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A COMPERHENSIVE ON ANTI VIRAL DRUG USED IN THE SKIN INFECTION

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INTRODUCTION

Antiviral drugs are prescription medicines (pills, liquid, an inhaled powder, or an intravenous solution) that fight against viruses in the body Continuous intravenous infusion is recognized[1] as a superior mode of drug administration not only to bypass hepatic "first pass" metabolism, but also to maintain constant drug level in the body. This provides direct entry of drug into the systemic circulation but entails certain risks. Recently, the benefits of I.V. drug infusion can be duplicated without its hazards by using skin as the port of drug administration to provide continuous transversal drug infusion into the systemic circulation. Antiviral drugs are one class of antimicrobials, a larger group which also includes antibiotic (also termed antibacterial), antifungal and antiparasitic drugs, or antiviral drugs based on monoclonal antibodies. Most antivirals are considered relatively to the host, and therefore can be used to treat infections. They should be distinguished from viricides, which are not medication but deactivate or destroy virus particles, either inside or outside the body. Natural viricides are produced by some plants such as eucalyptus and Australian tea trees.

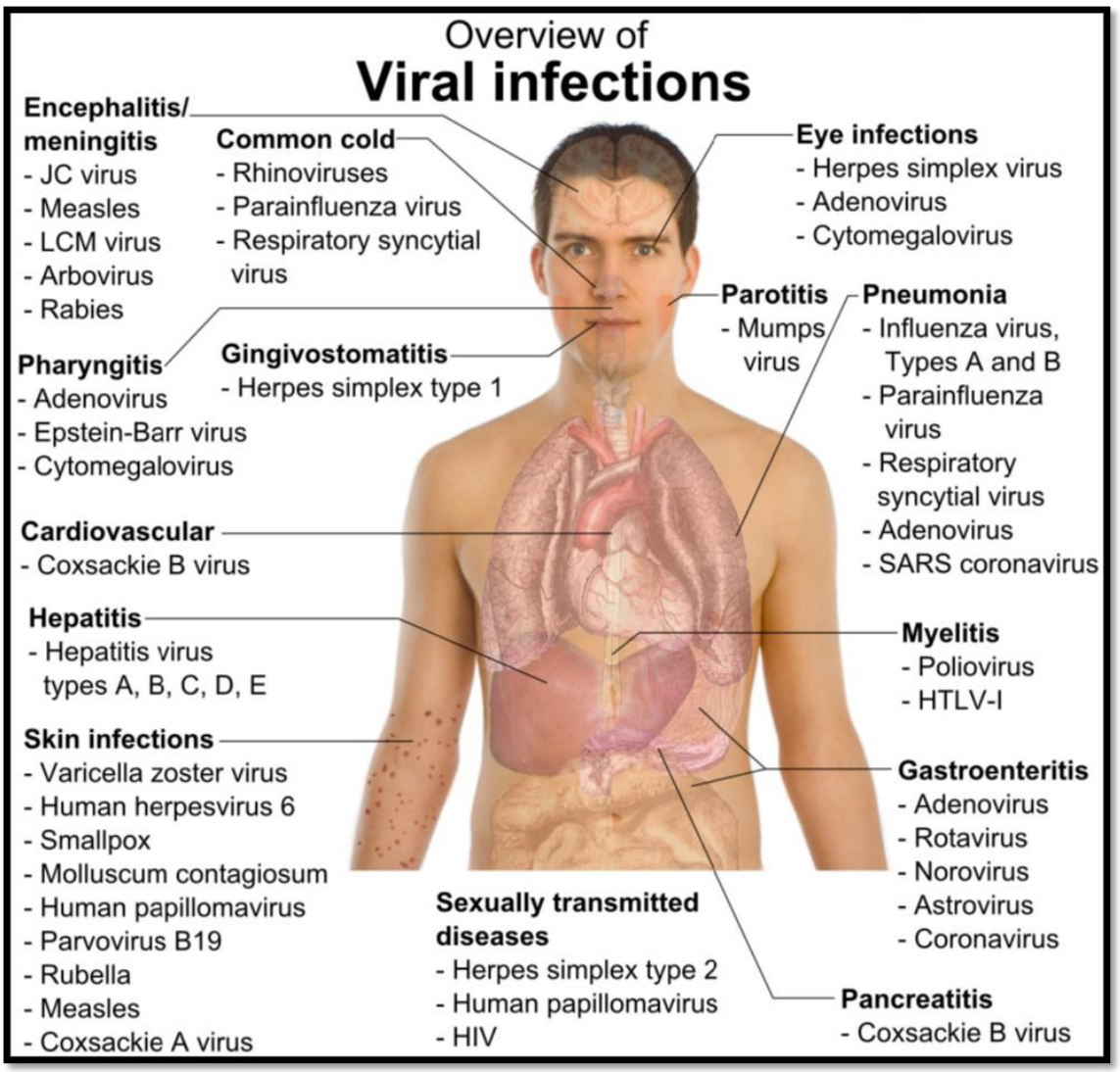

Fig no 1: Pictorial layout of viral infection.

