"Formulation and development of film forming system for anti- acne agents"

A Thesis Submitted to

NIRMA UNIVERSITY

in Partial Fulfillment for the Award of the Degree of

MASTER OF PHARMACY

IN

PHARMACEUTICS

BY

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Under the guidance of

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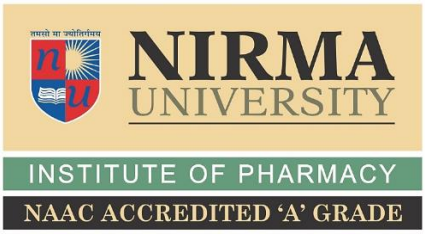

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june 2020

CERTIFICATE

This is to certify that the dissertation work entitled "Formulation and development of film forming system for anti- acne agents" submitted by Mr./Ms.DHARMIKA.S.GOHEL with Regn. No. (18MPH103) In partial fulfillment for the award of Master of Pharmacy in "Name of a Department" is a bonafide research work carried out by the candidate at the Department of Pharmaceutics, Institute of Pharmacy, Nirma University under my/our guidance. This work is original and has not been submitted in part or full for any other degree or diploma to this or any other university or institution.

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CERTIFICATE OF ORIGINALITY OF WORK

This is to undertake that the dissertation work entitled "Formulation and development of film forming system for anti- acne agents" Submitted by Dharmika.S.Gohel (18MPH103.) in partial fulfillment for the award of Master of Pharmacy in "Pharmaceutics." is a bonafide research work carried out by me at the "Pharmaceutics", Institute of Pharmacy, Nirma University under the guidance of "Dr.Mohit Shah". I am aware about the rules and regulations of Plagiarism policy of Nirma University, Ahmedabad. According to that, this work is original and not reported anywhere as per best of my Knowledge.

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DECLARATION

I hereby declare that the dissertation entitled "Formulation and development of film forming system for anti- acne agents", is based on the original work carried out by me under the guidance of Dr.Mohit Shah, Institute of Pharmacy, Nirma University. I also affirm that this work is original and has not been submitted in part or full for any other degree or diploma to this or any other university or institution.

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In providing concrete shape of my article, there are number of people who have play major role, I take this opportunity to express my deepest gratitude my guide **Dr. Mohit Shah,** Assistant Professor, Department of Pharmaceutics, Institute of Pharmacy, Nirma University for his valuable guidance and support for the project. His expensive knowledge and helpful nature played pivotal role in shaping my project.

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Chapter 1:

AIM OF PRESENTATION INVESTIGATION

Skin is considered as a main course of commercial creativity of medicines for both close by and basic properties. The practicality of topical cure based upon the physical and chemical employments of the medication what's more, adherence of the patient to the action dull essentially as the premise's capacity to protect fast to skin over the span of the treatment to support therapeutic medication entrance through the pores and skin limit. Conventional data for topical and dermatological organization of molecule have sure imprisonments like awful adherence to skin, negative vulnerability and haggled tireless consistence. For the treatment of sicknesses of casing tissues and wounds.[1]

Topical film shaping are such emerging medication transport process suggested for topical use to the pores and skin, which hold to the body, confining a small straightforward film and flexibly movement of the dynamic fixings to the body tissue.[1] These are anticipated for pores and skin utility as emollient or defensive and for near to intrigue or transdermal invasion of medicament for central hobby.

The straight forward is a huge part of this film former setting which unmistakably impacts the influenced individual affirmation. In the present dispatch, the film framing plan are delineated as an auspicious selection for topical and transdermal cure transport.[1]

Chapter : 2

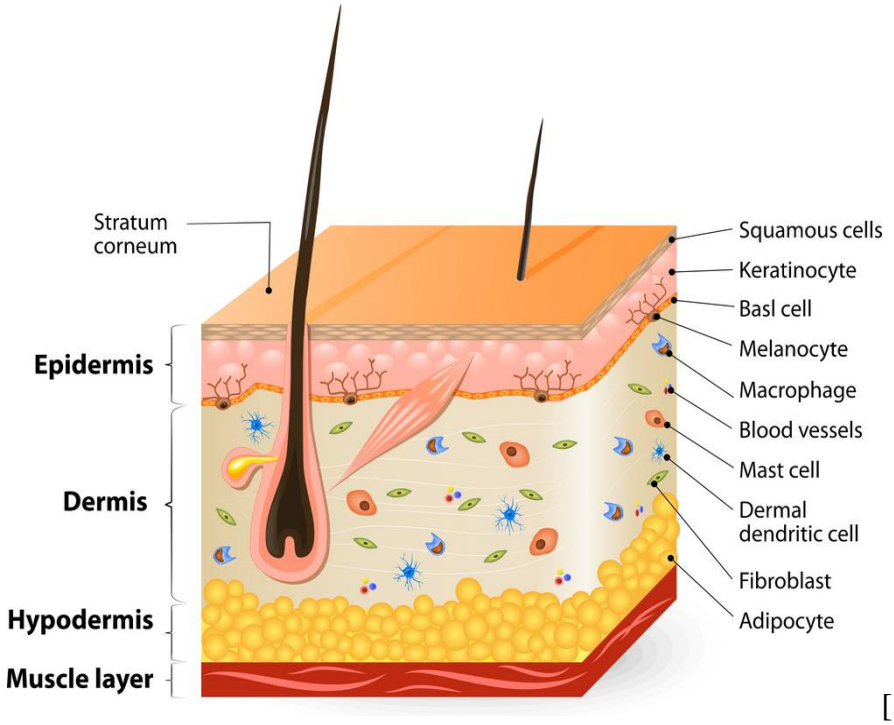
INTRODUCTION

2.1 Anatomy of Skin

The skin is the greatest extreme speedily available organ of the body and goes about as a limit contrary to the littler scope and bacteria of the earth in gentle of its less transparency to such materials. The skin of a normal human body has cycle 2 m2 surface zone and it gets around 33% of the full scale blood flowing sooner or later of the casing. Percutaneous ingestion of medications through pores and skin for the most segment happens by layer corneum.[2]

Skin layer is made up of dead cells, keratinized and non-keratinized epidermal cells. Normally upper layer of skin has a thickness of 10 mm which act as a main main barrier for transferring the drug. As such conveyance of drug flotsam and jetsam over the skin is troublesome. The skin is the most outer body organ which is almost continuously get in contact with outer atmosphere. Simultaneously large number of bacteria and micro-organisms present inouter atmosphere. Here impermeable skin's upper layer act as a protective barrier. Outer skin has very large surface area up to 2 m^2. It also gets 33% of outright blood sooner or later of the body. Percutaneous ingestion of medication by means of skin primarily occurs by method of layer corneum.[2]

Upper layer of skin is also known as stratum corneum which also act as barrier for micro-organism as well as active pharmaceutical ingredient. Actually it is part of body's nature protective system.Thus, conveyance of prescription particles over the skin is extreme.[2]



[3]

The skin is the biggest organ of the animal body. It protects the whole body by forming a cover on the all organs. It fills in as a protecting watchman contrary to warmth, mellow, harm, and confusion. The skin as well:

- Regulates inward warmth degree
- maintain fat and water level
- Is a very important body organ
- Prevents liquid fiasco
- creates protective layer against living organisms (bacteria and fugus)
- Acts as a limit among the home being and its situation
- its help in the production of vitamin D, with the presence of sun light[3]

Skin is covering part of the body an available as the various surface and thickness. For example, head skin has higher hair follicles than anywhere else. Hard and rigid skin is

available at the lower part of foot. Besides, the bottoms of your toes and the fingers of your palms are parts harder than skin available on the other parts of the body.[4]

Skin generally made up of three different layers, and each layer has certain limits with the permeability:

1. Epidermis
2. Dermis
3. Hypodermis[5]

Epidermis[6]

It is the outlying or furthermost layer of human body. It is slightly cover by the stratum corneum.

Cells presents in the epidermis is divided in these 3 parts:

1. Squamous cells. The fringe layer is as often as possible shed is alluded to as the layer corneum.
2. Basal cells. Basal cells are watched for all intents and purposes beneath the squamous cells, at the base of the epidermis.
3. Melanocytes. Main function of this type of cells is to produce a melanin. This present at the base of stratum corneum.

