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A Review on Transdermal Drug Delivery System

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ABSTRACT

Transdermaldrugdelivery,asopposedtoconventional topicaldrug delivery,isthetermfordrugdeliverythrough the skin to obtain a medicine's systemic effect. Transdermal drug delivery systems (TDDS) aredosage forms in which a significant portion of the drug is transferred into the systemic blood circulationwhile the remaining portion is delivered to the epidermal and/or dermal tissues of the skin for localtherapeutic impact. Currently, 74% of prescriptions are for drugs to be taken orally, yet studies haveshown that oral medications frequently have lower efficacy rates due to first-pass metabolism andunstabledrugbloodlevels.Thefundamentaldrawb ackoftransdermaldeliverymethodsis that onlydrugswith small molecular sizes may be administered using this technique because the skin functions as anextremely effective barrier method. This review article describes the overall introduction of transdermalpatches including their types, method of preparation, advantages, disadvantages, the pathway of drugabsorptionthroughtheskin,marketedpreparation ,Evaluationparameter,andfuturetrends.

I. INTRODUCTION

The term "transdermal patch" often refers to the topical delivery of substances to healthy, intact skin,either for localized therapy of tissues beneath the skin or for systemic delivery. Compared to conventionaldosing forms or controlled-release oral systems, transdermal patches have significant benefits. As thelargest penetration barrier for drugs is within the stratum corneum, a key drawback of drug deliverypatchesisthat they usually fail to deliverthe necessary active componentthrough the skin.Due to thehigh barrierto penetration acrossthe skin,which isassociated primarily with the biological barrier,theuse of transdermal distribution to a wider spectrum of medications is constrained stratum corneum,theepidermis' toplayer.[1],[2]

In contrast to other routes of drug administration, transdermal drug delivery systems avoid a number ofproblems, including first-pass hepatic metabolism, enzymatic digestion, drug hydrolysis in acidicenvironments, gastrointestinalirritation, drugfluctuations,adverseeffects,therapeuticfailure, andtheriskof disease transmission. Additional benefits include regulated drug release, cheap cost, and patientcompliance.[3]

The first transdermal patch device, which contains scopolamine (hyoscine) to reduce nausea and vomitingbrought on by motion sickness, was introduced in 1979. Since then, it has been a desirable method ofmedication delivery as well as a difficult field of study. This early technique consisted of a tissue layersupporting a thick layer of adhesive hydrogel that contained the active ingredient. Later, patches includeda "reservoir" system with an exterior backing layer, a raised reservoir with the medicine either soluble inan alcohol solution or in solid or gel form, and a polymeric sticky membrane to separate the reservoirfromthe epidermisandadjusttheagentdistribution.[2],[4]

However, Different transdermal DDS designs have been put forth, from the simplest, which relies on thepassive delivery of drugs with little to no permeability enhancement, to the most sophisticated, whichenablesthedelivery ofbothsmalland largemolecules.In ordertoenhancethepharmacologicaleffects ofdrugs, drug carriers (either at the nano- or micro-scale) can be inserted in patches, leading to moreeffectivetreatmentof suchdevices.[5]

Transdermal medication delivery devices are used for treating a variety of skin conditions, as well asangina pectoris,pain, quittingsmoking, andneurologicalconditionslikeParkinson'sdisease.T hisstudysummarizes the work that has been done in recent years to produce patches with various designs andexplore their potential as medication delivery systems. Future prospects and the advantages anddisadvantagesof

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thesystemsthatarenowinusewillbe explored.[5],[6]

Anatomy and physiology of skin:

The skin is the largest organ in the body and a has surface area of about 1.5 to 2 sq. meters in adults andincludesglands,hair,andnails.Therearetwomainlayerstheepidermisandthedermis.

Epidermis:

The epidermis is the topmost layer of skin and is made up of stratified keratin squamous epithelium,whichvariesinthicknessdependingonwhereonthebodyitislocated.Thepalmsofthehandsandthebottoms of the feet are where it is thickest. The dermis' interstitial fluid, which supplies oxygen andnutrients and drains away as lymph, bathes the different layers of the epidermis, which contains bloodvesselsornerveendings.[7]

a) Stratumcorneum:

The skin's topmost layer is referred to as this horny layer When it is roughly 10µm thick when dry butswellstomanytimesthisthickness whenwhollyhydration. 10to25deadlayersarepresent.Corneocytesare keratinized cells. Though adaptable pretty impenetrable. In the stratum corneum, there is the mainobstacle to drug entry. An example of how to model the Horney layer's architecture wall-likeconstruction. The keratinized skin in this simulation Incorporates lipid, cells that work as protein"bricks."“mortar.”