SKIN CHARACTERISTICS[2,3]

The purpose of topical dosage form is to conveniently deliver drugs across alocalized area of the skin. Medications are applied to the skin in the form of ointments, creams, gels etc. The absorption of substances from outside the skin, including entrances into the blood stream is referred to as percutaneous absorption. Itis necessary to understand the skin characteristics to develop an ideal topical dosage form.

SKIN

The skin is an organ because it consists of tissues structurally joined together to perform specific activities. It is one of the larger organs of the body in terms of surface area. For the average adult, the skin occupies a surface area of approximately2 sq.m (3000 sq.inches) It is a common site of administration for dermatological drugs to achieve a localized

pharmacological action. Here, the drug molecules diffuse to a target in the skin to produce its action before it is distributed to the blood circulation for elimination. The skin also serves as a port of administration for a number of systemically active drugs whereby those drugs applied topically are first absorbed into the blood circulation and then transported to the target for elicitation of its therapeutic effect.

STRUCTURE

Structurally, the skin consists of two principal parts. The outer, thinner portion, which is composed of epithelium, is called the epidermis. The epidermis is cemented to the inner, thicker, connective tissue part called the dermis. Beneath the dermis is a subcutaneous layer. This layer, also called the superficial fasica or hypodermis, consists of aerolar and adipose tissues. Fibers from the dermis extend down into the subcutaneous layer and anchor the skin to it. The subcutaneous layer, in turn, is attached to underlying tissues and organs. The pH of the skin is normally between 5.0-6.0.