Dermis that is two types keratinised and non-keratinised. In that specifically keratinized part is made up of squamous cell outer line in four to five different layers. Although outer most part called stratum corneum does not show any vasculature inside it. Specifically, skin with four different layers known as “Modest Skin”. These four layers are named as Basale layer, spinosum layer, granulosum layer and corneum layer. Skin is the largest part of the body which covers highest surface area copare to any other part. Sometimes fifth layer also shown which is known as layer lucidam, mostly found between the corneum and granulosm layer.

Keratinocytes can be defined as the cumulative layer regardless of basale layer. Keratin is a very important protein that is involve in many biological process and human body parts like hair, nails. Main function of keratin is to provide equal hardness to the skin and water safe hormones. Keratin present inside the skin layer can swamp easily and being used by needful cells.

Stratum Basale[6]

It is the most significant layer of epidermis or stratum corneum which is also known as germinativum layer. It interfaces between epidermis and basal lamina that also covers the dermis. Two layers are bind together with each other through collagen fibres which causes the basement film. Dermal papilla present inside this has finger like projection. Also dermal papillae improve the contact between dermis and epidermis.

The layer basale is the single layer that is created by basal cell bodies. It is a versatile cell having a cuboidal shaped. Apart from this, cells are also acting as a precursor in protein synthesis like keratin. Mostly this cellis present on the surfaces of palms and toes. Moreover, two specific types of cells named as Merkel and melanocytes. Melanocytes are the cells that prepare the melanin. Melanin is a protein that provides black color to theskin and hair. In addition to this melanin also protect the skin from the harmful UV radiation. Second type of cells are Merkel which act as a receptor and responsible the quickening the cerebrum nerves. This cells are often go through the mitosis cycle to make new cells.

Stratum Spinosum[6]

As the name proposes, the layer spinosum is spiked in appearance because of the sticking portable administrative work that be a piece of the layer through a structure known as a desmosome. The desmosomes interlock with each other and meat up the bond among the cells. It is interesting to focus on that the "horny" thought of this is a relic of the recoloring procedure. Perfect dermis tests don't show this trademark look. The layer spinosum is produced using 8 to 10 layers of keratinocytes, encircled on account of portable division inside the layer basale.

Stratum Corneum[6]

It is the shallowest layer which also act as the entry level for the micro-organism and active pharmaceutical ingredients. Also the extended keratinization would see that known as cornification.There are typically fifteen to thirty layers of cells in the layer corneum. This dry, dead layer hinders the passageway of microorganisms and the drying out of essential tissues, and gives a mechanical security towards scratched spot for the extra sensitive, central layers. Cells on this layer are shed now and again and are displaced by utilizing cells pushed up from the layer granulosum (or layer lucidum because of the arms and bottoms of toes). The whole layer is displaced at some phase in a period of cycle a month. The total layer of cells will be replaced by new cells at specific time interval. Because of this reason skin pores keeps open and skin looks new and glossy.

Dermis[7]

The epidermis is the middle layer of the pores and skin. The dermis comprises of the going with:

- Blood vessels
- Lymph vessels
- Hair follicles
- Sweat organs
- Collagen packs
- Fibroblasts
- Nerves
- Sebaceous organs

The epidermis is held by and large by methods for a protein alluded to as collagen. This layer empowers skin versatility and. The epidermis also comprises of torment and connect with receptors.

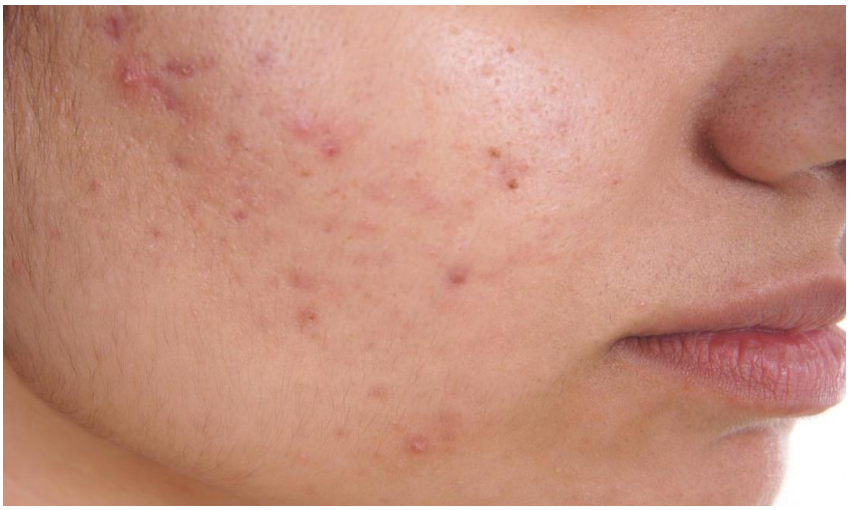
Subcutaneous fat layer[7]

The subcutaneous portly sheet is the most extreme significant layer of pores and skin. It involves two types of different cells; collagen and fat cells. It helps proportion the body's warm temperature and shields the casing from damage by means of going roughly as an ensure.

2.2 Disorders of skin

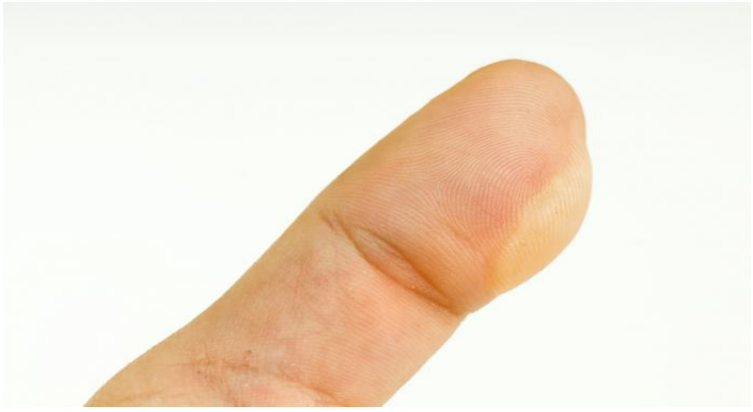
Acne[2]

- Commonly arranged at the face, neck, shoulders, chest, and top again
- Breakouts at the pores and pores and skin produced using pimples, whiteheads,
- pimples, or significant, hard rankles and handles
- May leave scars or hard to perceive the pores and pores and skin if untreated



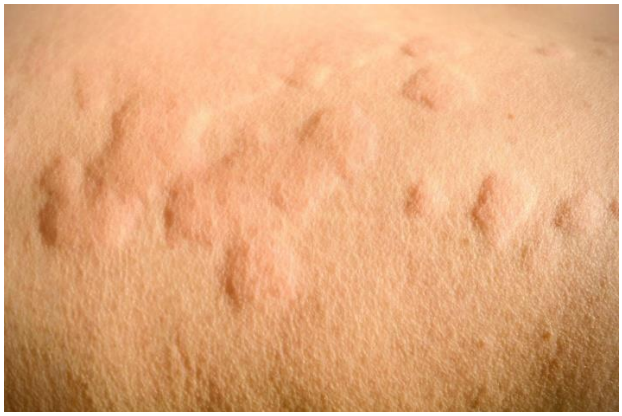
Blister[2]

- Portrayed by method of watery, spotless, fluid stuffed territory at the skin
- May be tinier than 1 cm (vesicle) or greater than 1 cm (bulla) and occur all alone or in social events. Can be found wherever on the body



Hives[2]

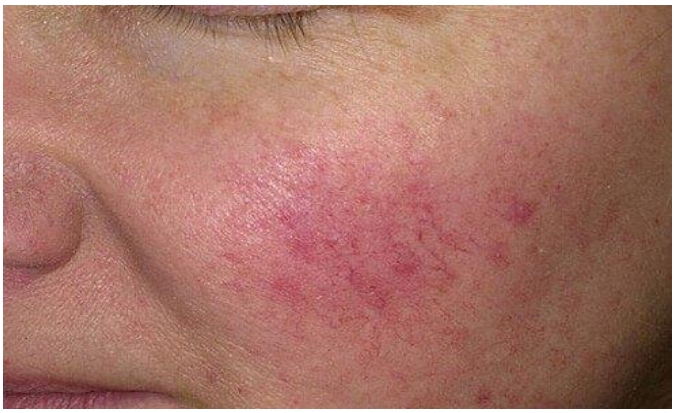
- Itchy, raised welts that show up after introduction to an allergen
- Red, warm, and very anguishing to the touch
- Can be pretty much nothing, circular, and ring-shaped or huge and erraticallyframed.