b) Viableepidermis:

This layer,which lies underthestratumcorneum,rangesinthicknessfrom0.06 mmontheeyelids to0.8mm on the palms. It is composed of different layers as it moves inward, including the stratum basal,stratum lucidum, stratum granulosum, and stratum spinosum. The epidermis is continuously renewed bycell division in the basal layer, which makes up for the loss of dead Horney cells from the skin's surface.The basal layer's outward-moving cells undergo morphological and histochemical changes as theyundergokeratinization toformthestratumcorneum'stopmostlayer.[8]

Threesteps arenecessarytokeeptheepidermishealthy:

1) Thekeratinizedcell's surfacedesquamation
2) Thecelliseffectivelykeratinizingasitapproachesthesurface.
3) Constantcelldivisioninthe deeperlayers,wherefreshlycreatedcellsarepropelledtothesurface.[7]

Dermis:

The dermis is a 3 to 5-mm thick layer made up of a connective tissue matrix that houses nerves, bloodvessels, and lymphatic vessels. The control of body temperature relies heavily on the cutaneous bloodsupply. While removing pollutants and waste, it also gives the skin nutrition and oxygen. Most moleculesthat penetrate the skin barrier sink in capillaries, which are located 0.2 mm from the skin's surface. Thus,the blood supply maintains a very low dermal concentration of a permeant, and the ensuing concentrationgradientacrosstheepidermisisnecessaryfortransdermalpenetration.[8]

Hypodermis:

The dermis and epidermis are supported by the hypodermis or subcutaneous fat tissue. It functions as aplacetostorefat.Thislayeraidsintemperatureregulation,offersnutrientsupport,andprotectsmechanically.Principalbloodarteries,nerves,andpossiblypressure-sensingorgansarecarriedthereto the skin. For transdermal drug administration, the medication must pass through all three of these layersandenterthebloodstream,whereasfortopicaldrugdelivery,juststratumcorneumpenetrationisnecessary,andthe drugshouldthenberetainedintheskinlayers.[7]

Pathwayofdrugabsorption throughtheskinTransfollicularAbsorption:

Thetrans follicularrouteisthequickestrouteforadrugtotakeinorderto gettothesystemiccirculation,which offers a vast region for drug dispersion. The skin has numerous sweat glands, oil glands, hairfollicles, and pores that open to the skin's outside surface through their ducts. These ducts provide acontinuous channel across the stratum corneum for the transport of medications, although manyparameters, such as gland secretion, the composition and volume of secretion, etc., alter the transport ofpharmaceuticals through this route. The trans follicular route is the quickest route for a drug to take inorder to get to the systemic circulation, which offers a vast region for drug dispersion. Skin has numeroussweatglands,oilglands,hairfollicles,andporesthatopentotheskin'ssurface.[9]

TransdermalAbsorption:

Thetransdermaldrug deliverysystemworks

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byallowingdrugmolecules todiffusethroughtheepidermallayers of the skin from the drug reservoir in the transdermal patch. As a barrier, the stratum corneum,which is regarded as the rate-limiting membrane in transdermal drug delivery systems, poses a significantimpediment. Partitioning into the stratum corneum is the initial step in trans epidermal permeation, afterwhich tissue-to-tissue diffusion occurs. Since the epidermis lacks a direct blood supply, the permeatingdrug must diffuse across it in order to reach the wet cell mass of the epidermis. The epidermal cellmembranes are tightly packed together, and there are no intercellular spaces for ions and polar nonelectrolytemoleculestodiffuselypassthrough.[10]

IntercellularRoute:

Drugs are transported by the continuous lipid matrix in the intercellular route. For two reasons, thisapproach presents a major challenge. In contrast to the relatively direct course of the transcellular route,the interdigitating nature of corneocytes produces a complex conduit for intercellular drug absorption,which brings to mind the "bricks and mortar" model of the stratum corneum. An area of alternatelystructured bilayers makes up the intercellular domain. Thus, a medication needs to repeatedly diffusethrough aqueous and lipid domains and progressively partition into each. Small, uncharged moleculescommonlyentertheskinbythis pathway,whichis widelyacknowledgedas themost prevalentone.[11]

