



Use of Gels in Wound Healing

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Abstract:

Topical drug delivery is application of dosage form directly to the skin as for wound healing or any other disorder related to the skin. Topical drug delivery show the local effect. It cover various dosage forms as semisolid, liquid, solid fine powders and Sprays. Gels comes under the category of Semisolid dosage form. Gel shows the advantages over topical semisolid dosage forms as ointment and creams. The main components in formulation of gel are mixture of gelator, API, Solvent, with other excipients. Gels may be classified into two categories as organogels and hydrogels. Gel show better stability and application suitability too. In wound healing gel show promising effect.

1.1 GELS:

Gel is a semi solid formulation that has a pair of components which is liquid phase in rich. After the application of gel the liquid phase get dry by the evaporation and a film of gel having drug covers the skin^[1].

Gels are as compare to the creams and other ointments give better drug release. These are highly bio-compatible that's why minimum risk of adverse reaction and inflammation. The dermatological use of gels have many property as thixotropic, easily remove, non-greasy, desirable spreadable, non-staining, emollients, compatible with the many excipients. Topical drug delivery systems are apply as directly on the body surface as external part by spraying, rubbing, spreading. The topical route for of administration are very common and it is use as treatment of skin disorder and local effects.^[2] Gels are often topically applied as emollients, or as occlusive dressing and also as protective for the local and systemic medication. Gels are defined as significant extent dilute cross linked system that is in the steady state no flow. Gels are sometimes called jellies.

The word gel was invented by 19th century by Scottish chemist Thomas graham by the clipping from gelatin. Gels are semisolid systems that are a polar phase is constrained within a three dimensional polymeric matrix in which high degree of physical and sometimes chemical cross linking has been introduced. The polymers apply in the preparation of pharmaceutical gels including natural gum semi synthetic and synthetic materials. Natural gums as tragacanth, pectin, agar, alginic acid, carrageen and such semisynthetic materials

as carbopols, sodium alginate, methyl cellulose, carboxymethyl cellulose, hydroxyethyl cellulose, where is synthetic polymer such as vinylpolymers with ignitable carboxyl groups. Gels are prepared by mainly fusion process by the gelling characters of gallant^[3]. According to USP definition of gels "Gels are semisolid system consisting of the dispersion made of either small inorganic particle or large organic particles enclosing and interpenetrated by liquid". Gels are bi-phasic system in which inorganic particles are not soluble or dissolved but merely it will dispersed the continuous phase randomly coiled in the flexible chains^[4].

1.1.1. Ideal properties of Gels^[2,5]

- It should be inert with healthy skin.
- Site specific drug delivery.
- It should show satisfactory rheological behavior.
- It should be less greasy.
- Their absorption should be better.
- It should be water washable.
- Topical gel should not be tacky and should show better spreadability.
- Ophthalmic gel should be sterile.
- It should be stable during storage condition and should not lead any alteration in its viscosity.

1.1.2. Advantages of Gels^[6]

- Gels can be self-applied by patient to the affected area.
- Applied only disease affected area.
- Minimum risk of adverse effect.
- Low inflammation.



- Easily washed from applied area due to irritation.
- It is for local therapeutic effect.
- Natural polymer may be used.
- Effective cost.
- It is achieved cutaneous and percutaneous drug delivery.
- It also avoid gastrointestinal drug absorption.
- These also avoids enzymatic activity.

1.1.3. Disadvantages of gels

- Longer or time consuming treatment.
- Stability as well as storage problems.
- Possible to allergic reaction.
- Low permeability of some drugs through skin.
- Time taking preparation.
- Carefully apply the gel on target area.
- Irritation may cause on applied area.
- Local inflammation may cause.
- Some larger particles of drug are not absorbed by skin.
- Many times spread to unaffected area that lead to damage or affect healthy tissue.

1.1.4. Factor affecting Gel Formulation [7]

➤ **PH of myofibriller protein:** These are strongly pH dependent. The myofibrillar protein, pH 5.3 required at the isoelectric point. The pH is affected on gel formulation for the myosin reached for these pH values are required pH 6.