Rosacea[2]

- Chronic skin disorder that reviews examples of obscuring and fall away from the faith
- Relapses may be initiated through warm sustenance, blended fluids, sunlight, strain, and the intestinal microorganisms Helicobacter pylori
- There are four subtypes of rosacea comprising of a broad combination of caution signs. Common perspective results involve facial flushing, raised, pink thumps, facial redness

- skin dryness, and skin affectability

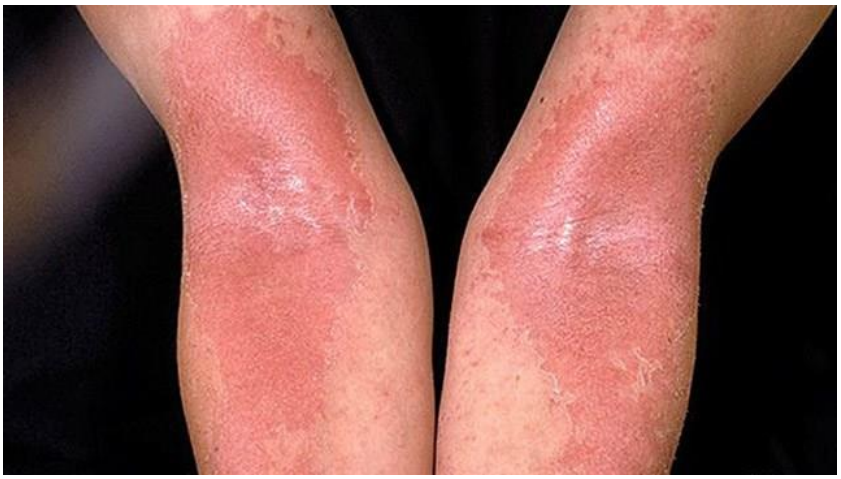


Latex allergy[2]

- Rash may also appear internal minutes to hours after prologue to a latex object
- Warm, vexatious, red wheals on the page of touch which could handle a dry, crusted appearance with reiterated introduction to latex
- Airborne latex particles may also cause hack, runny nostril, wheezing, and irate, watery eyes
- A extreme unfavourably susceptible response to latex can thought process creating and bother unwinding

Eczema[2]

- Yellow or white textured patches that piece off
- Affected regions might be red, bothersome, oily, or smooth
- Hair misfortune might also appear within the vicinity with the rash



2.3 Acne

Acne types[3]

Obstructed pores motive skin break out itself. These might be attributed to:

- extra formation of emollient (sebum)
- bacteria
- hormones
- useless skin cubicles
- ingrown hairs

Skin break out is generally connected with hormonal changes experienced sooner or later of more youthful years, anyway developed joined statescan happen upon skin escape, as

appropriately. Around 17 million Americans have skin bothering, making it one of the most extreme notable skin conditions a portion of the youths and adults.

Perceiving which kind of skin avoid experiencing is basic to incredible cure. Skin break out may be noninflammatory or combustible. Subtypes of skin get away from inner these two characterizations comprise of:

- blackheads
- whiteheads
- papules
- pustules
- nodules
- cysts

Noninflammatory skin break out[8]

Noninflammatory pores and skin irritation incorporates zits and whiteheads. These fundamentally don't reason developing. They in like manner respond normally pleasantly to over the counter (OTC) medications.

Salicylic destructive is as often as possible showcased for pores and skin break out with everything taken into account, anyway it all things considered works top notch on noninflammatory skin escape. It regularly sheds the skin, clearing dead skin cells which can start off zits and whiteheads. Quest for it in substance mixes, toners, and creams.

Zits[9]

Blackheads show up while a pore is plugged up through a blend of sebum and dead skin cells. The greatest purpose of the pore remains open, regardless of its the rest being blocked. This impacts inside the trademark darkish concealing seen on a shallow stage.

Whiteheads[10]

Whiteheads can in like manner outline while a pore gets deterred by sebum and dormant pores and skin cells. In any case, by no means like with zits, the absolute best factor of the pore stops for the afternoon. No doubt a little thump distending from the pores and skin.

Whiteheads are step by step difficult to manage in light of the fact that the pores are starting at now shut. Things containing salicylic destructive can be valuable. Topical retinoids

convey the quality impacts for comedonal skin disease. Starting at now, adapalene (Differin) is available over the counter as a retinoid.

Incendiary Acne[10]

Pimples that are purple and swollen are implied as ignitable skin break out. Although sebum and dead pores and skin cells add to red hot pores and skin break out, microorganisms can in like manner accept a movement in forestalling up pores. Microorganisms can reason a malady far underneath the pores and skin's surface. This may likewise achieve troublesome skin escape spots which may be difficult to put off.

Products containing benzoyl-peroxide may likewise help reduce expanding and dispose of minute living beings inside the pores and skin. These can in like manner empty excess sebum. Your main consideration wellbeing professional may suggest either an oral or topical enemy of pollution along the benzoyl-peroxide to manage your combustible pores and skin break out. Topical retionoids are besides a decent estimated bit of combatting red hot papules and pustules.

Papules[11]

Papules happen while the dividers enveloping your pores break free extreme exacerbation. This results in intense, deterred pores which can be touchy to contact. The skin around those pores is commonly pink.

Pustules[11]

Pustules can moreover shape while the dividers around your pores independent. In contrast with papules, pustules are stacked up with release. These takes come out from the pores and skin and are commonly red in concealing. They much of the time have yellow or white heads on apex.

Knobs[11]

Nodules show when plugged up, swollen pores bear what's more exacerbation and end up being bigger. In contrast with pustules and papules, handles are more prominent significant underneath the pores and skin.

Because handles are so significant in the pores and skin, you can not by and large treat them at household. Doctor pushed sedate is indispensable to help tidy those up.

Sores[11]

Sores can make when pores are plugged up through a blend of microorganisms, sebum, and dead skin cells. The plugs up seem significant inside the pores and skin and are comparably underneath the floor than handles.

These extensive red or white thumps are routinely anguishing to contact. Developments are the most significant kind of skin disturbance, and their affiliation commonly impacts from an inordinate disease. This sort of skin escape is moreover the appropriately at the way to scar.

2.4 Different types of dosage forms[12]

1. Gastrointestinal systems: oral and rectal route
2. Parenteral systems: Subcutaneous, Intramuscular, Intravenous etc.
3. Trans-mucosal systems: Buccal
4. Topical systems
5. Trans nasal systems
6. Transdermal Systems

2.4.1 Topical dosage form[13]

A topical cure is a formulation this is applied to a precise site on or in the edge. Routinely topical company suggests programming to body area, as an occasion, the skin or mucous layers to cure sicknesses through an extensive extent of classes comprehensive of lotions, balms, creams, froths, gels. Several topical medications are percutaneous, telling that they might be applied directly to the skin. Topical API can likewise in like way be inhalational, for case, asthma remedies, or completed to the outside of tissues beside the pores and skin, for instance, eye drops applied to the conjunctiva, or ear drops put in the ear, or prescriptions applied to the open air of a teeth. Topical medication association is a constrained drug movement body anyplace in the casing through ophthalmic, rectal, vaginal and skin as topical distributions.

Skin is one of the greatest immediately open organs on human casing for topical manager and is principal course of topical medicine movement system.

Advantages of topical dosage form[1]

- Low danger of fundamental unfriendly occasions and medication cooperation.
- Higher convergence of the anti-toxin when applied to the influenced territory.
- Smaller measure of medication is utilized.
- Lack of impact on intestinal florae.
- Low cost.
- Ease of organization to a small kid.

Disadvantages of topical dosage form[1]

- Potential creation of aggravation and hypersensitive contact dermatitis.
- Decreased infiltration in the influenced region.
- Potential quick appearance of bacterial obstruction.
- Potential change of cutaneous greenery.

1.4.2 Types of topical formulation:[14]

Cream[15]

A cream is of an emulsion type dosage forms of oil and water in around equivalent degrees. It enters the layer corneum outside layer of skin divider. Cream is heavier than lotion, and keeps up its shape while removed from its holder. It will when all is said in done be gentle in immersing tendency. For topical steroid objects, oil-in-water emulsions are customary. Creams have a vital peril of delivering immunological cleaning on account of added substances and have a high pace of affirmation with the guide of patients. There is a choice range in fixings, affiliation, pH, and opposition among nonexclusive makers.