TYPESOFTRANSDERMALDRUGDELIVERY SYSTEM

A. ReservoirSystem:

Inthisdrugsystem,adrugreservoiris heldbetweentheSupport layerandvelocitycontrolmembrane.medicine Release from rate-controlled microporous membranes. The drug can be in the form of asolution,suspension,orgelDispersedinasolidpolymermatrixinthereservoirsection.[12]

B. MatrixSystem

1) Drug-in-adhesivesystem-

for the formation of drugs After dispersing the drug in the adhesive polymer, Dispersion of MedicatedPolymer Adhesives with Solvents Melt cast or glue (use hot melt adhesive) on an impermeable carrierlayer.[11]

2) Matrix-dispersionsystem

The drug is dispersed in a matrix dispersion system Uniform in a hydrophilic or lipophilic polymermatrix.This containing polymer is then immobilized together with the drug Obstructing base plate in thecompartmentoftheDrugimpermeablebacksheet.Theadhesivespreads Surroundinginsteadofapplyingtothesurfaceof thedrugReservoirsforformingadhesive edgestrips.[12]

C) Micro-ReservoirSystem

Thissystemisacombinationofreservoirandmatrixdispersion systems.Heretheactiveingredientissuspended in an aqueous solution.Disperse the solution after dispersing the water-soluble polymerHomogeneous with lipophilic polymer, thousands of Non-leaching microscopic spheres of drugreservoirs.[11]

D) Single-layerdruginadhesive:

This is a type that contains a drug in the adhesive layer . Adhesive layers are not only used to gluedifferent layerstogether,buttheyarealsoresponsiblefortherelaseofdrugsSkin.Adhesivelayeristemporarilyenclosed bylinerandpads.[11]

E) Multi-layerdruginadhesive:

Thistypeisalsosimilartothesingle-layertype,buttheDrugimmediatereleaseinlayerand otherlayerscontrol the release together with the adhesive layer.The adhesive layer is responsible for the release ofactiveingredients.[11]

F) Vaportransdermalpatches

Transdermal vapor patches consist of a single layer of adhesive polymer containing vapor-releasingproperties.Various steamskinpatchesis availableonthemarketandusedforvarious purposes. NicoDermforexampleCQ®is atransdermalnicotinepatchthatcontainsessentialoils uponrelease.Helpsquitsmoking.Thisproductwasintroducedtothe Europeanmarketin2007.[3]

KineticsofTransdermalPermeation:[9]

The main mechanism by which drugs are absorbed Transdermal is the passive diffusion of drugs throughtheskininwhichthedrugisabsorbedaccordinglyConcentrationgradientduetohighdrugconcentrationResides in the skin or within the skin Drug

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molecules diffuse from the reservoir into the systemcirculation through the skin. drug absorption rate Diffusion by passive diffusion is controlled by Fick'slaw.
ThetransmittancedQ/dt is givenbydQ/dt=Ps(Cd-Cr)……(1)

whereCdisthedonorphaseconcentration,i.e.SkinsurfaceandCristhedrugconcentration inthereceptorphased.H.WholebodyapplicationtotheskintrafficjampublicrelationsistheoverallpermeabilityandisgivenbyThefollowingformula:
Pr=(KsDss/hs)……(2)
WhereKsis thepartitioncoefficientofthedrugandDssistheApparentdiffusivityofthedrugandhsisthethicknessoftheskin. Therefore,themagnetic permeabilityPscanbeconsideredas
Ks, Dss, and hs (from Equation 2) areConstant under certain conditions. that's why a constant diffusionrateisachievedwhenCd>Cr.soevaluate ThespreaddQ/dtinEquation1canbereducedtodQ/dt= Ps.Disc……. (3)
To keep the penetration rate (dQ/dt) constant, CdThe value should remain constant throughout thepenetrationProcessthroughtheskin.Tokeep themedicationconstantReleaserate(Rr)mustalways begreater than the absorption rate (Ra), i.e. (Rr) > (Ra). Therefore, the concentration of drugs on the skinsurface is always given Greater than the saturation solubility of the drug in the skin (Ces) i.e. Cd >Cesandmaximumskinpermeability(dQ/dt)misthen (dQ/dt)m=Ps.Ce

Componentsoftransdermalpatch:

1.Backinglayer

External protection of macromolecular drug reservoirs Provide environment, support, and accept print.Carrier webs must have optimum elasticity and flexibility toPrevent drug diffusion to prevent drugloss.That Must be compatible with polymers, excipients, and drugs ,do not provoke any reaction. It's aforgery of aluminum foil, polyethylene, polyester, polyvinyl chloride, heat seal layer, polyurethane, andcoverfoampad.[9]