➤ **Muscles types:** Generally in human body there are three types of muscles, visceral, cardiac, and skeletal muscles. We study about red and white muscles there is required stronger gel formulation for the white muscles than the red muscles because the red muscles are thin as compare to the white muscles. Red muscles are lazy contraction. In the red muscles the heavy amount of myoglobin are responsible for red color. In the white muscles minimum amount of myoglobin are present. In the white muscles lactic acid are accumulated.

➤ **Protein concentration:** For the formulation of gel necessary or required the critical protein concentration. The amount of protein concentration is increases due to the increasing of hardness of gel.

➤ **Temperature:** Temperature is important factor for the gel formulation. Due to application time at the pH 6 temperature required 60° c to 70° c for the inducing gelation of myosin. Temperature is also affected on the storage condition of gel.

➤ **Skin condition:** skin is a barrier layer of our body which protects us from external environment. For the therapeutic effect of gel should be need the cross the skin layer. Skin is consisting of three layer epidermis, dermis, and hypodermis. Epidermis is responsible for

the thin and thick skin. Thick skin has five layers as stratum corneum, stratum spinosum, stratum granulosum, stratum lucidum and stratum basal, and in the thin layer absence of stratum lucidum.

➤ **Age:** The absorption of gels is dependent on patient age. In the geriatrics or elderly patient slow absorption and permeation rate of drug due to their skin condition as the compare with adult. The skin of the geriatric patients is rough and dry.

➤ **Density of sweat gland:** Sweat glands are produced sweat which major role play in thermal regulation in body. Sweat production are good then the drug absorption rate are good and their permeability also increased.

➤ **Fat content:** Fat content of applied area are responsible for drug release. Fat contact has a marked effect on gelation properties of meat product.

➤ **Other Factors :-** Races, Nature of exposure to applied skin (Chemical, Radiation)

➤ 1.2 ADDITIVES OF GEL [8,9]

➤ The polymers are utilized for supporting the structural network for the gel preparation. Which polymers are classified as below

➤ 1. Natural polymers

➤ A. Proteins

➤ Collagen, Gallatin

➤ B. Polysaccharides

➤ Gellum Gum, Pectin, Agar, Alginate acid, Cassia tora, Sodium carrageen, Potassium carrageen, Xanthan gum, Guar gum.

➤ 2. Semisynthetic polymer

Cellulose derivatives

Hydroxyl propyl methyl cellulose [HPMC], Hydroxylpropyle cellulose [HPC], Carboxyl methyl cellulose [CMC], Methyl Cellulose.

3. Synthetic polymer

A. Carbomer

Carbomer -940

Carbomer-934p

Carbomer- 941

B. Poloxamer

C. Polyvinyl alcohol

Poly vinyl propyl [PVP]

D. Polyacrylamide

4. Surfactant

Allyl alcohol, Propylene oxide, Butylene oxide, Vinylpyrrolidon
Vinyl alcohol, Brij-96.



5. Inorganic polymer

Silicon, Polysilane, Aluminum hydroxide,

1.3 Types of gel^[10]

These are categorized on the basis of following:

1. Based on colloidal system
2. Based on nature of solvent system.
3. Rheological properties
4. Based on physical nature

1. Based on colloidal system

- a. Organic gel
- b. Inorganic phase

2. Based on nature of solvent system

- a. Organic gel
- b. Hydrogel
- c. Xerogels

a. Based on rheological behavior Pseudo plastic gel

- b. Plastic gel

3. Based on physical nature

- a. Elastic gel
- b. Rigid gel

1.4 SKIN^[11,12]

1.4.1. Anatomy and Physiology of Skin

Skin is the outermost part of our body. It is the largest organ which makes a barrier on the surface of the body. Skin is defending the internal organ damage through the external atmosphere, external microbes and other elements. Skin is maintained the body temperature and water loss through the sweat gland, also provide the touch sensation, hot, cold, and pinch. The transdermal drug delivery system, there is drug should be either pass through stratum corneum of epidermis or go through the hair follicles or pass the sweat gland then reached the site of action. Area of skin which covering of human body, in adult person approximately 2 square meter [22 square feet] and weight about 4.5-5 kg that is 16% of total body weight.