Ointment[15]

A treatment is a similar, gooey, semi-vigorous status, most extreme ordinarily a slick, thick (oil 80% - water 20%) with an over the top constancy, that is conscious for external request to the pores and skin or mucous layers. Medications have a aqueous amount that portrays the greatest serious proportion of water that it might incorporate. They are used as emollients or for the use of energetic components to the skin for protective, therapeutic, or preventative determinations and in which a level of deterrent is needed.

Medicines are regularly very soaking, and valuable for thirsty skin. They have a typically protected of cleaning due to having once in a while any ingredients the base oil or fat, and espresso pestering risk. There is routinely little capriciousness between makers of restorative treatment. They are regularly disliked by patients as a result of sleekness

Gel[15]

Gels are heavier than liquids. Gels are routinely a semi solid formulation basically an emulsion and sporadically use alcohol as a solvent for the dynamic preservative; a few gels consolidate at inner warmth degree. Gel will in favoured be cellulose lessen with alcohol or CH3)2CO. Gels will in mainstream act obviously drying, will in across the board have enormously thing fixings among producers, and pass on a basic danger of starting over the top delicateness because of fragrances and added substances. Gel is advantageous for bristly locales and body folds. In utilizing gel one have to avoid fissure

inside the skin, because of the stinging effect of the alcohol base. Gel acknowledges an over the top beat of affirmation in view of its remedial greatness

Spray/Solution[15]

Topical arrangements can be promoted as drops, washes, or showers, are for the maximum part of low thickness, and often use liquor or water within the base. These are commonly a powder disintegrated in liquor, water, and right here and there oil; albeit an answer that utilizes liquor as a base fixing, as in topical steroids, can purpose drying of the skin. There is noteworthy changeability among brands, and some arrangements may additionally reason bothering, contingent upon the preservative and smells utilized within the base.

2.5 Aim of project

Formulation and development of film forming system for anti- acne agents.

Objective[16]

- Topical anaesthetize conveyance basis has consistently been a significant course of administration for both area just as fundamental impact.
- Conventional plans for dermatological & topical organization of medications have positive constraints like low adherence to skin, low porousness and traded off patient consistence.
- Film framing DDS are the one which conquer these impediments by better permeability, long haul impact and better consistence because of less tenacity and effectively pertinent.

2.5.1 Film forming formulation (spray/solution)[11]

Film moulding courses of action and sprinkles is a charming procedure in transdermal estimations structure. In this the film former course of action is enforced to the skin as a

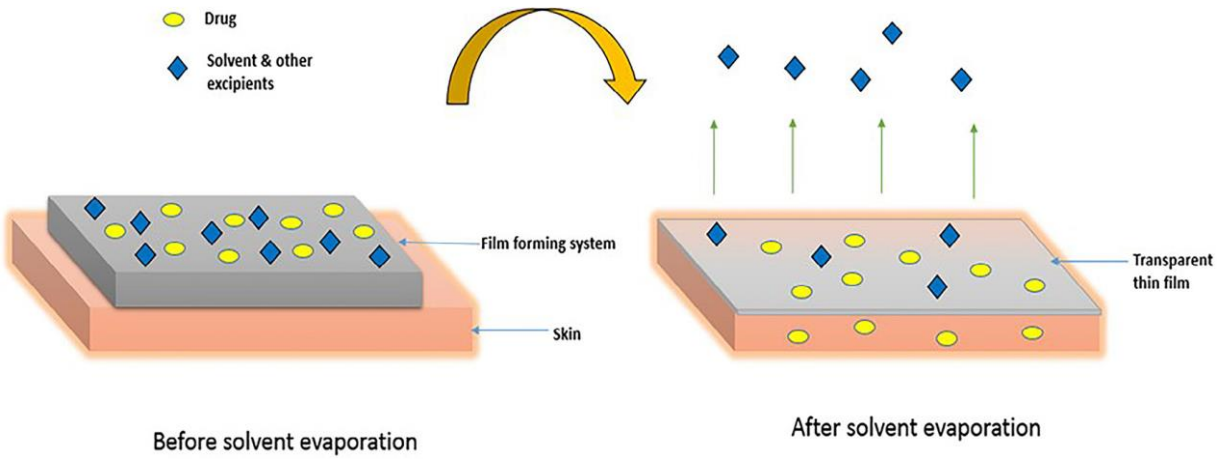
solution or sprinkled on the skin and structures a for all intents and purposes clear film by dissolvable evaporating.

The film shaping arrangement are involved four standard parts – cure, dissolvable structures for instance insecure and non-unusual solvents, film formers and passageway increses. The non-flimsy fragment available in the dissolvable premise shields the drug from rushing in plan when the unusual dissolvable section vanishes. The non-precarious fragment is picked with the ultimate objective that it itself allocates into the layer corneum and moreover helps in separating of the prescription into the layer corneum, similarly as manufactures quiet diffusivity by upsetting the organized lipids between cellular region and overhaul infiltration. This kind of transport system makes an imperceptible distribution centre of drug in the layer corneum from which the prescription can be gradually acclimatized into the crucial course. Along these lines a proceeded and updated infiltration of drug over the skin can be practiced after once consistently application.

• Film framing arrangement can be enforce with an execute to the skin surface and wait to dry. Film moulding shower is made as an evaluate partition siphon device to give fixed proportion of medicine and it is sprinkled on the topical site to outline a film. These processes structure a consistent speedy drying, non-exasperating imperceptible film generate which the prescription is open for transdermal treatment.

Mechanism[17]

Film framing framework is tested clearly to the skin and it shapes a slight, direct movie in situ upon dissolvable disappearing. After usage of the arrangement to the skin, the association of the formulation surrounding system changes essentially as a result of the loss of the flimsy fragments of the solvent which achieves advancement of extra film on the skin superficial. In this system the intermingling of prescription grows, showing up at drenching level and with the chances of showing up at full saturation level on the skin superficial. Full saturation achieves the improved medicine movement through the skin by growing the thermodynamic action of the arrangement deprived of impacting the skin's limit, as needs be reducing the indications or unsettling influence.



2.5.2 Excipients used in film formulation[18]

Polymers	Properties
Hypromellose HPMC	• generate a little weight, non-sleek equal film with incredible surface • Do't assistant inside and out with various fixings • Surface powerful administrator, along these follows adsorbs water giving basic dissipating, lubricity and ease sense in occlusive state on utility to pores and skin
Polyvinyl pyrrolidine (PVP) (PVP K30, PVP VA64)	• water dissolvable and particular solvents • Adhesive and restricting possessions • Acts as a bioavailability enhancer
Ethyl cellulose	• Harmless, no irritating, non-allergic material • Better film moulding assets that structure more diligently film.

HPC	• Non-ionic, pH cold-hearted polymer • dissolvable in aqueous media
PVA	• dissolvable in water • Exceptional film framing and glue properties • Harmless and bio-good
Eudragit (polymethacrylates copolymer) Eudragit	• Clear, adaptable, self-glue • Virtuous association to the skin

Solvents	**Types**
Glycols.	PG, PEG 200, PEG 400
Alcohols	Ethanol, IPA, benzyl liquor, butanol, lanolin alcohols, greasy alcohols

Plasticizer	**Properties**
glycerine, PEG, sorbitol, PG, dibutyl phthalate, triethyl citrate	Plasticizers are utilized in the film framing frameworks to pass on adaptability to the film types of formulation and enhance the stretchable intensity of the film moulded.