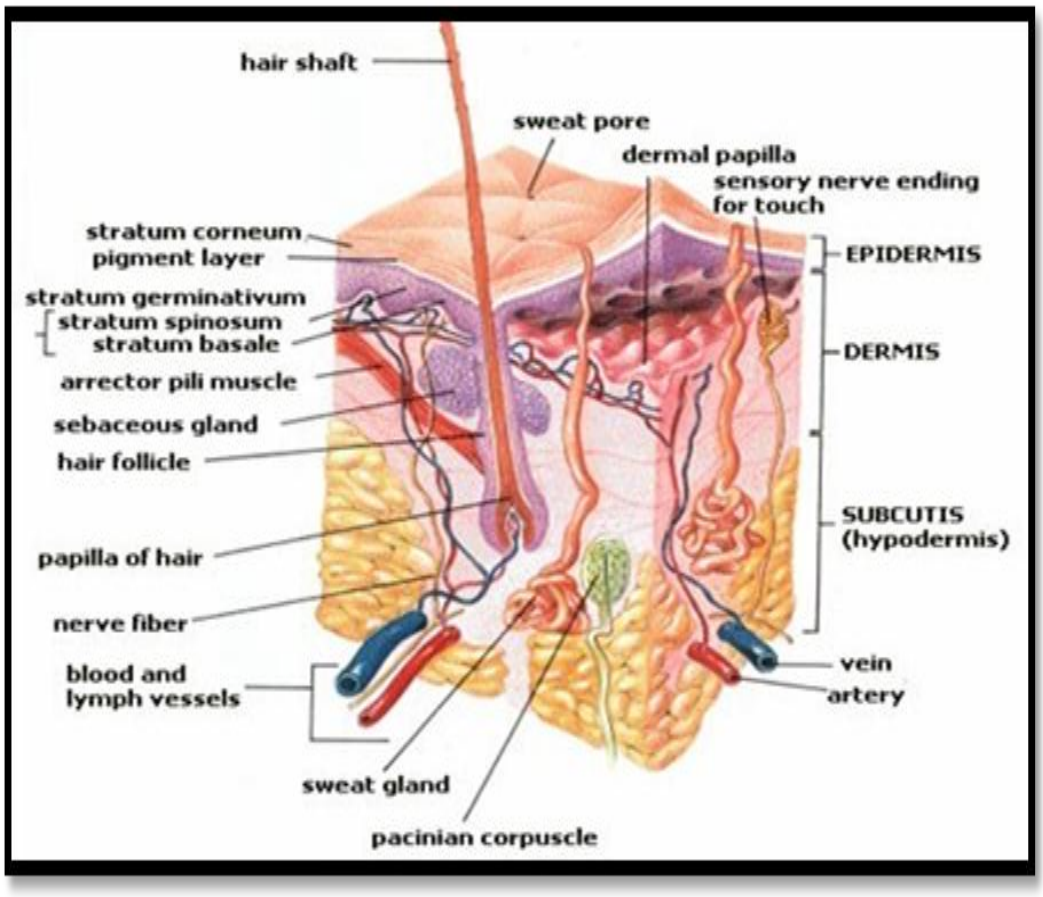

Fig. no 2: Structure of skin underlying subcutaneous tissue.

Epidermi

The epidermis is composed of stratified squamous epithelium and contains four distinct types of cells. They are 1) Keratinocytes 2) Melanocytes Non- pigmented granular dedtrocytes formerly known as 3) Langerhans cells and 4) Granstein cells. The keratinocytes of the epidermis are organized into the following cell layers, from the deepest to the most superficial region.

1. Stratum basale
2. Stratum sponosum
3. Stratum granulosum
4. Stratumlucidum
5. Stratum corneum.

Dermis

The second principle part of the skin, is composed of connective tissue containing collagenous and elastic fibers. Numerous blood vessels, nerves, glands and hair follicles are embedded in the dermis. The upper region of the dermis, about one fifth of the thickness of the total layer is named the papillary region or layer. It consists of loose connective tissue containing fine elastic fibres. Its surface area is greatly increased by small, finger like projection called dermal papillae (pa-PIL-e). These structures project into the epidermis and many contain loops of capillaries. Some dermal papillae also contain corpuscles of touch, also called Meissner's corpuscles, never endings that are sensitive to touch. The remaining portion of the dermis is called the reticular region or layer. It consists of dense, irregularly arranged connective tissue containing interlacing. Bundles of collagenous and coarse elastic fibers. A small quantity of adipose tissue, hair follicles, nerves, oil glands and the ducts of sweat glands occupy spaces between the fibres. The combination of collagenous and elastic fibers in the reticular region provides the skin with strength, extensibility and elasticity.

The reticular region is attached to underlying organs, such as bone and muscle, by the subcutaneous layer. The subcutaneous layer also contains nerve endings called lamellate or paining corpuscles that are sensitive to pressure.

1. The permeability barrier of the skin consists of
2. The stratum corneum (10-50 micro meter thick)
3. The viable epidermis (100 micro meter thick)
4. The papillary layer of dermis (100-200 micro meter thick)

Transdemal Permeability

The principle of transport mechanism across mammalian skin is by passive diffusion[5] through primarily transepidermal route at steady state or throughl route at non-steady state. The factors influencing and causing in transdermal permeability can be classified into three major categories:

1. Physico chemical properties of penetrants
2. Physico chemical properties of drug delivery system
3. Pathological & Physiological conditions of the skin.

Various physico-chemical propreties of the drug like partition co-efficient, concentration in the vehicle, conditions, molecular size and molecular weight play a vital role in deciding the percutaneous absorption.

The affinity of the vehicle for the drug[6] molecules solubility of the drug in thevehicle, pH of the vehicle can influence the release rate of the drug. The composition

Viral Disease[8]

The Herpes virus family contains over a hundred species of enveloped DNA viruses that affect humans and animals. They are characterized by their ability to establish latent infections enabling the virus to persist indefinitely within infected hosts and to undergo periodic reactivation Herpes simplex virus belongs to a family of viruses called *Herpesviridae*. They are composed of a central DNA core and a protein capscid with 162 hollow cylindrical apsomers. This nucleocapsid is surrounded by an envelope forming a virus particle with an overall diameter of 130-180nm.[9]

Herpes simplex virus usually affects tissues of ectodermal origin, such as skin, mucous membrane and the nervous system. After the attachment to specific receptors on the surface of the human cells the virion loses its envelope to the cell membrane and enters the cells by pinocytosis. The DNA released into the cells travels to the nucleus. In namely thymidine kinase and DNA polymerase. Viral proteins synthesized in the cytoplasm are transferred to the nucleus where the nuleocapscid is assembled. The nucleocapscids packed with such particles before it ultimately undergoes cell lysis and releases the infectious particles.[10]

Table no 1: Short description of antiviral drug in tabular format.