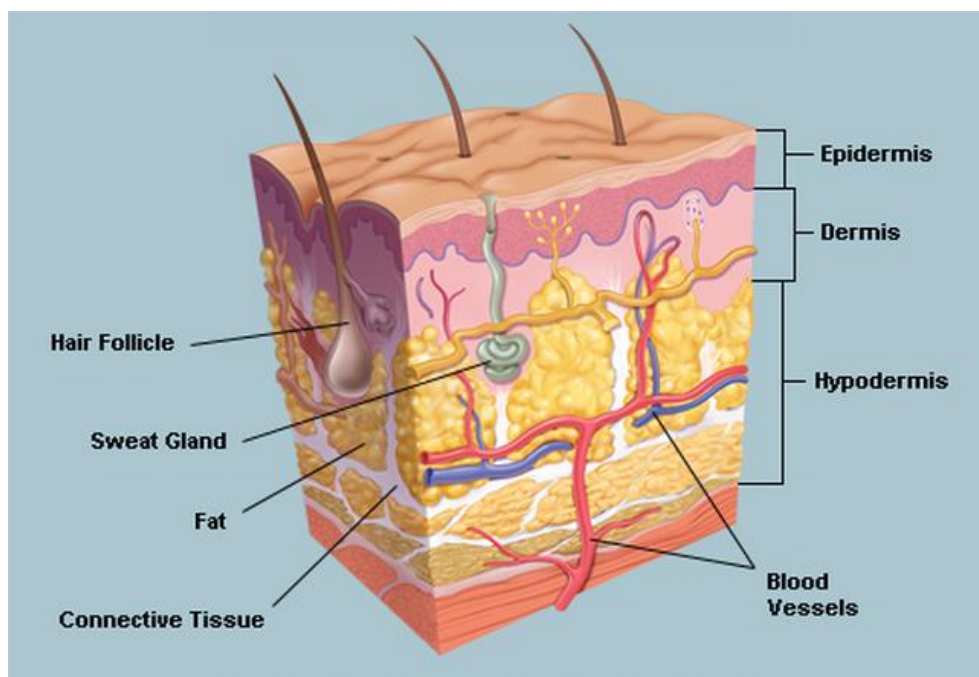


Figure - Anatomy of skin

Skin is consist of three layer

1. Epidermis
2. Dermis
3. Hypodermis

1. Epidermis: Epidermis is external layer of the skin which is work as water-proof barrier of body. Epidermis layer of skin are composed the keratinized stratified squamous epithelium tissue and contains the four types

of cells: Markel cells, Melanocytes, Langerhans cells, and fourth are Keratinocytes. Epidermis cells are very important role play in our body as it is protect our internal organ through the external environmental microbes and other elements. It also defends the cold and hot air that can be give negative effect on our body. The keratin protein is produced by the keratinocytes of epidermal cell which helps to protect the skin and tissue from the heat, microbes and other chemical. In the



epidermal layer the melanocytes are very effective role play in our body. Melanin enzymes are secreted by the melanocytes of epidermal cells. Approximately 8% of epidermal cells are melanocytes. Melanin has yellow-red and brown –black pigment which are supply skin colors and damaging ultra- violet light. The epidermal cells are consist five types of layer as stratum basal, stratum spinosum, stratum granulosum, stratum

lucidum, and stratum corneum. These layers of epidermal cells are responsible for the thick and thin skin. In the thick skin there is available all layer of epidermal cells and thick stratum corneum are present but in case of thin skin there is four layer are available and fifth layer as stratum lucidum are absence and the thick stratum corneum is replaced by thin stratum corneum.