Chapter: 3

RESEARCH PLAN

3.1 Physiochemical properties of drug[19]

Drug profile

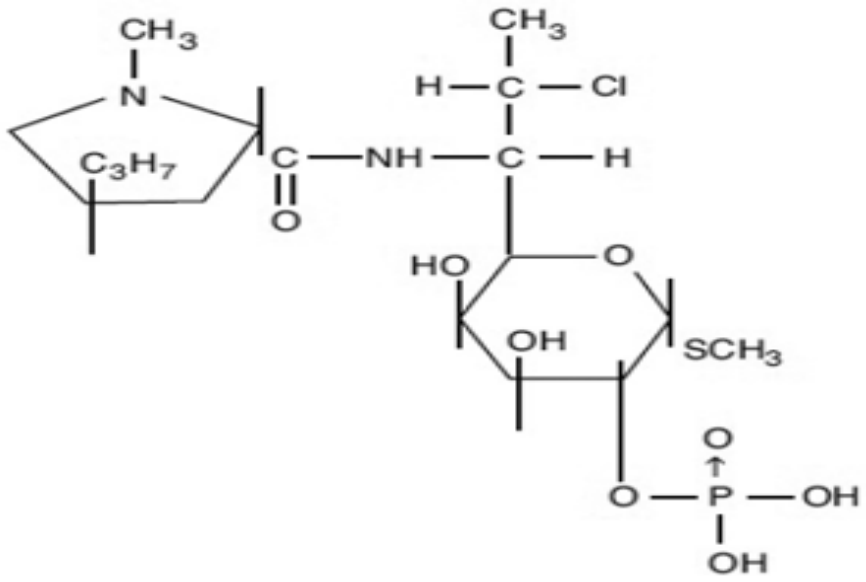
1) Name:

Clindamycin phosphate

2) General indications: [19]

Clindamycin is an anti-microbial utilized for the treatment of numerous bacterial contaminations, along with bone or joint contaminations, pelvic provocative illness, strep throat, pneumonia, center ear sicknesses, and endocarditis. It can likewise be applied to treat zits,and some instances of methicillin-safe Staphylococcus aureus (MRSA). In combo with quinine, it has a tendency to be applied for jungle fever. It is on the market with the aid of mouth, by using infusion right into a vein, and as a cream to be applied to the skin or within the vagina.

3) Structure



4) CAS Number:[20]

24729-96-2

5) Molecular weight

Average: 505 g/mol

6) IUPAC NAME:

[(2R,3R,4S,5R,6R)-6-[(1S,2S)-2-chloro-1-[[(2S,4R)-1-methyl-4propylpyrrolidine-2- carbonyl] amino] propyl]-4,5-dihydroxy-2-methylsulfanyloxan-3-yl] dihydrogen phosphate

7) Other properties:[19]

Sr no	Property	Value
1	Water solubility	200 and 300 mg/mL
2	Log P	2.2
3	Pka	7.56
4	Bioavailability	1
5	Physical state	Solid
6	Melting point Point	114°C

7	Solubility in solvent	Insoluble

8) BCS CLASS:

Class 2 Low solubility and High permeability

9) Mechanism of clindamycin phosphate[21]

Clindamycin has a principally bacteriostatic impact. At higher c ncentrations, it might be bactericidal. It is a infective protein blend inhiitor by restraining ribosomal trans-location, along these lines to macrolides class of anti-biotics. It does as such by authoritative to the 50S rRNA of the huge bacteria ribosome subunit, covering with the coupling destinations of the oxazolidinone, pleuromutilin, and macrolide anti-infection agents, among others. The coupling is reversible. Clindamycin is more compelling than lincomycin.

The X-beam precious stone structures of clindamycin bound to ribosomes (or ribosomal subunits) got from Escherichia coli,Deinococcusradiodurans, and Haloarcuramarismortui have been resolved; the structure of the firmly related anti-toxin lincomycin bound to the 50S ribosomal subunit of Staphylococcus aureus has likewise been accounted for echanism of clindamycin phosphate.

10) Dosage form available[20]

Sr no	Dosage form	Dose
1	Cream	1gm
2	Ointment	10mg
3	Gel	1gm

3.2 Literature review

• Kashmira Katheas: "Film framing frameworks for topical and transdermal medication conveyance". This Book or reference gives information about the general contemplations with respect to transdermal drug movement. The film encircling system shows a novel and unique stage to pass on drugs through the skin both type of route topical and transdermal. These film confining structures are fundamental and offer central purposes of straightforwardness, non-slick, lower skin aggravation, clean up deterrent, longer upkeep, progressively significant extended portion versatility, improved patient consistence and elegant appearance . [1]

• Radhakrishnan et al: "Shower wrap framework in topical prescription transport Topical film or dressing that can be formed by sprinkling makes the new circumstance in pharmaceutical medicine movement, thusly investigate towards this bearing began from 1966. Various associations and scientist has taken this to pramoted level by solidifying medicaments like NSAIDs, against bacterial, antagonistic to septic, steroids, etc., in like manner fitting to cover minor cuts and expend wounds. Further smoothing out the itemizing framework to get quick dry non tenacious shower wrap will have a huge solidarity to move the current topical medicine transport grandstand. [14]

• Linda A. Felton "Instruments of polymeric film improvement" Film course of action from polymer game plans occurs as the dissolvable evaporates, since the polymer chains are by and by mixed. On the other hand, polymer scatterings require dissolvable dispersal just as mix of the individual polymer circles and following interpenetration of the individual polymer chains to outline the chain.[22]

• Ines Zurdo etal: "Improvement and depiction of film forming polymeric responses for skin sedate movement" Film surrounding arrangements were

successfully arranged with polymers from different manufactured social events, for instance, acrylates and its different derivaties, Dermacryl, polyurethane-acrylates, cellulose auxiliaries, polyvinylpyrrolidones and silicones. This says one of the polymers, an unusual dissolvable and other optional excipients, for instance, plasticizers and were fixed manifestations concerning the groupings of all excipients included. The made rating structure, regardless of the way that subject to essential test strategies, gave a not too bad reason to the evaluation of the made insights about the five key estimates thickness, drying time, outward diligence, cosmetical drawing in quality or reliability on the skin.[11]

- Sandeep Karki et al: "Slight movies as a developing stage for sedate conveyance" option in contrast to ordinary dose structures, polymeric slender movies are relied upon to stand apart as a measurements structure to defeat the constraints presented by existing dose structures. The film measurements structure experiences a few difficulties during the periods of plan advancement and production. Such issues ought to be routed to streamline the general detailing much in the wake of moving to huge scope fabricating. [23]