2) Polymermatrix:

Thedrugisreleasedfromthe devicebelowpolymercontrol.[13]

3) Drug

Drugsubstancesaredirectlyattachedtothereleaseliners..[12]

- DrugsneedmolecularWeightlessthanabout 1000Daltons.
- HasbothlipophilicandhydrophilicphasesRequiredfordrugaffinity.
- Drugmusthavealowmeltingpoint.
- Foradrugtowork,Dailydosesofafewmilligrams shouldbesufficient.
- Ashorthalf-life(t1/2)is required.anallergicorirritant reactiontoDrugs shouldnotoccur.[13]

4) Releaseliner

It is a reliable and essential packaging material. Peel off the patch while using the patch on the skin.Consists of the non-occlude able base layer (e.g. paper tissue) or occlusive such as polyethylene, PVC.[14]

5) Adhesive

The glue keeps the patches in constant contact Skin. Use your finger to apply it to the skin Pressureshould be applied to hold the patch in place longer period. Patch selection criteria are Patch type anddesign, and adhesive properties. It should be Non-irritating and compatible with other ingredients .Theformula is gentle on the skin and can be easily removed. for example. ,Polyisobutadiene, polyacrylate,siliconeadhesivepolymer.[9]

6) Permeationenhancers:

Permeation enhancers are used to increase the permeability of the stratum corneum (SC) layer.Drugcandidates achieve higher therapeutic levels. Structural components of the stratum corneum, such asproteins Lipids are affected by permeation enhancers. Changes in protein and lipid packaging SCsisdone by penetration enhancers, thus chemically modifying skin barrier function leading to increasedtransparency.

PenetrationenhancerforTDDS

1. Solvents-Methanol,Ethanol,Dimethylsulfoxide
2. AnionicSurfactant–SodiumLaurylSulfate
3. NonionicsurfactantPluronicF68,PluronicF128
4. Essentialoils –cardamomoil, cuminoil, lemonoil,menthol(SinghMC et al.,2010)Pressuresensitiveadhesive(PSA)[15]

VARIOUSMETHODSFORPREPARATIONOFTDDS:

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1) AsymmetricTPXMembraneMethod:

Using as the backing a polyester sheet (type 1009, 3m) with a concave diameter of 1cm prototype patchcould be created for the membrane.The concave membrane is covered by poly (4-methyl-1-pentene)-asymmetric membrane (TPX), which is then affixed with an adhesive.[13]Preparation of asymmetric TPXmembranes a dry/wet inversion is used to create them. To prepare polymer solution with dissolved TPXCyclohexane with non-solvent additive, 60°C.With a gardening knife, the polymer solution Pour into aglassplateat40°C for24hours.Dissolvethecastfilmat50°Cfor30minutes Secondsbeforemeltinginto a clot Bath (temperature is kept at 25°C).Then you can start removing and drying the membrane Soak[10minutesinanovenat50°C].[13]

2) MercurySubstrateMethod:

This approach involves dissolving the needed amount of medication in a solution of polymer andplasticizer. Stirring the aforementioned remedy for a fewIt takes some time to create a homogeneousdispersion,soafterwaitingforthelastoft heairbubbles todisappear,it is pouredintoaglassringthat isputoverthemercurysurfaceinaglasspetridish.Byput tinganinvertedfunneloverthepetridish,the paceat whichthesolventevaporatescanbemanaged.Thefilms shouldbekept inadesiccatorafterdrying.[16]

3) CircularTeflonmould method-(BakerandHeller1989):

As an organic solvent, polymeric solutions in various ratios are utilized. The answer is then split into twohalves. The medicine is dissolved in one-half of the calculated amount and in the other half.Two halvesare combined once the enhancers at various concentrations have been dissolved. The drug-polymersolution is supplemented with a plasticizer, such as Di-N-butyl phthalate. The entire mixture must bestirred for 12 hours before being placed into a circular Teflon mould. In a laminar flow hood model withanairspeedof0.5 m/s,themouldsmustbesetuponaflatsurfaceandcovere dwithaninvertedfunneltomanage solvent vaporization. For 24 hours, the solvent is allowed to evaporate. The dry films must bekeptfora further24hoursat250.5°C.[12]

4) GlassSubstrateMethod:

Then keep the polymer solution on one side and let it swell Add the required amount of plasticizer andactive ingredient solution Stirred for 10 minutes. Also, for some, it's the page Eliminate trapped air, thentime pour Clean and dry the Anumbra Petri Plate. solvent rate Evaporation is controlled by inverting theglassfunnelPetridish.Afterovernight,removethed riedfilmRemoveandstoreitinadesiccator.[16]

5) "IPMMembranemethod

- in this method medicineDispersed in a mixture of water and propylene glycol Contains Carbomer 940polymerandisstirredfor12hourswithamagneticsti rrer.ThevariancemustbeneutralizedTriethanolamine was addedtothicken.BufferpH7.4canbeusedto obtainsolutionGels wheretheactivesubstance has a very high solubility in aqueous solutions poor. The formed gel is incorporated into theIPMfilm.[17]

6) Byusing"TheEVACmembranes"method

Manufacture of transdermal targeted drugs system, 1 x rbopol reservoir gel, polyethylene (PE),EthyleneVinyl Acetate Copolymer (EVAC) Membrane is Used as a speed control diaphragm. If the drug does notdissolve Make a gel using water and propylene glycol. medicine is Add Carbopol resin dissolved inpropyleneglycolAddtotheabovesolutionandneutra lizeusing5%w/wSodiumhydroxidesolution.Putmedi cine (gel) A backing that covers a designated area. Place the rate-limiting membrane on top of thegel,Edgesareheatsealedtopreventleaksdevice.[12]

7) AluminiumBackedAdhesiveFilmMetho d:

Transdermal drug delivery systems can be unstable Matrix for loading >10 mg.The aluminum-coatedadhesivefilmmethodis suitable.Topreparethesame,chloroformisthesolvent ofchoice.Mostmedicinesand glues dissolvein chloroform. The drug is dissolved in chloroform,Add adhesive to the chemicalsolution,dissolution. Custom-made aluminum formers are lined up Wrap in aluminum foil and seal theendstightlycorkblock.[16]

8) Freefilmmethod:-

The free film of cellulose acetateis made by casting on a mercury surface. polymer A solution of 2%w/wshouldalsobepreparedchloroform.Theplastic izeris aConcentration of40%byweightofpolymer weight. 5mlPour the polymer solution into the glass ring, and Placed on the mercury surface of a

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Volume 8, Issue 3 May-June 2023, pp: 3457-3467 www.ijprajournal.com ISSN: 2249-7781

glassPetri dish.The evaporation rate of the solvent is to Place the inverted funnel on top of the petri dish. Thefilm Detect formation by observing the mercury surface after complete evaporation of the solvent dry filmorganizedandstoredbetweenleavesandWaxpaperuntiluseinadesiccator.[17]

Tableno.1-TDDSMARKETEDPRODUCTS[18], [19]

ProductName	Drug	Manufacturer	Indication
Alora	Estradiol	TheraTech/Proctol andGamble	Postmenstrualsyndrome
Androderm	Testosterone	TheraTech/GlaxoSmithKline	Hypogonadisminmales
Catapres-TTS	Clonidine	Alza/BoehingerIngelheim	Hypertension
Climaderm	Estradiol	EthicalHoldings/Wyeth-Ayerest	Postmenstrualsyndrome
Climara	Estradiol	3MPharmaceuticals/BerlexLabs	Postmenstrualsyndrome
Deponit	Nitroglycerin	Schwarz-Pharma	Anginapectoris
Duragesic	Fentanyl	Alza/JanssenPharmaceutica	Moderate/severepain
Estraderm	Estradiol	Alza/Norvatis	Postmenstrualsyndrome
Fematrix	Estrogen	Ethical Holdings/Solvay HealthcareLtd.	Postmenstrualsyndrome
FemPatch	Estradiol	Parke-Davis	Postmenstrualsyndrome
Habitraol	Nicotine	Novartis	Smokingcessation
Minitran	Nitroglycerin	3M Pharmaceuticals	Anginapectoris
Nicoderm	Nicotine	Alza/GlaxoSmithKline	Smoking cessation
Transderm-Scop	Scopolamine	NovartisConsumerHealth (Parsippany,NJ,USA)	Motionsickness
Neupro	Rotigotine	Schwarz Pharma(Mequon, WI, USA)	Parkinson'sdisease
Exelon	Rivastigmine	Novartis	Dementia

Applicationoftransdermalpatch[17]

1) Transdermal nicotine patches to be released Controlled dose of nicotine to help quit smokingsmokeacigarette
2) NitroglycerinpatchsometimesItwasprescribedfor thetreatmentofanginapectoris.
3) clonidine,antihypertensivesandketoprofen,non-steroidalanti-inflammatorydrugsItisavailableintheformof atransdermalpatch.
4) MAOIselegilinetransdermalabsorptiontypewas ingestedFirst meansoftransdermaladministrationofantidepressants.
5) TransdermaldrugforattentiondeficitHyperactivitydisorder(ADHD).