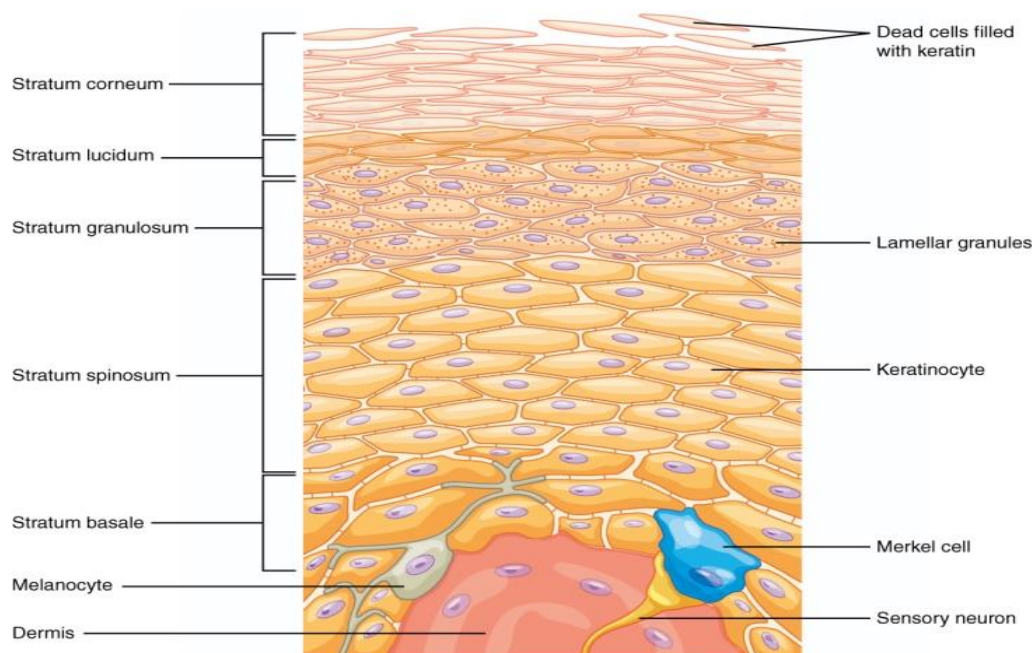


Figure- epidermis layer

1. Dermis: It is the far down or lower layer of the skin and it is the large part of skin. Dermis is composed connective tissue, blood vessels, nerve, hair follicles, and gland. Dermis is categorized in to papillary region and reticular region. The papillary region is made up the one fifth part of total layer. It is also composed of connective tissue. The dermis surface area is increased by a little finger like structure that's called dermal papillae. There is present reticular region which are attached to the subcutaneous layer. The subcutaneous layer is act on the time of transdermal drug delivery absorption and permeation. The subcutaneous layer composed the fibroblast and collagen bundle, and some fibrous elastic. Fibrous elastic and collagen are supply the skin strength, elasticity, and covering or extensively.

2. Hypodermis: It is the deeper part after the dermis of the skin. Hypodermis layer are composed by fat, and connective tissue also consist the some part of hair follicle and sweat gland nerve are also available here. Actually the hypodermis is not a part of skin but it is counting in the third layer of skin. It is made up of areolar and adipose tissue.

Accessory structure of the skin:

Hair, skin gland, and nails-

These are the accessory and supportive structure of the skin. These all are being developed from embryonic epidermis. Hair and nails are protecting the body part and their internal organ. Hair are defends the external microbes, or elements and protect the skin from any damage. Nails are worked to support the fingers and also protect that's. Nature of hairs and nails are continuous growth. Melanin is responsible for the hair color as white and black.

The sweat glands are helps the maintained the body temperature. It is maintained by the help of sweat secretion in the body. When the temperature of body is arise that's time the sweat gland are secreted the sweat juice which is fall down the arise temperature of the body then body temperature will be maintained. If the body temperature decreased that's time thermoregulation activity will be start and blood flow rate is increased that's why body temperature increased and it will be maintained.



1.4.2 Function of the skin

The skin are provides to regulation of body temperature, blood storage, protect from external microbes and elements, heat and cold sensation, excretion and absorption, synthesis of vitamin D in the body, thermoregulation are including these.

Thermoregulation:

Thermoregulation is a process which is maintained the body temperature by the homeostatic regulation with the help of two methods as the release sweat and other is adjusting through the blood flow in the dermis. The standard baseline temperature of healthy person are temperature between 98°F [37°C] to 100°F [37.8°C]. When the elevated temperature of body the increased the sweat production and that is evaporated from surface of body then temperature will be maintained. When the body temperature are loss for the recovery of it's the blood vessels of skin in dermis that is more blood flow which is increased the amount of loss of heat and recover the losing heat.

Blood reservoir:

The skin are play as a blood reservoir because the dermis have affecting large area network of blood

vessels that is carry the 8-10% of total blood flow in adult person.

Protection:

Skin are make available for use to protection of body by the microbes, Absorption, heat, and chemical, dehydration, hold entry of water duration of shower and swimming for across the skin. Skin also protects the body from the ultraviolet light. When ultra violet light is attack on the body that's time melanin pigments are active or secreted and that defend the UV light.

