

A Comprehensive Overview of the Epidemiology of Skin Disorders: A Systematic Review

Rupendra V. Doshi¹, Vishal B. Babar¹, Sudarshan N. Nagrale¹, Manoj N. Phadtare², Prajкта S. Jagtap¹,

Harshada S. Deshmukh^{3*}, Priyanka B. Parekar⁴, Shivraj S. Shivpuje⁵

¹DKSS's Dattakala college of Pharmacy, Swami-Chincholi, Pune, Maharashtra, India 413130

²Sou. VenutaiChavan Pharmacy College, Phaltan, Satara, Maharashtra, India 415523

³DKSS's Institute of Pharmaceutical Science and Research (for Girls), Swami-Chincholi, Pune, Maharashtra, India 413130

⁴Chetana College of Pharmacy, Sardewadi, Indapur, Pune, Maharashtra, India 413106

⁵School of Pharmacy SRTM University, Nanded, Maharashtra-431606.

Date of Submission: 20-12-2024

Date of Acceptance: 30-12-2024

ABSTRACT

The skin, an organ found on the outermost layer of a live organism, shields the body beneath it from environmental dangers such as shocks, temperature changes, UV rays, and toxins. The epidermis, dermis, and subcutaneous fat tissues are the three layers that make up the skin, starting from the exterior. The skin is human body's major organ. It provides a layer of protection over the body's underlying structures. It keeps the body protected from being mentered by microorganisms which makes it the body's first line of defence.

Keyword: Skin, Epidermis, Dermis, Tissue, Defence

I. INTRODUCTION:

The largest organ in the body is the skin.[1] The integumentary system is composed of the skin and its byproducts, including the hair, nails, perspiration, and oil glands. Protection is one of the skin's primary roles. It shields the body from environmental elements like temperature, chemicals, and pathogens.[2,3] As seen in Fig. 2, the skin is separated into multiple layers. Keratinocytes make up the majority of the epidermis. The basement membrane, sometimes referred to as the dermo-epidermal junction, is a narrow, multilayered tissue that lies beneath the epidermis and serves as an anchor between it and the dermis. Fat makes up the majority of the hypodermis, the layer beneath the dermis. Below is a description of these structures.

Three main surfaces of skin:

1. The epidermis-surface of the skin (5 layers)
2. The Dermis

3. Hypodermis/subcutaneous layer [2]

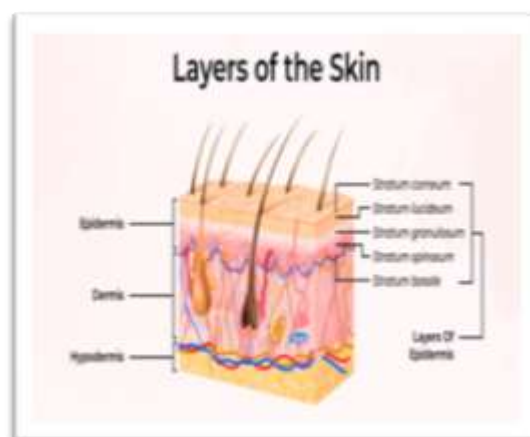


Fig.1. Human Skin

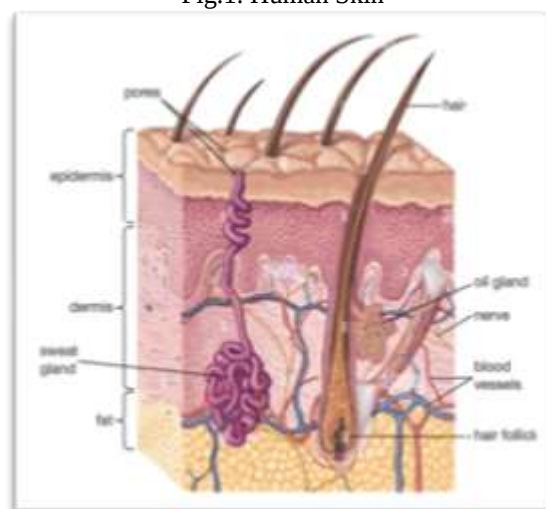


Fig no. 2 Cross section of human skin

Define Skin:

The skin the stratified squamous epithelium that makes up the epidermis, the skin's outermost layer, is mainly made up of keratinocytes in various stages of development (Amirlak and Shahabi, 2017).