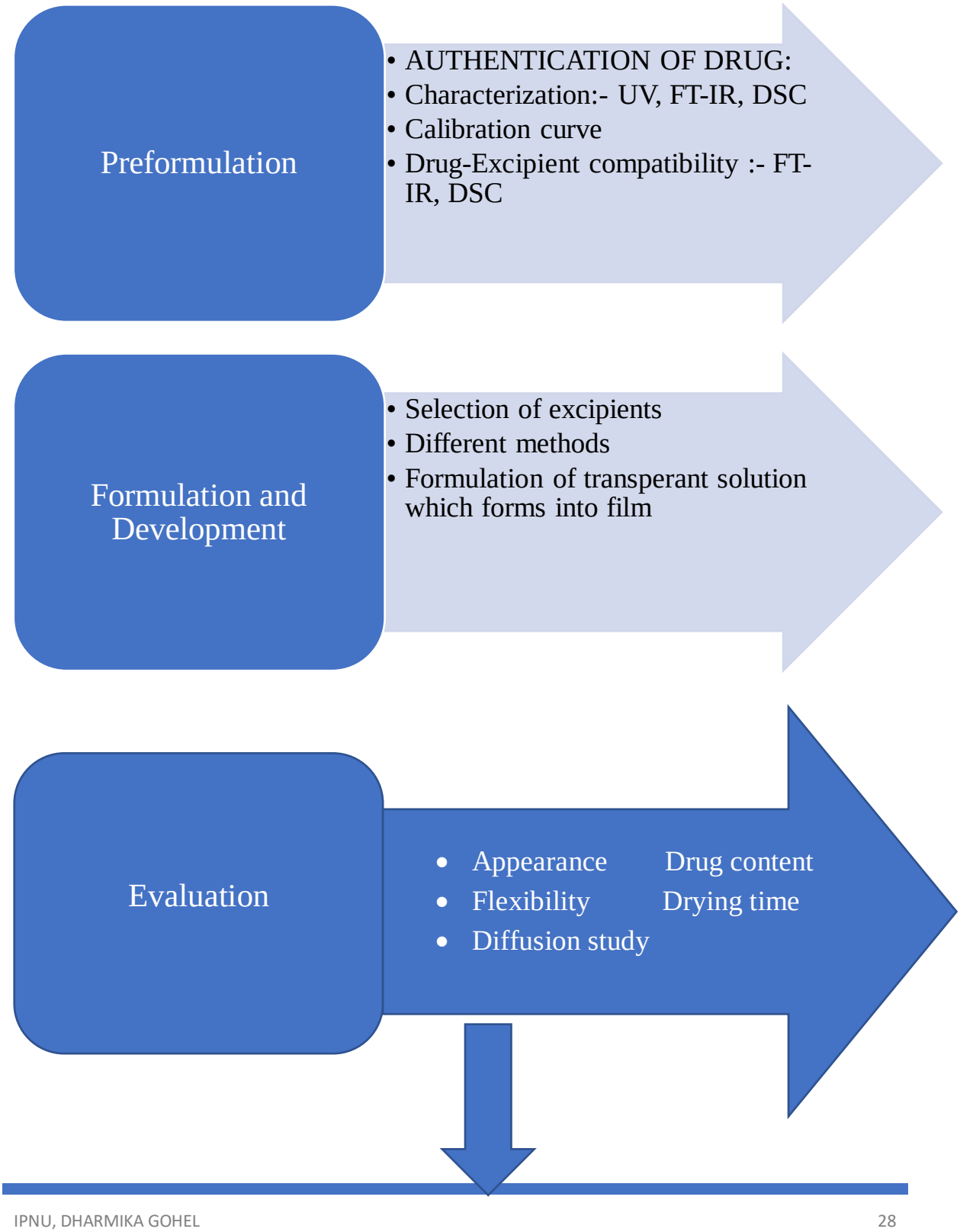
Chapter: 4

EXPERIMENTAL WORK

4.1 Preformulation study

4.2 Formulation and Development

4.3 Evaluation of formulation



OPTIMIZATION OF THE FORMULATION & EVALUATION OF OPTIMIZED FORMULATION BY DOE

In-vitro study

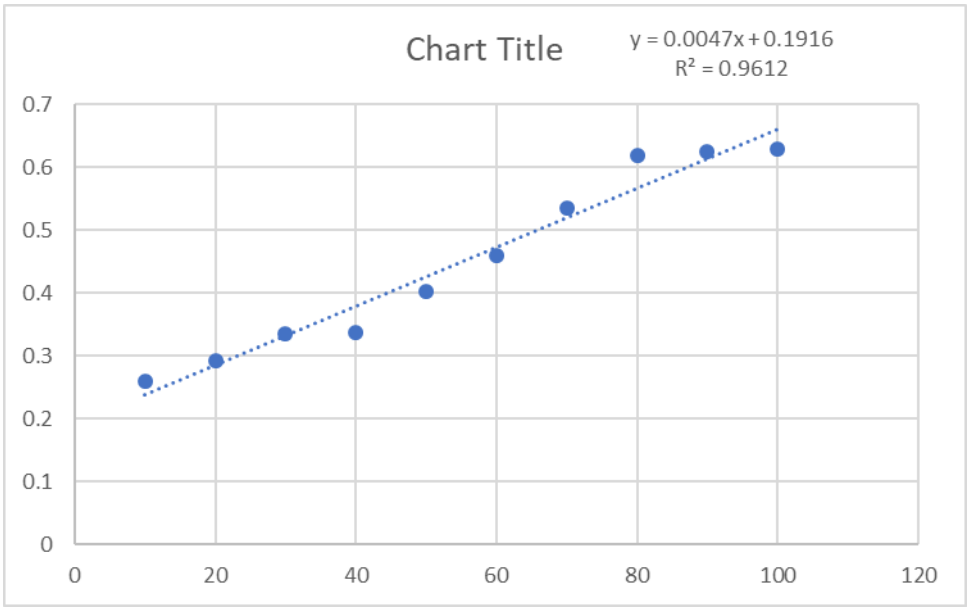
4.1 Preformulation study

4.1.1 UV Spectroscopy in Phosphate buffer PH 5.5[24]

10 mg of Clindamycin phosphate was broken down in adequate measure of Phosphate cushion at pH 5.5 and final volume was made to 100 ml with it (100 µg/ml). The arrangement arranged (100 µg/ml) was examined in the scope of 200 - 400 nm utilizing Phosphate cushion as clear in Jasco UV - noticeable spectrophotometer V - 210to decide the frequency of most extreme absorbance.

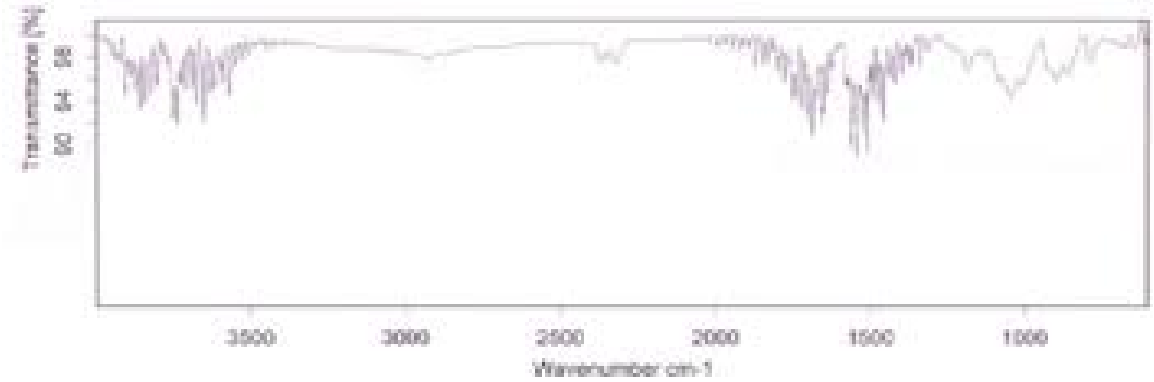
SR no	µg/mL	Abs
1	5	0.2590
2	10	0.2924
3	15	0.3341
4	20	0.3358
5	25	0.4027
6	30	0.4593

7	35	0.5348



4.1.2 IR spectroscopy of Clindamycin Phosphate[25]

• The character of medication was affirmed by contrasting IR range of medication and revealed range of Clindamycin Phosphate. The IR spectra of Clindamycin indicated trademark groups like writing and are portrayed in the spectra.

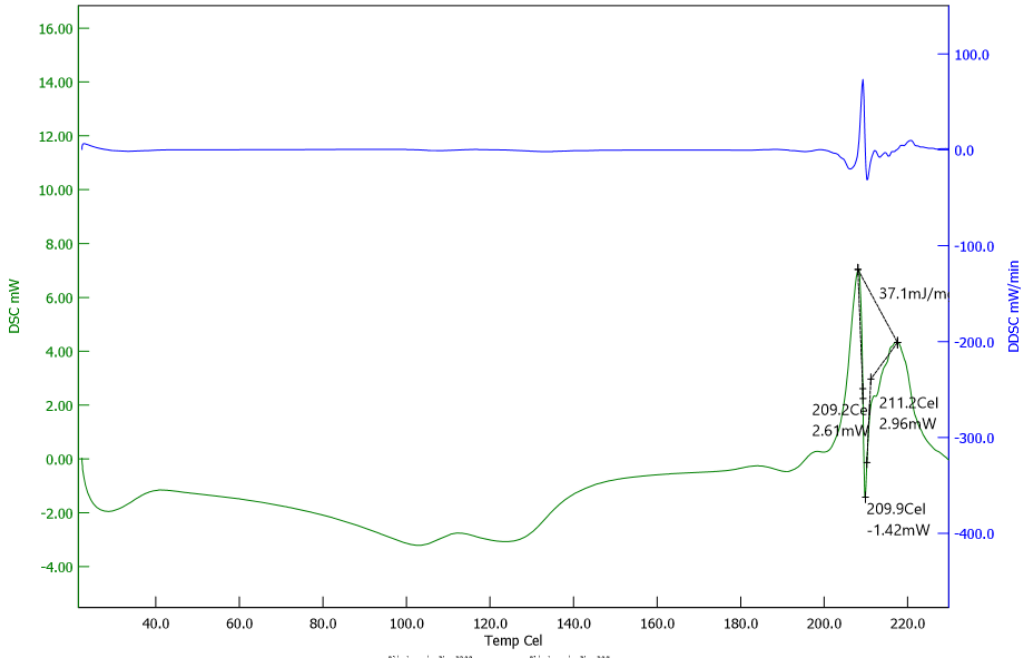


Frequency (cm^{-1})	Type of streching	Functional group

1564.56	C=C stretch	Aromatic (unsaturated)
604.06	c-cl strech	Carbon-chlorine
2300-2400	NH3 strech	Ammonium ion
1240.56	CH3 stretch	Methyl

4.1.3 Differential Scanning Calorimetry analysis[26]

• DSC thermograph of the CP displayed a sharp endothermic top at 232.4°C affirming the personality of the medication.