ADVANTAGES[8],[13],[16]

1. Preventfirst-passgastrointestinalandhepaticmetabolism.
2. Makesurethecontrolabsorptionis constant.
3. lessensnegativeeffects
4. Limitexposuretoharmfulmetabolites.
5. Increasedpatientcompliancebecausemultipledosingis nolongernecessary.
6. Increasetheeffectiveness oftherapy.
7. Simpletouseandtakeaway.
8. Painlessandminimallyinvasive
9. Self-governance.
10. Functionswellformedicationswithbriefbiologicalhalf-livesandrestrictedtherapeutic windows.
11. Simpletostop dosingintheeventofabadreaction.
12. Repeatedsustainrelease.
13. Transdermal drugdeliverymakesit possibletoavoidgastrointestinalabsorptionanditassociatedrisksofenzymatic andpH-relateddeactivation.
14. Refrainingfromfirst-passmetabolism.
15. Drugsrequiringrelativelyconstantplasmalevelsareexcellentcandidatesfortransdermaldrugdeliverybecausetheabsenceofpeaksinplasmaconcentrationcanlowertheriskofsideeffects.

Inplaceoftheoralroute.

17. Thepatchalsoallows forcontinuousdosingratherthanthepeaks andvalleysin medication levelcommonwithorallyadministeredmedications.
18. Theabilitytoquicklystop theeffects ofadrugbyremovingapatch,aswellas

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Volume 8, Issue 3 May-June 2023, pp: 3457-3467 www.ijprajournal.com ISSN: 2249-7781

quicknotifications ofmedicationinanemergency

Limitations

1. Drugsrequiringhighbloodlevelscannot beadministered.
2. Adrugorits formulation mayirritateandsensitisetheskin.
3. Theskin'sabilitytoactasabarriervariesfromonesit etoanotheronthesameindividual,frompersontop erson,andwithage.
4. Notfeasibleif thedrugis heavily metabolisedintheskinandifthemolecularsizeis too largetoallowthemoleculestodiffusethroughthes kin.
5. Mightleadtoanallergicreaction.
6. Consistencyover timeischallenging.
7. Ionic medicationscannotbedeliveredusingatransderm aldrugdeliverysystem.
8. High druglevels inthebloodcannotbeachieved.
9. Itisunabletodevelopfordrugswithlargemolecula rweights.
10. Itisunabletodelivermedicationpulse-by-pulse.
11. Itcannot developif themedicationorformulationirritatestheskin.
12. Apossiblelocalinflammatoryreactionat theapplicationsite.
13. Might leadtoanallergicreaction.

Tableno.2-PolymersUsedIn TransdermalPatch

Sr.No.	Polymers	Reference
1	EC	[1]
2	HPMC K4M/K100/PVP	[20]
3	PVA	[21]
4	SiliconeElastomer	[22]
5	HPMC/Chitosan	[23]
6	Carbopol	[24]
7	HPMC	[25]
8	Eudragit,PVP	[26]
9	PG	[27]
10	PEG	[28]

EC- Ethyl CellulosePVA-PolyvinylAlcohol
PVP-PolyvinylPyrrolidone
HPMC- Hydroxypropyl methylcellulosePG-PropyleneGlycol
PEG-Polyethyleneglycol

ADVANCEDDEVELOPMENT INTDDS:

Medicine in adhesive technology Systems is Recommended for Passive Transdermal Delivery has twoareas of formulation research Focus on adhesives and secondary materials. glue Research Focuses onAdhesiveCustomizationImproves adhesiontotheskin when worn duration,improvesdrugstabilityandsolubility,

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Volume 8, Issue 3 May-June 2023, pp: 3457-3467 www.ijprajournal.com ISSN: 2249-7781

Decreases latency, and increases speed delivery. Free size glue None can absorb all drugs andformulation chemistry, adjustment adhesive chemistry allows percutaneous absorption Formulator foroptimizingtheperformanceof transdermalpatch.Richresearchfieldsinthe last10-15years[29]

Concentration Development of transdermal absorption technology Increase using mechanical energydrug flow across the skin by changing either the Skin barrier (mainly stratum corneum) or increasedenergy of drug molecules. This so-called"Active" transdermal techniques include:Iontophoresis uses alow-voltagecurrenttopowerthechargeddrugthroughthesk in.