Groups	Species (Official name)	Species (Common name)	Site of latentinfection
	Human herpes virustype 1	Herpes simplex virus type1(HSV-1)	Neurons
Alpha-herpes virus	Human herpes virustype 2	Herpes simplex virus type2(HSV-2)	Neurons
	Human herpes virustype 3	Varicella zostervirus (VZV)	Neurons
Beta-herpes virus	Human herpes virustype 4 Human herpes virustype 5	Cytomegalovirus Human B cell lymphtropic virus	Secretory glands, kidneys, other organsand tissues Lymphoid tissues
	Human herpes virustype 6	R K virus	Lymphoid tissues
Gamma-herpes virus	Human herpes virustype 7 Human herpes virustype 8	Epstein-Barr virus --------	Lymphoid tissues -------

ANTI-VIRAL DRUG MECHANISM OF ACTION

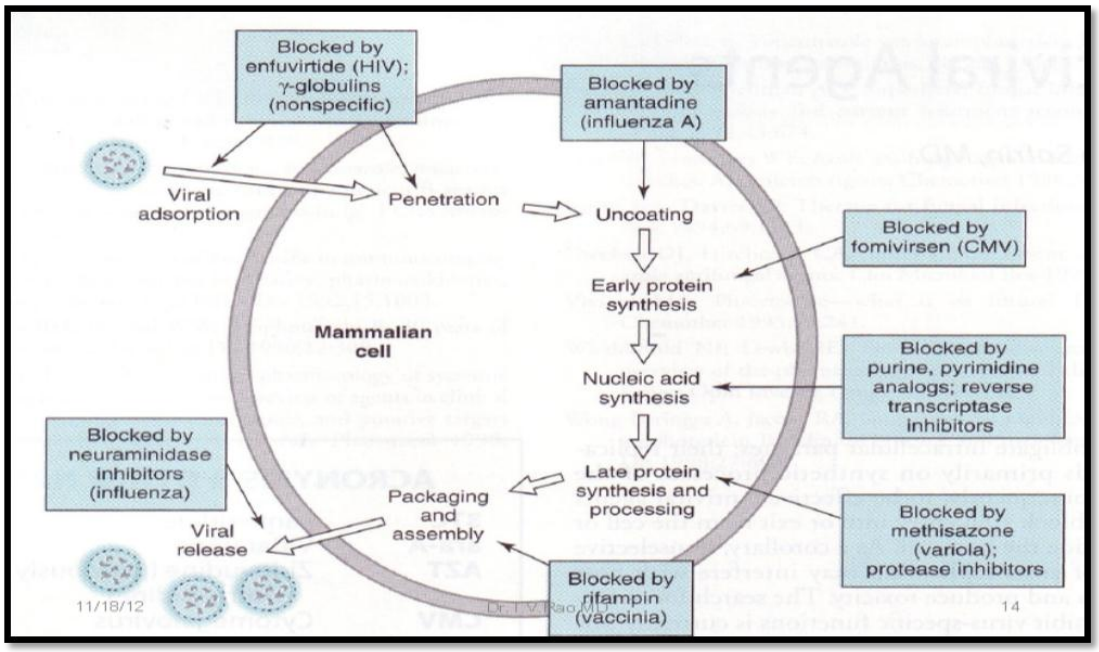

Fig no 3: Anti-Viral Drug Mechanism of Action.

Anti-viral drugs

Therapeutic uses Interferons

1. Chronic hepatitis B and C (complete disappearance is
2. Seen in 30%).
3. HZV infection in cancer patients (to prevent the
4. Dissemination of the infection)
5. CMV infections in renal transplant patients

6. Condylomata acuminata (given by intralesional
7. Injection). Complete clearance is seen ~ 50%.
8. Hairy cell leukemia (in combination with zidovudine)
9. AIDS related Kaposi's sarcoma

Table no 2: Antiviral drug use in common diseases.

Virus	Diseases	Drug(s) of choice	Alternative drugs
FLU	Influenza	Amantadine	Rimantadine
RSV	Pneumonia, bronchiolitis	Ribavirin (aerosol)	
HSV	Genital herpes	Acyclovir	Foscarnet
	Keratitis Conjunctivitis	Trifluridine	Idoxuridine Vidarabine
	Neonatal HSV infection	Acyclovir	Vidarabine

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