Cutaneous sensation:

Cutaneous sensation are help the tactile sensation like touch, pressure, vibration, heat, cold, pain, another like pinch are informed about these all of sensation.

Percutaneous absorption:

Percutaneous is a part of skin and for the drug release the required of the percutaneous absorption. Some drug as like emollients, antimicrobial, and deodorants role play as fundamentally on the surface of skin. The desirable area of maximum dermatological disorder stays in the viable epidermis. The skin penetration diffusion is necessary. The drug penetration through the skin as following-

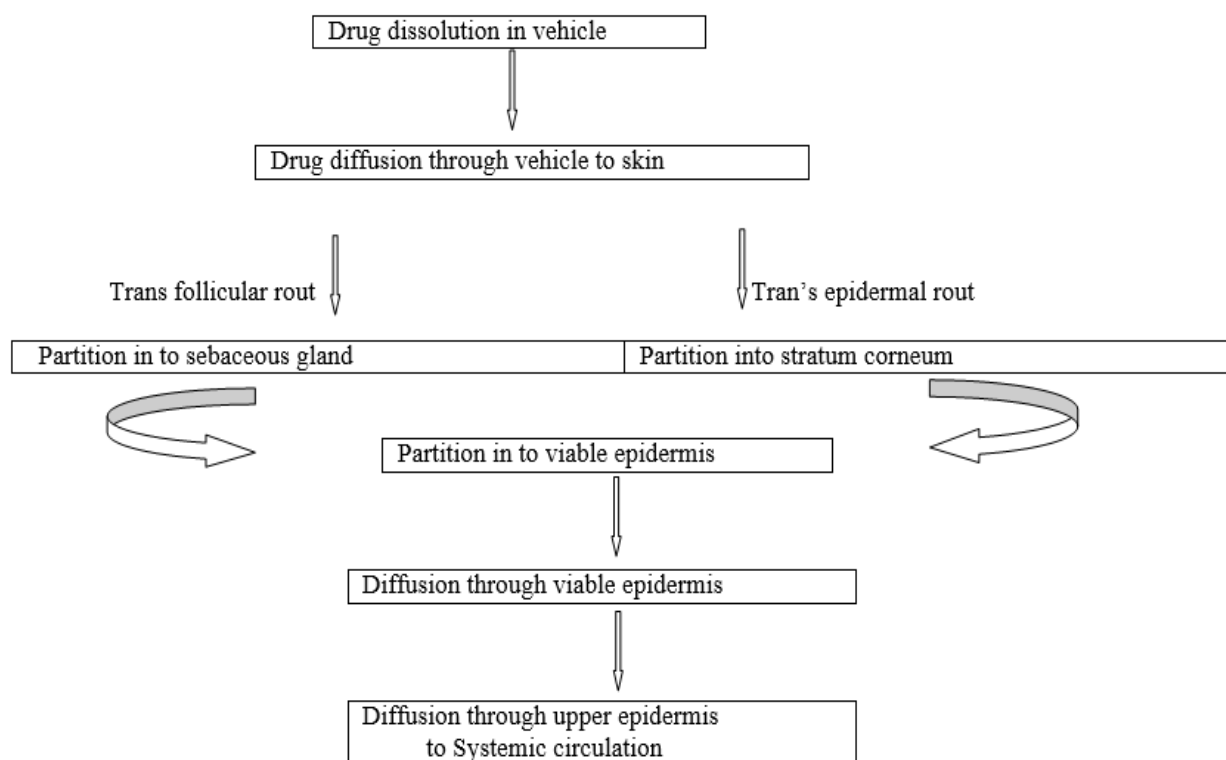


Diagram of Percutaneous absorption



Excretion and absorption:

The skin is little role play in the excretion system. The terminated of substance from the body and absorption the passage of some material from the outer environment in to the body cells. 400ml of water are evaporate per day by stratum corneum of body. Carbon dioxide, ammonia, urea, and little amount of salts are excretion from body. Lipid soluble materials do penetrate the skin along vitamin A, D E & K, some drug and some gases oxygen & carbon di oxide, and water soluble substance are negligible that absorption.