Keratinocytes are the main cells that make up the epidermis and are responsible for producing the protein keratin. The underlying dermis is completely responsible for the delivery of nutrients and the removal of waste through the basement membrane because the epidermis is avascular (has no blood vessels). The epidermis' primary job is to serve as a biological and physical barrier to the outside world, keeping allergens and irritants out. In addition, it keeps internal homeostasis and stops water loss (Gawkrödger, 2007; Cork, 1997). Layers make up the epidermis; the thickest skin has five layers, whereas the majority of body parts have four. The stratum lucidum, which is only present in thick skin, such as the palms of the hands, the stratum corneum, or horny layer[4]

Epidermis:

Consist of several zones.

1-Basal layer (stratum basale): columnar dividing cells.

2-Spinous layer (stratum spinosum): Polyhedral(cuboidal)cells attached by desmosomes.

3-Granular layer (stratum granulosum): flat cells containing keratohyaline granules.

4-Cornified layer (stratum corneum): dead cell with no organelles

The epidermis consists of many cells 95% are Keratinocytes, and other prominent cells are melanocytes, Langerhans cells, and merkel cells.

- The epidermis doesn't have blood vessels it obtains its nutrients from the blood vessel of dermis diffusing through the dermoepidermal junction (papillary layer of dermis).

- Very important layer for the protection of the skin against chemical agents and pathogens

1-Basal cell layer: (Stratum basale):

There is only one layer rest on the basement membrane; it keeps dividing and rises. Dendritic cells called melanocytes are arranged in a 1:10 ratio between basal cells. They produce the melanin that is kept in melanosomes. The epidermal melanin unit is formed when melanosomes are transported to neighbouring cells via dendrites; each melanocyte produces 36 keratinocytes, and the presence of the equal distribution helps to

maintain the skin's homogeneity. White and black skin is distinguished by the size of their melanosomes and packaging. White and dark skin has the same quantity of melanocytes. Additionally, melanocytes can be found in

- The iris
- Inner
- Ear meninges
- Mucus membranes
- Hair, Nail

2-Spinous cell layer:

Adhere to each other by Desmosomes (complex Modification of the cell membrane). Desmosomes appear like spines hence the designation Stratum Spinosum. Langerhan cells are antigen presenting present in Abundance. (They are found in all skin layers unlike the melanocytes which are only confined to the basal epidermal layer.)

3-Granular cell layer (stratum granulosum)

Flat cells in the shape of diamonds. Keratohyaline granules are found in the cytoplasm.

The stratum corneum layer's thickness is directly proportionate to this layer's thickness.

There are one to three cell layers in thin skin and ten layers in thick skin, such as palms and soles. Knowing where the biopsy was taken from is useful since the skin on the lid is the thinnest layer, while the skin on the palms and soles is the thickest.

4-Cornified layer (Stratum corneum) : -

This layer's cells are nucleus-free. There are 25 layers of cells. Cells are chemically resistant due to their thick envelope. Offers defence against infections and chemicals. The pattern is basket weave.

5. The stratum lucidum

Which located under the stratum corneum in thick skin, It is defined as clear and empty. The lucid zone, which is an empty space between the stratum corneum and granular layer, dissolves when a skin sample is processed with formalin. The stratum lucidum feature is visible when the skin is thick, and the pattern becomes compressed rather than basket weave.

Basement membrane –

It is a uniformly pink, undulating region that lies between the dermis and epidermis. It is the location of assault harm in blistering diseases. It is

made up of several proteins, including laminin, which is attacked in certain bullous diseases. Blisters have two layers: the lamina lucida and the lamina densa. They will dissolve or ulcerate if they are traumatised. -Hemidesmosomes allow keratinocytes to adhere to the basement membrane. The basement membrane is made up of hemidesmosomes and the basal cell's plasma membrane.

1. Lamina Lucida:

There are the thin, transparent, amorphous space. It is abundant in antigens and proteins. A region with a high electron density.

2. Lamina Densa:

Fibrillar anchors that bind the epidermis to the dermis

Dermis:

Made of dense connective tissue that is tough, elastic and flexible. It gives strength, shape, elasticity and smoothness to the skin.

Dermis is divided into:

1. Papillary dermis
2. Reticular dermis

Consists of:

Collagen fibers: Provide strength thin fibers in papillary dermis but thick and coarse in the Reticular dermis. Elastic Fibers: Provides elasticity protection against shearing forces.