4.2 Formulation and Development

4.2.1 Selection of excipients[27]

Following Excipients were finalized:

Sr.no	Excipients	Role
1	Methanol	Solvent
2	Water	Solvent
3	Eudragit L100	Polymer
4	PEG400	Plasticizer

4.2.2 Finalization of basic formula[28]

Sr.no	Excipients	Quantity
1	Clindamycin phosphate	1%
2	Methanol	14 ml
3	Water	1ml
4	Eudragit L100	1.05gm
5	PEG 400	1ml

1.Methanol as Solvent[29]

Methanol was tried with different concentration. Methanol was tried with concentrations of 3 to 5% The main parameter affected by solvent that Used into the preparation of transparent film. Also used change in the drug release and drug permeation.

2. Eudragit L100 as polymer[29]

Eudragit L100 grade us as polymer in film forming because eudragit L100 polymer is soluble in solvent and compatible with polymer.Eudragit l100 used as film forming polymer and also used to penetration enhancement.

3. PEG 400 as plasctisizer[29]

PEG 400 is soluble in water and methanol. Because of PEG 400 use in formulation the flexibility of film formulation is better. plasticizer is tried with Different concentration.

4.2.3 Design of experiments

- DESIGN EXPERIMENT
- 3^2 FACTORIAL DESIGN
- Excipient: Solvent and Polymer
- Solvent : Methanol(3 to 5%)
- Polymer : Eudragit L100 (2 to 4%)
- Parameters affected: DRYING TIME
  DRUG RELEASE
  DRUG PENETRATION
  FLEXIBILITY

4.2.4 Batches with variation in Polymer and solvent

SR.NO	Polymer in gm	Solvent in ml
1	1.05	12
2	1.05	8
3	0.5	12
4	0.512	7
5	0.5	7
6	0.512	8
7	1.05	7
8	0.5	8
9	0.512	12

4.3 EVALUATIONS

1.Film Appearance: [30]

The films are designed into glass Petri plate as in vitro parameters or on an extracted pig ear pores and skin as ex vivo parameters. Film-development is assessed and evaluated as complete and uniform, incomplete or non-uniform, with or without precipitation of the film-framing polymer. The restorative elements of the film are given as far as straightforwardness or obscure, clingy or dry, peel able or non-peel able.

2.Drying time:[31]

For the measurement of the drying time of the film, first solution is spry on the volunteer's lower arm inner side. After a specific time interval a pitcher slide is situated at the film with no pressure. If no fluid is seen at the glass slide after elimination, the film is mulled over dry. In the event that stays of the fluid are noticeable on the glass slide the test is rehashed with a development in drying time. A reasonable FFS must have a base drying time to evade long prepared time for the influenced individual.

3.Stickiness: [32]

The tenacity of the formulation moulded is dictated by methods for dire cotton fibre fleece at the dry film with less weight. Contingent upon the amount of fibres which may be held through the formulation, the tenacity is evaluated high if there's thick aggregation of fibers on the film, medium if there is a thin fibre layer on the film and espresso if there might be an incidental or no adherence of fibers. This appraisal parameter is basic, as the segments ought to be non-clingy to keep away from adherence to the garments

4.Flexibility:[1]

Swab investigate should be possible to assess the house time of film shaping device. For attachment checking out, glass got utilized as a highly polar, lipophobic materials. Glass

transformed into chose as investigate surface in light of the fact that films clinging emphatically to it would likewise show strong adherence to skin on the grounds that every substance shows a polar floor shape

5.Dry swab check:

This check shows the conduct of FFS above pores and skin in dry situation. Dry gauze test might be finished on a glass plate. The glass plate is marked with 6 squares of 1 × 1cm ^{2}. Created equation is executed in this place. Dry q-tips of the indistinguishable degree are taken. Cleaning on the functional formulation is performed at zero minute, thirty minute, two hour, four h, six hour and eight hour and checked for medicate content material after extraction of medication from the swab.

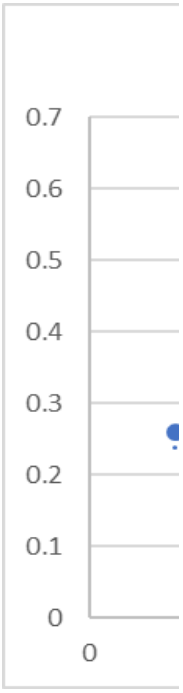
6.Wet swab check:

By use of this method check delineates the conduct of FFS while it interacts within H2O or perspiration. The strategy for the wet gauze check is equivalent to dried gauze check other than the gauze given is absorbed water sooner than after which the details are cleaned with this wet gauze.

7.Diffusion:[33]

The in vitro dispersion contemplates are utilized to are expecting the penetration qualities of medication in-vivo. Franz dissemination assembly is utilized to deciding the discharge rate of the medication from the formulation shaping machine. The cell is made up using cubicles, the unit and the beneficiary unit among which the dispersion layer is snared. The giver unit is presented to the environmental factors and the acceptor unit contains the dispersion medium. The inspecting arm in the acceptor unit takes into account testing. Foreordained amount of the medication containing film framing segments is situated on the benefactor unit. film are amassed and dissected by appropriate UV analysis method for sedate discharge.

Sr. No.	Time	Abs,	Conc (µg/ml)	Dilution factor	µg/20ml	Error	Total Conc.	CDR	CPR
1	1 min	0.1384	0.113	1	2.27	0	2.27	2.27	1.265219
2	3 min	1.8889	1.864	1	37.28	0.1138	37.40	39.67	22.04366
3	5 min	1.4307	1.406	1	28.12	1.978239	30.10	69.78	38.76679
4	7 min	1.1149	1.090	1	21.80	3.384409	25.19	94.97	52.76224
5	9 min	0.2254	0.200	1	4.017	4.474779	8.49	103.46	57.48011
6	10 min	1.106	1.081	1	21.62	4.675649	26.30	129.76	72.09402
7	15 min	0.2695	0.244	1	4.89	5.757118	10.65	140.42	78.01431
8	20 min	0.9307	0.906	1	18.12	6.002088	24.12	164.55	91.41736



SR.NO.	CONC.	ABS.
1	0	0
2	10	0.259
3	20	0.2924
4	30	0.3341
5	40	0.3358
6	50	0.402
7	60	0.4593
8	70	0.5348
9	80	0.6193
10	90	0.6235
11	100	0.6277

Chapter 5

CONCLUSION

CONCLUSION

The film provides a better result on the conventional dosage forms like pills. It can be cure both types of the disease topical and transdermal. Film is good in the transparency, irritation of skin is also reduced, non-greasy formulation compares to the lotion and cream type of the formulation, easily remove from the skin when required, prolong release treatment is also given, flexibility on the skin surface and looks good in the appearance. Although tremendous work has been done on the system, now not decent arrangement data are to be had on its vehicle efficiency. Hence their fore the showcased items accessibility are the less. Additional considers is yet the got outcomes are empowering for additional advancement of this novel topical medication giving over time.

Chapter 6

REFERENCES

[1] K. Kathe and H. Kathpalia, “Film forming systems for topical and transdermal drug delivery,” *Asian J. Pharm. Sci.*, vol. 12, no. 6, pp. 487–497, 2017, doi: 10.1016/j.ajps.2017.07.004.

[2] M. B. Brown, G. P. Martin, S. A. Jones, and F. K. Akomeah, “Dermal and transdermal drug delivery systems: Current and future prospects,” *Drug Deliv. J. Deliv. Target. Ther. Agents*, vol. 13, no. 3, pp. 175–187, 2006, doi: 10.1080/10717540500455975.

[3] S. C. Weiss, “Conventional topical,” *Dermatol. Ther.*, vol. 24, pp. 471–476, 2012.

[4] H. Garvie-Cook, K. Frederiksen, K. Petersson, R. H. Guy, and S. N. Gordeev, “Biophysical elucidation of the mechanism of enhanced drug release and topical delivery from polymeric film-forming systems,” *J. Control. Release*, vol. 212, pp. 103–112, 2015, doi: 10.1016/j.jconrel.2015.06.015.

[5] K. Frederiksen, R. H. Guy, and K. Petersson, “Formulation considerations in the design of topical, polymeric film-forming systems for sustained drug delivery to the skin,” *Eur. J. Pharm. Biopharm.*, vol. 91, pp. 9–15, 2015, doi: 10.1016/j.ejpb.2015.01.002.