Synthesis of vitamin D:

Vitamin D is present in the body in the form of inactive and for the activation of its required the UV rays. Ultraviolet rays are activate the vitamin D precursor molecules. The best source of ultra violet rays are sunlight. More active form of Vitamin D is found in calcitriol.

1.5. WOUND HEALING

1.5.1 Wound [13, 14]:

Wound is defined as the any damage or mechanism failure in the defensive mechanism of the skin due to external condition as surgery, cuts, and accidental. Due to damage condition the loss of consistent existence and change the anatomy of the epithelial tissue or epithelium, may or may not loss of the latent connective tissue as like muscles, bone, and nerve. Types of the wound are also required for the diagnosis of these. There is cut wound, surgical wound, accidental wound, shape as curved wound, straight cut. Season is also role play in wound. High heat and high cold are negative effect on the wound. Wounds are infected by external environmental condition as heat, cold, and other bacterial attack, Microbes will be grow. In the autumn season minimum chances of infection or microbial grow.



Figure- Image of wound on skin

1.5.2 Wounds are classified as following

1. Infected wound:

This type of wound is older, which are long term treatment. It consist dead tissue and cells. These type of wounds are required carefully treatments or maintained.

2. Contaminated wound

It is wound as like open and may be surgical that is major cut or surgery with the help of sterile process which are allow to visible the inflammation.

3. Clean wound

Such type of wounds is operational or surgical in hospital or trauma. On the surface of such type wound no microbes are stable due to their maintenance and treatment.

Clean and contaminated wound

This type of the wounds is not infected that's non inflammation. It is surgical wound and under the supervision of doctor, and hospital staff as junior doctor.

1.5.3 WOUND HEALING

Wound healing is the fundamental process that response to connective tissue. The Process of wound healing is the recovery of normal cells or tissue from the injured or damage tissue. Wound size and shape are also important for the incision or medication. The site of wound also play a major role in wound healing.

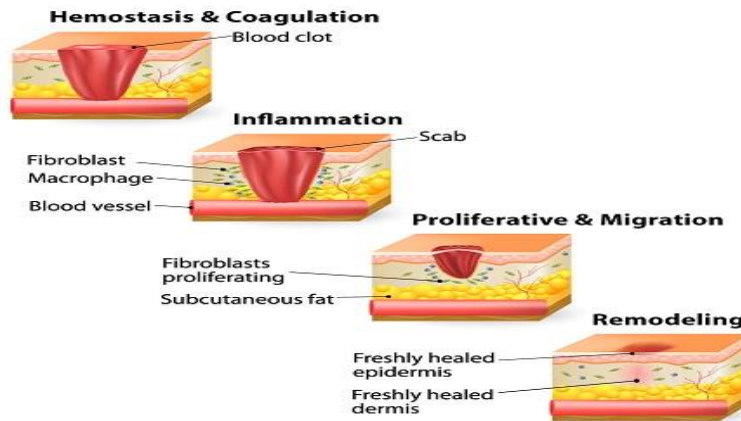
A long time ago a physician from Egypt who treats the open wound by using the grease, honey paste and skin removed for the wound healing. 400 BC Hippocrates discusses, in the Greek medication system for the wound healing, surgical method applies and for that a tinny pipe are push in the wound cavity and wound healing drainage. This method is not existence to long time. Every-one know about that cleaning washing and bandage according to the type of wound. Now a day Wound are cleaning and washing by the hot water or sterile water, and other chemical like savlon antiseptic liquid, Dettol. Ancient time a Greek physicians treat the patient for wound healing using wine that is contains 98% of alcohol, grease and fragrant which is bactericidal. First manufacturer of sterilize cotton, gauze, and other product for the treatment of wound and other surgical equipment was Johnson and Johnson company.