Ground substance:

Binds water and maintains the skin turgor and makes the skin soft and smooth. Blood vessels to nourish the overlying epidermis also. Remember the epidermis is avascular Fibroblasts to produce the above elements.

Function of dermis:

It provides nourishment to the epidermis and interact with it during wound repair It gives the skin its strength, elasticity, and softness.[5]

Hypodermis:

A region that produces and stores fat. It is composed of areolar tissue (loose with collagen, elastin, and reticular fibres) and adipose tissue (energy reserve, support, and protection). By stopping heat loss via the skin, the hypodermis aids in bodily insulation.

Functions of skin:

1. Secretion - of sweat and sebum. Sweat helps regulate body temperature and eliminates waste from the skin. The sebaceous glands produce sebum, which is the skin's natural moisturiser and barrier. Acid mantle is the result of sweat and sebum combining on the skin's surface. a barrier that keeps microorganisms out.
2. Heat regulation - The body can either retain or lose heat thanks to the skin. It accomplishes this by using the blood flowing via the blood vessels. Vasoconstriction is the tightening of blood capillaries to prevent blood flow to the epidermis. If the body gets cold, it occurs. There will be no heat loss through radiation, conduction, or convection if there is no blood reaching the skin's surface. When the blood capillaries relax, a large amount of blood can reach the skin's surface. This is known as vasodilation. As a result, heat is lost through radiation, conduction, or convection, and the skin flushes. In order to raise body temperature, the body can also encourage shivering.
3. Absorption -While the skin is a waterproof covering, it is unable to absorb many things. The epidermis's pores and follicles allow the absorption of medications, essential oils, and certain conditioning lotions.
4. Protection - The skin acts as a multilayered, natural barrier to keep out germs and other pathogens. Additionally, it has an acid mantle that prevents bacteria from developing on the skin's surface. Melanin, a pigment, shields our skin from UV radiation. Langerhans cells strengthen the immune system and shield us from infection. Nerve endings alert us to danger and harsh situations. A waterproof coating keeps vital bodily fluids from evaporating.
5. Elimination - toxins such as salts, urea and waste water are lost through sweat glands of the skin.
6. Sensation - the nerve endings and other receptors of the skin can detect pain, cold, heat, pressure and touch. Different receptors lie at different levels in the skin.
7. Vitamin D production -Ergosterol, which is found in sebum, is transformed into vitamin D by sunlight. For healthy teeth and bones, vitamin D is necessary for the metabolism of calcium and phosphorus. Children who are deficient in vitamin D get rickets.

8. Melanin production - Sunlight's UV rays enhance the release of melanin, the natural pigment of the skin. This pigment shields us from harm and burning by absorbing the sun's harmful rays.[6]
9. Thermoregulation- Protecting the body from heat or cold and preserving a steady core temperature are two of the skin's vital roles. Changes to the blood flow via the cutaneous vascular bed accomplish this. The skin reddens, the vessels dilate, and sweat beads appear on the skin's surface during warm weather (vasodilatation = increased blood flow = greater direct heat loss). Vasoconstriction prevents heat from leaving by constricting the blood vessels during cold weather (less blood flow = less heat loss). Sweat from the skin's surface is secreted and evaporated, which aids in cooling the body.[7]

Causes of Skin Diseases:

1. Bacteria trapped in your pores or hair follicles
2. Effect on thyroid kidney or immune systems
3. Contact with environmental triggers
4. Allergens
5. Contact with another person's skin
6. Genetics
7. Fungus or parasites of skin
8. Medication
9. Viruses
10. Diabetes
11. Sun [8]

Symptoms Of Skin Diseases

Symptoms of skin diseases might differ greatly depending on the illness you have. Skin illnesses are not usually the cause of skin changes. For instance, wearing shoes that don't fit well can cause blisters. On the other hand, skin changes that appear for no apparent reason could be a sign of an underlying illness.