[6] M. Donkerwolcke, F. Burny, and D. Muster, “Tissues and bone adhesives historical aspects,” *Biomaterials*, vol. 19, no. 16, pp. 1461–1466, 1998, doi: 10.1016/S0142-9612(98)00059-3.

[7] R. B. Saudagar and P. A. Gangurde, “Formulation, development and evaluation of film-forming gel for prolonged dermal delivery of miconaole nitrate,” *Res. J. Top. Cosmet. Sci.*, vol. 8, no. 1, p. 19, 2017, doi: 10.5958/2321-5844.2017.00003.6.

[8] A. M. Master, M. E. Rodriguez, M. E. Kenney, N. L. Oleinick, and A. Sen Gupta, “Delivery of the photosensitizer Pc 4 in PEG–PCL micelles for in vitro PDT studies,” *J. Pharm. Sci.*, vol. 99, no. 5, pp. 2386–2398, 2010, doi: 10.1002/jps.

[9] H. Garvie-Cook, K. Frederiksen, K. Petersson, R. H. Guy, and S. Gordeev, “Characterization of topical film-forming systems using atomic force microscopy and Raman microspectroscopy,” *Mol. Pharm.*, vol. 12, no. 3, pp. 751–757, 2015, doi: 10.1021/mp500582j.

[10] M. Preis, K. Knop, and J. Breitkreutz, “Mechanical strength test for orodispersible and buccal films,” *Int. J. Pharm.*, vol. 461, no. 1–2, pp. 22–29, 2014, doi: 10.1016/j.ijpharm.2013.11.033.

[11] I. Zurdo Schroeder, P. Franke, U. F. Schaefer, and C. M. Lehr, “Development and characterization of film forming polymeric solutions for skin drug delivery,” *Eur. J. Pharm. Biopharm.*, vol. 65, no. 1, pp. 111–121, 2007, doi: 10.1016/j.ejpb.2006.07.015.

[12] S. Ranade, A. Bajaj, V. Londhe, N. Babul, and D. Kao, “European Journal of Pharmaceutical Sciences Fabrication of topical metered dose fi lm forming sprays for pain management,” *Eur. J. Pharm. Sci.*, vol. 100, pp. 132–141, 2017, doi: 10.1016/j.ejps.2017.01.004.

[13] M. C. Gohel and S. A. Nagori, “Fabrication of modified transport fluconazole transdermal spray containing ethyl cellulose and eudragit® RS100 as film formers,” *AAPS PharmSciTech*, vol. 10, no. 2, pp. 684–691, 2009, doi: 10.1208/s12249-009-9256-8.

[14] A. Radhakrishnan, G. Kuppusamy, and V. V. S. R. Karri, “Spray bandage strategy in topical drug delivery,” *J. Drug Deliv. Sci. Technol.*, vol. 43, pp. 113–121, 2018, doi: 10.1016/j.jddst.2017.09.018.

[15] N. M. An, D. D. Kim, Y. H. Shin, and C. H. Lee, “Development of a novel soft hydrogel for the transdermal delivery of testosterone,” *Drug Dev. Ind. Pharm.*, vol. 29, no. 1, pp. 99–105, 2003, doi: 10.1081/DDC-120016688.

[16] Z. Dong, Q. Wang, and Y. Du, “Alginate/gelatin blend films and their properties for drug controlled release,” *J. Memb. Sci.*, vol. 280, no. 1–2, pp. 37–44, 2006, doi: 10.1016/j.memsci.2006.01.002.

[17] D. Mukherjee and S. Bharath, “Design and Characterization of Double Layered Mucoadhesive System Containing Bisphosphonate Derivative,” *ISRN Pharm.*, vol. 2013, pp. 1–10, 2013, doi: 10.1155/2013/604690.

[18] N. L. Calvo, L. A. Svetaz, V. A. Alvarez, A. D. Quiroga, M. C. Lamas, and D. Leonardi, *Chitosan-hydroxypropyl methylcellulose tioconazole films: A promising*

alternative dosage form for the treatment of vaginal candidiasis, vol. 556. Elsevier B.V., 2019.

[19] W. Head, "CLINDAMYCIN PHOSPHATE (CLINDAMYCINI PHOSPHAS) REVISED DRAFT MONOGRAPH FOR INCLUSION IN The International Pharmacopoeia," no. August, pp. 1–13, 2016.

[20] B. Laboratories, "Clindamycin phosphate injection," vol. 7, [Online]. Available: http://dailymed.nlm.nih.gov/dailymed/lookup.cfm?setid=166d6d61-e9ce-4c8a-91ec-72d7a9d0af8d#nlm34068-7.

[21] L. A. Felton, "Mechanisms of polymeric film formation," *Int. J. Pharm.*, vol. 457, no. 2, pp. 423–427, 2013, doi: 10.1016/j.ijpharm.2012.12.027.

[22] X. Li *et al.*, "Preparation and characterization of sustained-release rotigotine film-forming gel," vol. 460, pp. 273–279, 2014.

[23] S. Karki, H. Kim, S. J. Na, D. Shin, K. Jo, and J. Lee, "Thin films as an emerging platform for drug delivery," *Asian J. Pharm. Sci.*, vol. 11, no. 5, pp. 559–574, 2016, doi: 10.1016/j.ajps.2016.05.004.

[24] A. Edwards, S. Qi, F. Liu, M. B. Brown, and W. J. McAuley, "Rationalising polymer selection for supersaturated film forming systems produced by an aerosol spray for the transdermal delivery of methylphenidate," *Eur. J. Pharm. Biopharm.*, vol. 114, pp. 164–174, 2017, doi: 10.1016/j.ejpb.2017.01.013.

[25] M. Iervolino, B. Cappello, S. L. Raghavan, and J. Hadgraft, "Penetration enhancement of ibuprofen from supersaturated solutions through human skin," *Int. J. Pharm.*, vol. 212, no. 1, pp. 131–141, 2001, doi: 10.1016/S0378-5173(00)00603-7.

[26] S. Gngr, M. Sedef, and Y. zsoy, "Plasticizers in Transdermal Drug Delivery Systems," *Recent Adv. Plast.*, 2012, doi: 10.5772/38156.

[27] V. Singh, M. Singh, G. Kukreti, A. Agarwal, and H. Bajaj, "Rheumatoid Arthritis: Treatment by Film Forming Gels," *J. Analg.*, vol. 3, no. 1, pp. 9–14, 2015, doi: 10.14205/2311-0317.2015.03.01.2.

[28] R. Guo, X. Du, R. Zhang, L. Deng, A. Dong, and J. Zhang, "Bioadhesive film formed from a novel organic-inorganic hybrid gel for transdermal drug delivery system," *Eur. J. Pharm. Biopharm.*, vol. 79, no. 3, pp. 574–583, 2011, doi: 10.1016/j.ejpb.2011.06.006.

[29] D. Lunter and R. Daniels, "In vitro skin permeation and penetration of nonivamide from novel film-forming emulsions," *Skin Pharmacol. Physiol.*, vol. 26, no. 3, pp. 139–146, 2013, doi: 10.1159/000348464.

[30] H. Zhai and H. I. Maibach, "Effects of skin occlusion on percutaneous absorption: An overview," *Skin Pharmacol. Appl. Skin Physiol.*, vol. 14, no. 1, pp. 1–10, 2001, doi: 10.1159/000056328.

[31] H. Chen, X. Chang, D. Du, J. Li, H. Xu, and X. Yang, "Microemulsion-based hydrogel formulation of ibuprofen for topical delivery," *Int. J. Pharm.*, vol. 315, no. 1–2, pp. 52–58, 2006, doi: 10.1016/j.ijpharm.2006.02.015.

[32] Y. C. Ng, Z. Yang, W. J. McAuley, and S. Qi, "Stabilisation of amorphous drugs under high humidity using pharmaceutical thin films," *Eur. J. Pharm. Biopharm.*, vol. 84, no. 3, pp. 555–565, 2013, doi: 10.1016/j.ejpb.2013.01.008.

[33] I. Šveikauskaite and V. Briedis, "Effect of film-forming polymers on release of naftifine hydrochloride from nail lacquers," *Int. J. Polym. Sci.*, vol. 2017, 2017, doi: 10.1155/2017/1476270.

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