In the wound healing process, there are four types mechanism are study

1. Homeostasis [blood clot]
2. Inflammation
3. Proliferation [tissue growth]
4. Maturation [tissue remodeling]



WOUND HEALING



Haemostasis:

Hemostasis

- Series of reactions to stop a bleed
- Phases:
 1. Vascular spasm
 2. Platelet plug
 3. Coagulation (clotting)
 4. Clot Retraction
 5. Fibrinolysis (Clot Eradication)

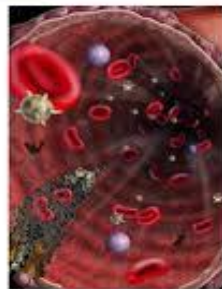
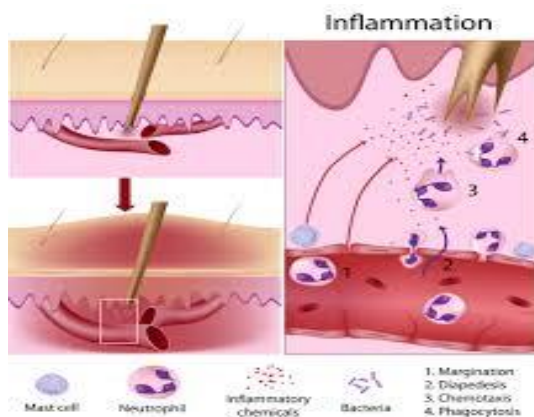


Figure Image of haemostasis

Haemostasis is primary phase of wound healing process. When the skin are damage by any caused there is protective mechanism are appear as haemostasis. It is the defensive mechanism of body which is exposed as time of any accidental, or damage of the tissues. When this is exposed after any damage on the body there is blood cloth and that tissue is red.

Inflammation:



Inflammatory

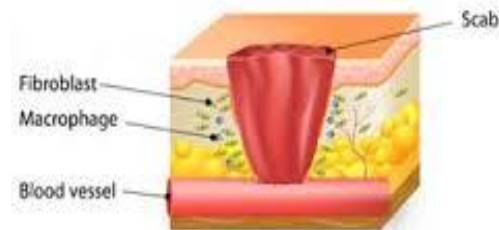


Figure-Images of inflammation

Starting phase of wound healing process include an acute inflammatory phase that is travel by synthesis of collagen and additional extracellular macromolecule which are change the structure to form a scar as a mark left on the skin. In the healthy skin epidermis which is surface layer and dermis which is deeper layer to provide a protective layer or barrier against the outer environment of the body. If the protective barrier is broken, the biochemical events of body are set a motion to recovery the damage of tissue or cells. In the inflammation when the breakdown the epithelial cells release cytokines which enhance integrands on the circulatory lymph.

Proliferative phase:

Proliferative

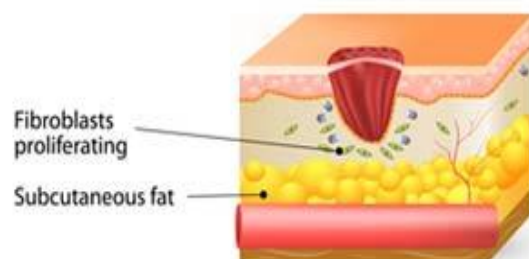


Figure - Image of proliferative stage



In such types phase the tissue are growing for the recovery of normal tissue. When the tissue Injured and it is break down, then for changing of damage or dead tissue to normal cell it will tissue recover.

Maturation:

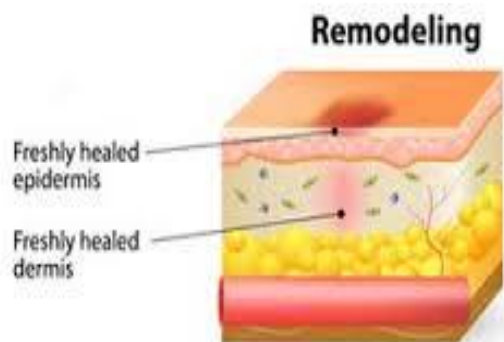


Figure : Maturation stage

This is the last phase of recovery the normal tissue from damage tissue. In this phase the tissue growth in the proliferation phase but there is a mark left. While this phase re-building of the injured tissue and recovery to normal tissue. In this final state of phase maturation of tissue recovery start from the third week to process recommended to long time as 9-12th month. In this phase collagen III are change in the form of collagen I which is tensile strength become make a greater size and recovery the 80% of normal tissue.

CONCLUSION:-

As we know that Wound healing is the fundamental process that response to connective tissue. The Process of wound healing is the recovery of normal cells or tissue from the injured or damage tissue .Wound size and shape are also important for the incision or medication. The site of wound also play a major role in wound healing .Gel show better patient compliance as easy to apply on the wound .

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