Generally skin diseases may cause:

1. Discolored Skin Patches
2. Dry skin
3. Open Sores
4. Lesions
5. Ulcers
6. Peeling skin
7. Rashes
8. Pain
9. Red, white or pus-filled bumps.
10. Rough skin[9]

Diagnosis And Test For Skin Diseases

Diagnosis

When examining the appearance of your skin, a physician may diagnose a skin condition. If examining your skin doesn't yield definitive results, your healthcare professional may employ tests like:

1. Biopsy- removing a small piece of skin to examine under a microscope
2. Culture- taking a skin sample to test for bacteria, fungus or viruses
3. Skin Patch Test- applying small amounts of substances to test for allergic reactions
4. Black/ Wood Light Test- using an ultraviolet (UV) light to view your skin's pigment more clearly
5. Diascopy- pressing a microscope slide against a skin patch to see if the skin changes colour
6. Dermoscopy- using a hand-held device called a dermatoscope to diagnose skin lesions.
7. Tzanck Test- examining the fluid from a blister to check for herpes simplex or herpes zoster[10]
8. Skin Tests-

In the **patch test**, many small samples of common and suspected reaction-causing substances, known as allergens, are applied to the skin (typically on the upper back) under adhesive tape and left on. The skin under the patches is evaluated 48 hours later after the patches are removed and then again at 96 hours. It often takes the skin several days to produce a visible reaction. If a substance produces a characteristic, usually itchy rash, the person is probably allergic to it. In people who have light skin, the color of the rash is usually red. In people who have dark skin, the color of the rash may have less contrast with surrounding skin and thus be more subtle. Sometimes the substances produce an irritation that is not a true allergic reaction. In the **prick test**, a drop of an extract of the suspected substance is placed on the skin. Then, the drop is pricked or punctured with a needle to introduce a very tiny amount of the substance into the skin. The skin is then observed for redness (or other color changes), hives, or both, which usually occur within 30 minutes. (See also Skin testing.) In the intradermal test, tiny amounts of a substance are injected under the skin. The area is then watched for redness (or other color changes) and swelling, which indicate an allergic reaction

9. Scrapings[11]

List of Skin Diseases:

1. Fungal skin Diseases

2. Bacterial Skin Diseases
3. Contaminated Skin Diseases
4. Vitamin Deficiency Skin Diseases
5. Insect Skin Diseases
6. Virus Skin Diseases
7. U.V. radiation Skin Diseases

Oral Medication used for Skin Diseases:

- Abrocitinib
- Aciclovir
- Acitretin
- Acne treatment
- Alitretinoin
- Amitriptyline
- Antiandrogens
- Antimalarials
- Antibiotics
- Antibiotics for acne
- Anticholinergics
- Anti histaminics
- Anti-oxidants
- Apremilast
- Azathioprine
- Baricitinib
- Bexarotene
- Cannabinoids
- Chloroquine
- Ciclosporin
- Clindamycin
- Clofazimine
- Cobimetinib
- Colchicine
- Cyproterone
- Cyclophosphamide
- Dabrafenib
- Dapsone
- Deucravacitinib
- Erythromycin
- Cyproterone
- Finasteride
- Fluconazole
- Fumaric Acid Esters
- Gabapentin
- Gold
- Griseofulvin
- Hormonal Treatment
- Horse chestnut extract
- Hydroxycarbamide
- Hydroxychloroquine
- HydroxyUrea
- Imatinib
- Isotretinoin
- Itraconazole
- Ivermectin
- Ketoconazole
- Leflunomide
- Leukotriene antagonists
- Melatonin
- Management of acne
- Methotrexate
- Minoxidil solution
- Mycophenolatemofetil
- Nicotinamide
- Oral Anti-fungal medications
- Oral Contraceptives
- Oral retinoids
- Penicillin
- Posaconazole
- Potassium iodide
- Quinacrine
- Propranolol
- Rifampicin
- Ruxolitinib
- Selenium
- Sirolimus
- Sonidegib
- Spironolactone
- Steroids
- Sulfasalazine
- Systemic Steroids
- Minoxidil solution
- Terbinafine
- Tetracycline
- Thalidomide
- Tofacitinib
- Tranexamic acid
- Treatment Of fungal infections
- Upadacitinib
- Vemurafenib
- Vismodegib
- Vitamin A
- Voriconazole[11]

1. Fungal Skin Diseases:

Mycosis, commonly referred to as fungal infections, is a condition brought on by a fungus (mould or yeast). While fungi (plural of fungus) are most frequently found on the skin or nails, they can also infect your mouth, throat, lungs, urinary tract, and many other areas of your body.[12]

Various Drugs are used in Fungal Skin Diseases[13]

- clotrimazole (Canesten)

- econazole.
- miconazole.
- terbinafine (Lamisil)
- fluconazole (Diflucan)
- ketoconazole (Daktarin)
- nystatin (Nystan)
- amphotericin.