Easy to use electroporation high voltage electric impulse Creates temporary watery pores skin.Sonophoresis(lowfrequencies that interferewithultrasonicenergystratumcorneum)andh eat energy(Increasedskinpermeabilityandweightgainenergyoft hedrugmolecule).

Also, cast magnetic energy was magnetophoresis studied as a means to increase its Drug flow across theskin.[18]

LIMITATIONSFOR SELECTIONOFTDDS:

Notalltypesofdrugs canbeadministeredthis wayRoot;thedrugshouldhavesomedesirablephysical properties.chemicalproperties.

- Notsuitablefor pharmaceuticalsrequiringhighplasmalevels.
- Notsuitableforagentsthatcauseskinirritationcont actdermatitis.
- Notsuitablefor highmolecular weightdrugs.
- Not suitablefordrugsmetabolizedduringthis timepassagethroughtheskin.Largeronescannotu se the transdermal route Since the skin is a very effective barrier, various drugs for drugpenetration.Onlypossibleatlowdosesmanag ed.[16]
- Medications thatrequirehighbloodlevelscannotbeadminister ed
- Medicationformulationsmaycauseirritationorse nsitization.[6]
- Drugsmetabolized duringthistimearenotsuitableto pass throughtheskinThismethod.[13]

EvaluationParametersofTransdermal Patch.

1) **Folding Endurance**:- strip of a specific area (2 cm∗2 cm)was cut evenly and repeatedly folded at thesameplacetillitbroke.Thenumberoftimes thefilmwas foldedatthesameplacewithoutbreaking gavethevalue of thefoldingendurance.[20]
2) **Tensile Strength**:-Using a tensiometer, the patch's tensile strength was assessed. There are two loadcell grips in it.Theupperonecouldbemoved,butthelowerone was fixed.Betweenthesecellgrips,2 x2cmfilmstripswerefastened,andforce wasgraduallyexerted.[20]
3) **Percentage Elongation Break Test:**- The length right prior to the breakpoint was used to determinethepercentage elongationbreak,whichwasthencalculatedusingt heformulabelow.Elongationpercentage= (L1−L2)/L2×100, whereL1isthefinallengthofeachstrip,andL2istheii nitiallengthof eachstrip.[20]
4) **Thickness**:-Using a digital micrometer, the thickness of the drug-loaded patch is measured at severalsites, and the average thickness and standard. To guarantee the created patch's thickness, deviation iscalculated. At various spots along the transdermal film, the thickness is measured using a travelingmicroscopedialgauge,screwgauge,orm icrometer.[20]
5) **Drug Content**:-In 100 mL of methanol, a predetermined patch area (2 cm x 2 cm) was dissolved, andthemixturewas continuallyshakenfor24hours.Next,theentire solutionwas ultrasonicallysonicatedfor15 minutes.Following filtering, the drug's concentration was evaluated by spectrophotometric estimationata wavelengthof 281nm.
6) **Percentage Moisture Content**:-For 24 hours, individually weighed patches are stored in desiccatorswithfusedcalciumchlorideatroomte mperature.Thepatchesmustbereweighedandme asured24hourslater.Aformulaisusedtodetermin ethepercentage moisturecontent. Percentagemoisturecontent:-(Initialweight-Final weight/Finalweight)x100[20]
7) **Percentage Moisture Uptake**:- The weighed films were keptin a desiccator at room temperature for 24h containinga saturated solution of potassium chloride in order to maintain84% RH. After 24 h, the filmswerereweighed,anddeterminethepercentag e moistureuptakefromthebelow-

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Volume 8, Issue 3 May-June 2023, pp: 3457-3467 www.ijprajournal.com ISSN: 2249-7781

mentionedformula:
Percentagemoistureuptake=Finalweight−Initial weight/Initialweight ×100….[20]

8) **WeightOfPatch**:-
Eachpatchfromaspecificformulationisweighedsepar atelyonadigitalbalancetodeterminethestandardd eviation.[18]

