3)	Mean±S.D.

Thicknessuniformity(mm)	0.17	0.16	0.15	0.16±0.01
Weightuniformity(mg)	0.606	0.703	0.756	0.688±0.07
Foldingendurance	80	85	83	82±2.51
Percentagemoistureabsorp	12.211	13.350	12.340	12.63±0.62
Percentagemoistureloss	2.245	3.271	3.554	3.02±0.68
Watervapourtransmissionrate	0.0023	0.0021	0.0023	0.0022±0.0001
Drugcontentuniformityoffilms(mg)	0.422	0.424	0.425	0.423±0.0015

EX-VivoReleasePermeationRateofDrug

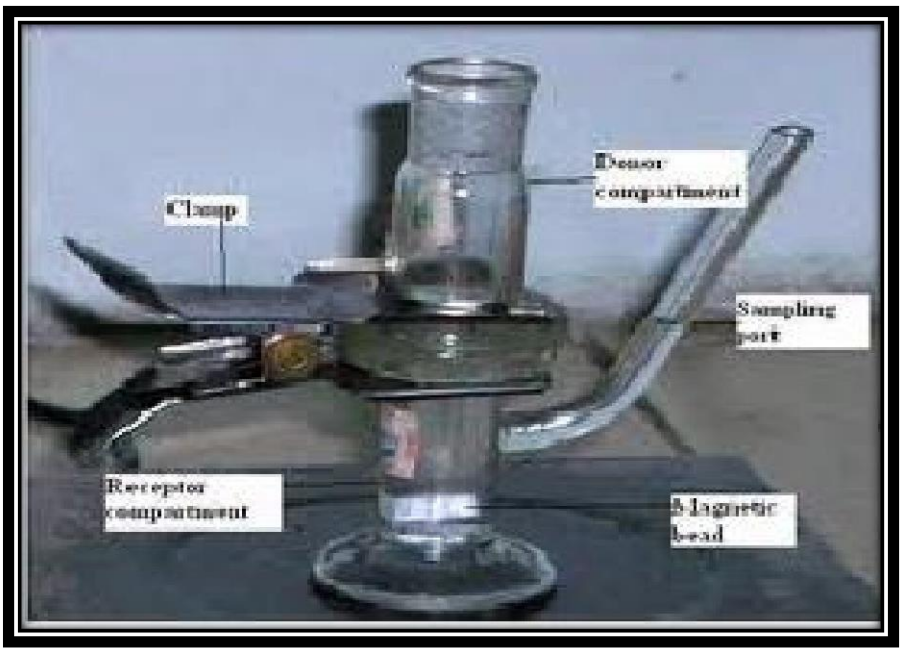
TableNo.5.24EX-Vivoreleasepermeationrateofdrug FormulationE

TIME	%OFDRUGRELEASE			
	EF1	EF2	EF3	EF4
0.5	1.1±0.18	2.1±0.21	3.1±0.22	4.3±0.26
1	2.2±0.21	3.2±0.23	4.3±0.18	6.5±0.20
1.5	4.3±0.22	6.3±0.22	6.1±0.27	8.1±0.31
2	6.3±0.21	8.3±0.25	8.1±0.22	9.3±0.23
2.5	9.7±0.25	9.3±0.26	11.3±0.19	12.3±0.21
3	13.4±0.26	11.4±0.21	12.1±0.22	14.3±0.25
3.5	14.3±0.23	13.5±0.23	14.5±0.21	15.5±0.26
4	16.3±0.27	15.3±0.21	16.1±0.24	18.2±0.24
4.5	18.3±0.22	17.5±0.22	17.9±0.26	20.1±0.28
5	19.3±0.26	18.9±0.27	20.9±0.27	22.1±0.31
5.5	21.3±0.21	21.4±0.26	22.3±0.27	25.1±0.24
6	23.5±0.28	23.7±0.21	26.1±0.24	28.1±0.28
6.5	24.5±0.26	24.7±0.26	27.3±0.26	31.1±0.22
7	26.3±0.23	28.1±0.22	28.2±0.21	33.5±0.24
7.5	27.7±0.26	31.1±0.28	32.5±0.19	35.1±0.20
8	32.9±0.21	33.2±0.20	35.4±0.24	40.1±0.25



FigureNo.5.17EX-Vivo releasepermeationrateofdrug Formulation E

FigureNo.5.18TransdermalPatchOfNifedipine



FigureNo.5.19DiffusionCell

4. CONCLUSION

TransdermalformulationofNifedipinewasdesignedbytakingdifferentpolymers.Thedifferentseriesi.e.formulation(A)haveethylcelluloseandPVPK-30asfilmformingpolymers. We try to optimize the ratio for thickness and drug release from their films anddesigned AF1 to AF4 formulation by altering the ratio of polymers. Firstly dibutylphathalatewasusedasplasticizerbutthefilmwasnotformulatedproperly.Thatmightbeduetothelargequantityof PVPK-30alongwithplasticizer.ThePEG-400containingfilmswereeasilypeeledoutfrompetridish.Sofurtherformulationsweredesignedandevaluatedforthinknessuniformity, weight uniformity, folding endurance, % of moisture absorption, % of moistureloss,watervapourtransmission rate,drugcontent uniformityandex-

vivopermeation study.
Similarytrialformulation(B)wasdesignedbytakingcombinationofECandHPCalongwithPEG-400 as plasticizer and IPA and DCM (1:4) as solvent. The formulation BF1 to BF4 hadpoorflexibility and somewhatrigid in naturesothefilms werenotstudied further.
Formulation CF1to CF4 was designed by taking combination of EC and HPMC K-15. PEG-400 was used as plasticizer along with combination of IPA and DCM (1:4) as solvent. Thepatcheshaverough surfaceand rejected dueto the roughness.
Formulation DF1 and DF4 were designed by taking combination of EC and Eudragit RS-100as film former along with PEG-400 as plasticizer. The formulations easily peeled off from thesurface.All thepatcheswereevaluatedfordifferenttests asthe discussedabove.
Formulation EF1 to EF4 were designed by taking combination of EC and Eudragit S-100 asfilm forming polymer along with PEG-400 as plasticizer and DMSO as permeation enhancer.All the formulation were easily peeled off and had smooth surface, uniform texture andtransparent.Theall filmswere evaluatedand resultswerereported.
Based on film characteristics Ethyl cellulose and Eudragit S-100 film were selected. The ex-vivo permeation was studied which revealed that formulation EF2, EF3 and EF4 showed33.2±0.20%,35.4±0.24%and 40.1±0.25% drugreleaserespectively.
The formulation EF4 was selected as finally optimized formulation as it showed 40.1±0.25%drugrelease.Furtheritfollowedzeroorderkineticsandcanbeusedasonceadaytransdermalpatch.
So in this work we optimize the ratio and weight of polymer required to achieve properthickness, elegance and other transdermal patch characteristics for Nifedipine transdermalpatch.

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Nil.

CONFLICTOFINTEREST
Authorsdeclaredfornoneconflictofinterest.

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