There are also separate leaflets in this series that deal with:

- candida skin infection(Yeast Infection)
- Fungal Scalp infection (Scalp Ringworm)
- Fungal Nail infection (Tineaunguium)

Antifungal shampoo

A shampoo containing ketoconazole is sometimes used to help treat scalp fungal infections and certain skin conditions.

Antifungal pessaries

Pessaries are tablets which are designed to be put into the vagina. Some antifungal medicines are used as pessaries to treat vaginal thrush particularly:

- Clotrimazole.
- Econazole.
- Miconazole.
- Fenticonazole

Antifungal mouth gel

There are multiple types. For example, nystatin is a liquid, and miconazole is an oral gel. The mouth receives their application. They are used to treat oral and throat thrush, which is caused by candida infections.

Antifungal tablets

Terbinafine, itraconazole, fluconazole, posaconazole and voriconazol are antifungal drugs that are available as tablets, which are absorbed into the body. They are used to treat various fungal infections. The one chosen depends on what type of infection you have. For example:

- Terbinafine is commonly used to treat nail infection which are usually caused by a tinea type of fungus.
- Fluconazole is commonly used to treat vaginal thrush, as an alternative to using antifungal cream. It is also used to treat and prevent certain fungal infections within the body.

There are also separate leaflets in this series dealing with Athlete's foot, ringworm and fungal groin infection.

Antifungal injections

These may be used if you have a serious fungal infection within the body. Amphotericin, flucytosine, itraconazole, voriconazole, anidulafungin, caspofungin, and micafungin are medicines that are sometimes used in this way. The one chosen depends on the type of fungus causing the infection. These are specialist medications that are used for people who are usually quite ill in hospital.[14]

Bacterial Skin Disease:

Bacteria (normally Staphylococcal or Streptococcal) can cause skin infections by either entering normal skin cells or by affecting the skin barrier (such as in surgical wound sites or skin damaged by atopic dermatitis). Our first line of protection against the environment is the skin. When this barrier of defence gets broken down, a systemic or local reaction is triggered. Both the usual skin microbiology and the external environment may contain microorganisms that infiltrate the skin. [15]

Various Drugs are used in Bacterial Skin Diseases-[16]

1. Sulphamethoxazole
2. Bactrim
3. Neosporin
4. Bacitracin
5. Co-trimoxazole
6. Neomycin
7. Bactrim
8. Antibiotic plus pain relief
9. Cortisporin Cream
10. Cortisporin ointment
11. Ammoniated mercury
12. Spetra
13. Spetra DS
14. Triple Antibiotic
15. Gentamicin
16. Cephalexin
17. Clindamycin
18. Amoxicillin
19. Fusidic Acid
20. Levofloxacin

Contaminated Skin Diseases:[17]

Infants and children are usually suffering from this type of virus, and spreads by come direct contact with a person with infected sores. Molluscum contagiosum: This virus can spread from person to person or by bites to other body parts.

Various Drugs are used in Contaminated Skin Diseases

1. Antibiotics
2. Antifungal Powder
3. Antifungal Spray
4. Antifungal ointment
5. Insecticides
6. Clindamycin
7. Erythromycin
8. Antiviral Drugs
9. Surgery – Laser

Vitamin Skin Diseases[18, 40-42]

Vitamin deficiencies can cause a variety of skin conditions, including:

Vitamin B deficiency: Can cause dry, flaky skin, wrinkles, acne, rashes, and cracked lips. It can also make skin more sensitive to sunlight and other irritants.

Vitamin B12 deficiency: Can cause skin hyperpigmentation, vitiligo, angular stomatitis, and hair changes.

Vitamin B3 deficiency: Also known as pellagra, this deficiency can cause dermatitis, dementia, diarrhea, and death.

Vitamin D deficiency: Can cause acne, eczema, rosacea, and irritated skin.

Vitamin E deficiency: Vitamin E protects against sun damage and helps treat skin inflammation.

Vitamin C deficiency: Can cause easy bruising because poor collagen production leads to weak blood vessels.

Iron deficiency: Can cause pale skin and brittle nails.

Zinc deficiency: Can cause dermatitis, brittle nails, and slow healing.