9) **Stabilitystudies**:InaccordancewiththeICHreco mmendations,stabilitystudiesmust becarriedoutbyholdingTDDS samplesat40°F and75RHforsixmonths.TheSamplesaretakenat0 , 30, 60, 90,and180daysandproperlyanalysedforthepresence of drugs.[30]

10) **Percentage Moisture Loss**:-The prepared patches are weighed separately and maintained indesiccators withanhydrouscalciumchlorideatroomtemperature for24hours.Thepatchesareweighedeverysoftenafterthefirst24hoursuntilasteadyweightisachieved.
Moisturelossiscalculatedbyusingthefollowingformulae:
Percentagemoistureloss= (Initialweight-finalweightt)/initialwt)X100.[31]

11) **In-vitro skin permeation studies**:-Using diffusion cell equipment, it is possible to measure how welladrugpenetratestheskin.Intheexperiment,pigearskinisprimarilyemployedandmountedbetweenthedonor and receptor compartments. Comparing the cumulative permeation profiles of skin that has beenmicroneedleanduntreatedskin.[32]

12) **Skin irritation evaluation:-**Albino rabbits (N = 15) were divided into 5 animals and a skin irritationtest (9) was conducted.Groups, 3 rabbits in each group. Group, I marked as control (no treatment),GroupIIwas alsopasted withcommerciallyavailableadhesivetape(Nichi poreSurgicalTape,Japan).considereda control group. Apply DXIBN transdermal patch to bare skin Group III and Group IV blank patch (nodrug) Standard stimulant was formalin Applied to Group V animals, the experiment was conducted over 7days.Group (reapply the new patch to the same location every 24 hours for 7 consecutive days)andapplicationsitesweresimilarlyratedonavisualrating.[21]

FUTURE TRENDS INTDDS

In the future, the transdermal route is the most preferred Medication management by improving patientcompliance, Dosage control, reduction of dosing frequency, etc. 2 Decades ago, nicotine patches weredeveloped for smoking Settings for transdermal use and many wins Very popularly. After that, manydrugs were prescribed Transdermal patches such as nitroglycerin and estradiol for angina pectorisFentanylforestrogendeficiency,fentanylforpain,etc.ThepatenttermencouragedresearcherstoFormulate drugs with new acceptable dosages to the application form. The popularity of transdermaldelivery systems Moreover, it is continuously increasing. Improved design and technology. leadership Apharmaceutical company is working on its TDDS, Many techniques for the transdermal route areWorking on these technologies with these companies' successful performance. new distribution systemssuchas Liposomes,niosomes,nanoparticles,microspheres,etc.Microemulsions areused intheformulation of TDDS. Increases solubility with improved absorption of Insoluble drugs. Other infiltrationtechniques Other improvements have also been made. B. use mechanical energy that increases drug fluxacross the skin by altering or increasing the physiology of the skin Velocity of drug molecules.electrophoresis, Iontophoresis, sonophoresis, and magnetophoresis are Other techniques studied forImproved drug delivery across the skin Drugs with molecular weight and insoluble drugs . The currentscenario has emerged as the safest and safest skin Acceptable route of drug delivery to the systemCirculatory,anti-oralroute[9]

II. DISCUSSION

This article provides valuable information and details of the evaluation process on transdermal drugdelivery systems as a ready reference for researchers working with TDDS. The foregoing indicates thatTDDS has great potential to exploit both hydrophobic and hydrophilic drugs into promising deliverabledrugs.Optimizingthisdrugdeliverysystemrequiresabetterunderstanding

ofthebiologicalinteractionsanddifferentmechanisms ofthepolymers.

The transdermal route of drug deliveryissafe and effective compared toother routes of administration.Many drugs are formulated withTDDS, such as hormone therapy, a wide range ofpain relievers, heartdisease drugs to avoid GI actionand first-pass metabolism. Due to several advantages and popularity oftransdermal drug delivery, which attract the attention of researchers and intendto introduce many newdrugs in transdermalform. The main function of the skin is to protectthe internal organs, buttransdermal administration of drugs can alter the physiology of the skin, so this should be consideredwhen designing a transdermaldeliverysystem that alters thenatural functions of the skinat leastpossible.Abetterunderstandingofthephysiology andanatomy oftheskin willhelpus moveforwardinthisfield.

However, thedesignandoptimizationoftransdermaldeliveryrequiresexcellent knowledgeandunderstandingoftheinteractionsbetweendifferentpolymersandskincomponents.

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