Omega-3 fatty acid deficiency: Can cause dryness, dermatitis, and early aging skin

Various Drugs are used Vitamin Skin Disease

1. Aquasol A Cap
2. Vitamin A Cap
3. Vitamin B12 Supplements and Injections
4. Cholecalciferol
5. Niacin
6. Follic Acid Pills

7. Vitamin E Supplements
8. Vitamin C Supplements
9. Ascorbic Acid
10. Oral/IV Iron Therapy
11. Zinc Supplements- Zinc citrate, Zinc oxide, Zinc acetate, Zinc Sulfate, Zinc Gluconate
12. Omega 3 Supplements
13. Fish oil
14. Algae based capsule
15. Nuts
16. Flaxseeds
17. Walnuts

Insect Skin Diseases[19, 37-39]

Some of these diseases are prevalent and more of a threat such as lice (pediculosis), while others are uncommon and life-threatening, like plague caused by bubonic plague. The majority of bug bites result in diseases with just skin-related symptoms. Scabies, head lice (pediculosis capitis), and pubic lice (pediculosis pubis) are a few examples.

Various Drugs are used in Insect Skin Disease[20, 31-36]

1. Cetirizine
2. Fexofenadine
3. Loratadine
4. Zinc acetate
5. Benadryl Extra strength itch stopping gel
6. Benzocaine
7. Diphenhydramine
8. Itch relief
9. Camphor
10. Benzyl alcohol
11. Anacaine
12. Callergy clear

Virus Skin Diseases[21, 26-30]

In primary care, viral skin infections are commonly observed. Some of the most common viral skin illnesses have been included in this study, including molluscum contagiosum, roseola, herpes zoster (shingles), and varicella zoster (chickenpox). Higher risk groups and guidelines for determining when to refer a patient to a specialist are also briefly covered in the review.

Various Drugs are used in Virus Skin Disease

Antibiotics.
Antihistamines.
Laser skin resurfacing.
Medicated creams, ointments or gels.
Moisturizers.

Oral medications (taken by mouth).
Steroid pills, creams or injections.
Surgical procedures

U.V. radiation Skin Diseases[22-25]

UV radiation is part of the natural energy produced by the sun. On the electromagnetic spectrum, UV light has shorter wavelengths than visible light, so your eyes can't see UV, but your skin can feel it. Tanning beds also emit UV radiation. Two Types of UV light are proven to contribute to the risk for skin cancer:

- ✓ Ultraviolet A (UVA) has a longer wavelength. It is mainly associated with tanning and skin aging but can also lead to sunburn.
- ✓ Ultraviolet B (UVB) has a shorter wavelength. It is mainly associated with sunburn

While UVA and UVB rays differ in how they affect the skin, they both do harm. Unprotected exposure to UVA and UVB damages the DNA in skin cells, producing genetic defects, or mutations, that can lead to skin cancer and premature aging. UV rays can also cause eye damage, including cataracts and eyelid cancers.

Treatment:

Phototherapy

REFERENCES:

- [1]. Benítez JM, Montáns FJ. The mechanical behavior of skin: Structures and models for the finite element analysis. *Computers and Structures*. 2017; 190: 75-107.
- [2]. <http://www.goldeneggholistic.com/Anatomy, Physiology and Pathology notes The skin notes pdf chapter 2 page no 1>
- [3]. SJ Wadher, SL Patwekar, SS Shivpuje, SS Khandre, SS Lamture. Stability Indicating Assay Methods for Simultaneous Estimation of Amoxicillin Trihydrate And Cloxacillin Sodium in Combined Capsule Dosage Form by UV-Spectrophotometric Method. *European Journal of Biomedical and Pharmaceutical sciences*, 2017; 4(10): 858-864.
- [4]. www.nursingtimes.net December 201/ Vol 115 issue 12 Clinical Practice Systems of life Skin Skin 1: the structure and functions of the skin page no. 30
- [5]. 432 Dermatology Team Structure and Function of the Skin page no. 4-9
- [6]. <http://www.goldeneggholistic.com/Anatomy, Physiology and Pathology notes The skin notes pdf chapter 2 page no 16>
- [7]. www.nursingtimes.net December 201/ Vol 115 issue 12 Clinical Practice Systems of life Skin Skin 1: the structure and functions of the skin page no. 33
- [8]. <https://my.clevelandclinic.org/health/diseases/21573-skin-diseases>
- [9]. <https://my.clevelandclinic.org/health/diseases/21573-skin-diseases>
- [10]. https://www.msmanuals.com/home/skin-disorders/biology-of-the-skin/diagnosis-of-skin-disorders#Diascopy_v87771817
- [11]. <https://dermnetnz.org/topics/>
- [12]. <https://my.clevelandclinic.org/health/diseases/4276-skin-fungus>
- [13]. Google
- [14]. <https://patient.info/infections/fungal-infections/antifungal-medicines>
- [15]. <https://dermnetnz.org/topics/bacterial-skin-infections>
- [16]. <https://www.drugs.com/condition/superficial-bacterial-skin-infection.html>
- [17]. <https://www.templehealth.org/services/conditions/contagious-skin-diseases>
- [18]. N Patre, S Patwekar, S Dhage, S Shivpuje. Formulation & Evaluation Of Piroxicam Bionanocomposite For Enhancement of Bioavailability. *European Journal of Molecular & Clinical Medicine*, 2020; 7(11): 9362-9376.
- [19]. MRP Rao, S Taktode, SS Shivpuje, S Jagtap. Optimization of Transmucosal Buccal Delivery of Losartan Potassium using Factorial Design. *Indian Journal of Pharmaceutical Education and Research*, 2016; 50(2): S132-S139.
- [20]. <https://www.drugs.com/condition/insect-bites.html>
- [21]. <https://wchh.onlinelibrary.wiley.com/doi/10.1002/psb.1907>
- [22]. <https://www.skincancer.org/risk-factors/uv-radiation/>
- [23]. Santosh A. Payghan Shivraj S. Shivpuje Shailesh L. Patwekar, Karna B. Khavane, Padmavati R. Chainpure. A Review on Different Preparation Method Used For Development of Curcumin Nanoparticles. *International Journal of Creative Research Thoughts*, 2021; 9(1): 4088-4101.
- [24]. Zeba Ashfaq Sheikh P. R. Chainpure, S. L. Patwekar, S. S. Shivpuje. Formulation and evaluation of Garciniacambogia and Commiphoramukul Herbal tablets used for Anti Obesity. *International Journal of*

- Engineering, Science and Mathematics, 2019; 8(4): 180-195.
- [25]. Pravin P Karle, Shashikant C Dhawale, Vijay V Navghare, Shivraj S Shivpuje. Optimization of extraction conditions and evaluation of Manilkarazapota (L.) P. Royen fruit peel extract for in vitro α -glucosidase enzyme inhibition and free radical scavenging potential. Future Journal of Pharmaceutical Sciences, 2021; 7(1):1-10.
- [26]. SheetalRathod P. R. Chainpure, S. L. Patwekar, S. S. Shivpuje. A Study Of Carica Papaya Concerning It's Ancient And Traditional Uses - Recent Advances And Modern Applications For Improving The Milk Secretion In Lactating Womens. International Journal of Research, 2019;8(2):1851-1861.
- [27]. Shivraj S. ShivpujeShailesh J. Wadher, Bhagwan B. Supekar. Development And Validation Of New Ft-Ir Spectrophotometric Method For Simultaneous Estimation Of Ambroxol Hydrochloride And Cetirizine Hydrochloride In Combined Pharmaceutical. International Research Journal of Pharmacy, 2019; 10(3):110-114.
- [28]. Shivraj S. Shivpuje, Shailesh J. Wadher, Bhagwan B. Supekar. Simultaneous Estimation of Ambroxol Hydrochloride and Cetirizine Hydrochloride in Combined Solid Tablet Formulations by HPTLC-Densitometric Method. Asian Journal of Biochemical and Pharmaceutical Research, 2019; 9(1):1-10.
- [29]. JW Sailesh, SS Shivraj, SI Liyakat. Development and Validation of Stability Indicating RP-HPLC Method for the Estimation of Simvastatin in Bulk and Tablet Dosage form. Research Journal of Pharmacy and Technology, 2018; 11(4): 1553-1558.
- [30]. Patil S. S. ShivpujeShivraj S. PatreNarendra G. Development and Validation Of Stability Indicating HPTLC Method For Determination of Nisoldipine (Niso) In Tablet Dosage Form. European Journal of Biomedical and Pharmaceutical sciences, 2017; 4(12):462468.
- [31]. W Shailesh, K Tukaram, S Shivraj, L Sima, K Supriya. Development and Validation of Stability Indicating UV Spectrophotometric Method for Simultaneous Estimation of Amoxicillin Trihydrate and Metronidazole In Bulk And In-House Tablet. World Journal of Pharmaceutical and Medical Research, 2017;3(8):312-318.
- [32]. J WadherShailesh, M KalyankarTukaram, S ShivpujeShivraj. Development and Validation of Stability Indicating Assay Method for Simultaneous Estimation of Amoxicillin Trihydrate and Cloxacillin Sodium In Pharmaceutical Dosage Form By Using RP-HPLC. World Journal of Pharmaceutical Research, 2017; 10(6):1002-1006.
- [33]. Shital S. Sangale, Priyanka S. Kale, Rachana B. Lamkane, Ganga S. Gore, Priyanka B. Parekar, Shivraj S. Shivpuje (2023). Synthesis of Novel Isoxazole Derivatives as Analgesic Agents by Using Eddy's Hot Plate Method. South Asian Res J Pharm Sci, 5(1): 18-27.
- [34]. Priyanka B. Parekar, Shivraj S. Shivpuje, Vijay V. Navghare, Manasi M. Savale, Vijaya B. Surwase, Priti S. Mane- Kolpe, Priyanak S. Kale. Polyherbal Gel Development And Evaluation For Antifungal Activity, European Journal of Molecular & Clinical Medicine. 2022; 9(03): 5409-5418.
- [35]. Jain AA, Mane-Kolpe PD, Parekar PB, Todkari AV, Sul KT, Shivpuje SS. Brief review on Total Quality Management in Pharmaceutical Industries, International Journal of Pharmaceutical Research and Applications. 2022; 7(05):1030-1036.
- [36]. Sumaiyya. K. Attar, Pooja P. Dhanawade, Sonali S. Gurav , Perna H. Sidwadkar , Priyanka B. Parekar, Shivraj S. Shivpuje. Development and Validation of UV Visible Spectrophotometric Method for Estimation of Fexofenadine Hydrochloride in Bulk and Formulation, GIS SCIENCE JOURNAL. 2022; 9(11): 936-944.
- [37]. SumayyaKasimAtar, PriyadarshiniRavindraKamble, SonaliSharadGurav, PoojaPanditDhanawade, Priyanka Bhanudas Parekar, ShivrajSangapaShivpuje. Phytochemical Screening, Physicochemical Analysis of Starch from ColocasiaEsculenta, NeuroQuantology, 2022; 20(20): 903-917.

- [38]. Priti D. Mane-Kolpe, Alfa A. Jain, Tai P. Yele, Reshma B. Devkate, Priyanka B. Parekar, Komal T. Sul, Shivraj S. Shivpuje. A Systematic Review on Effects of Chloroquine as a Antiviral against Covid-19, International Journal of Innovative Science and Research Technology, 2022;7(11): 989-995.
- [39]. Dr. Rohit Jadhav, Prof. Abhay D. Kale, Dr. Hitesh Vishwanath Shahare, Dr. Ramesh Ingole, Dr. Shailesh Patwekar, Dr. S. J. Wadher, Shivraj Shivpuje. Molecular Docking Studies and Synthesis of Novel 3-(3-hydroxypropyl)-(nitrophenyl)[1,3]thiazolo [4,5-d] pyrimidin-2(3H)-one as potent inhibitors of P. Aeruginosa of S. Aureus, Eur. Chem. Bull. 2023; 12(12): 505-515.
- [40]. Priyanka B. Parekar, Savita D. Sonwane, Vaibhav N. Dhakane, Rasika N. Tilekar, Neelam S. Bhagdevani, Sachin M. Jadhav, Shivraj S. Shivpuje, Synthesis and Biological Evaluation of Novel 1,3,4-Oxadiazole Derivatives as Antimicrobial Agents, Journal of Cardiovascular Disease Research, 2023; 14(8):611-624.
- [41]. Kavita R. Mane, Prachi A. Ghadage, Aishwarya S. Shilamkar, Vaishnavi A. Pawar, Sakshi B. Taware, Priyanka B. Parekar, Shivraj S. Shivpuje. Phytochemical Screening, Extraction and In-vivo study of Immunomodulation effect of Withaniasomnifera, Momordica dioica and Annonasquamosa leaves. Journal of Cardiovascular Disease Research, 2023; 14(9): 231-241.
- [42]. Harshada S. Deshmukh, Vishal B. Babar, Prajкта S. Jagtap, Rupendra V. Doshi, Shivarti V. Deokate, Ashwini V. Todkari, Amrata S. Mantri, Priyanka B. Parekar, Shivraj Shivpuje (2024). A Comprehensive Review Article on Herbal Cosmetics. South Asian Res J Pharm Sci, 6(3): 50-68.