



# Wound introduction



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TEHRAN UNIVERSITY  
OF  
MEDICAL SCIENCES



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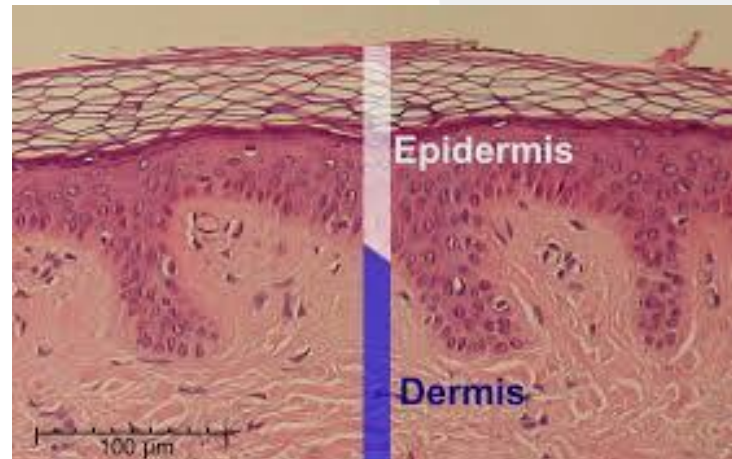
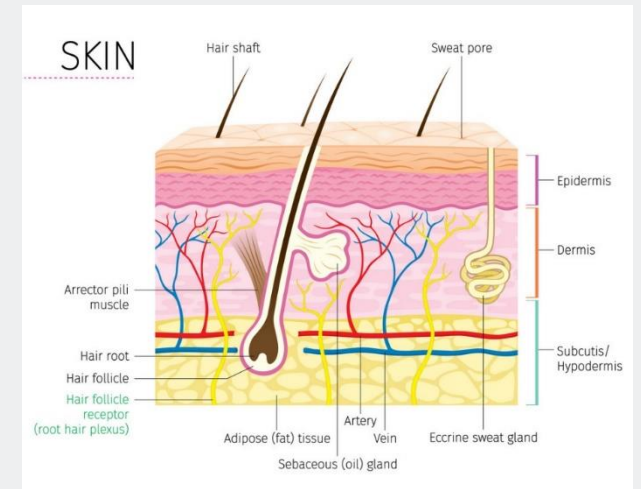


# Wound.....

- **Skin functions**

- largest organ
- barrier protection against external environment( micro organisms....)
- internal organ protection, internal environment protection( hydration, temperature)
- immunologic
- VitD synthesis
- protection from harmful light
- communication

....



Wound....

- **Injury to skin means:**

- entrance of micro organisms, existing of intercellular fluid, metabolite imbalance .....organ failure .....sepsis ..

- more than 10% of body surface injury = life threatened

- 1<sup>st</sup> : **repair** + inhibition of scar





# Wound....

- **Definition**

**Wound** : disruption of normal continuity of living structures ,caused by cut....



Wound...

- **Wound classifications:**

- different classifications goals : description, management, repair
- important keys to evaluate a wound:

- nature of injury: **abrasion, laceration, puncture, penetration**

- time and duration: acute vs chronic

- thickness of injury

- **Open Vs closed** : cut....Vs contusion, hematoma , crush ,,,



Wound .....

- Wound classification.....

- Timing :3 groups

acute <6 hrs

early <24 hrs

late > 24 hrs

- thickness



# Wounds

- Chronic wounds
  - More than 13 m. patients in the world Suffer from chronic wound
  - 15 b \$/ yr =m cost
  - is not easily defined :More than :
  - correction and stimulation of healing





Wound .....

## Wounds classification: closed contusion

hematoma



# Wounds....

- **Wounds : open**

abrasion



incision



laceration



# Wound classification.....

- Puncture

penetrating

perforating



Wounds...

- Wounds  
infected



clean





# Wounds .....

- abrasion



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Wounds....

- Wound assessment :
  - clinical
  - Bx
  - Perfusion measurements: thermography, dys, videoangiography
  - video microscopy
  - laser Doppler
- For emergency : telemetry, photography



Wound...

- **Burn rate in Iran**

- 180,000/year

- 30,000 admission

- 3000 death

- 20% electrical burn

- 6 th cause of death



# Wounds....

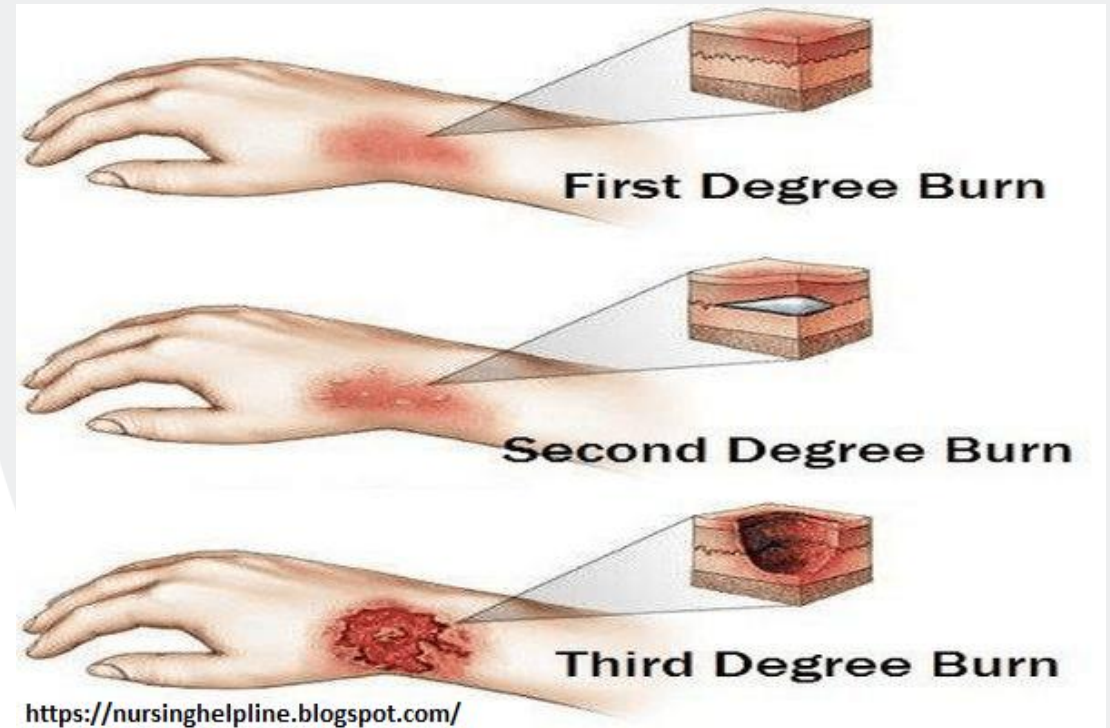
- Burn
  - depth : treatment , morbidity, scar
  - superficial ( heal rapidly)..... deep
  - clinical assessment for depth is 60-75% accurate





## Burn degrees

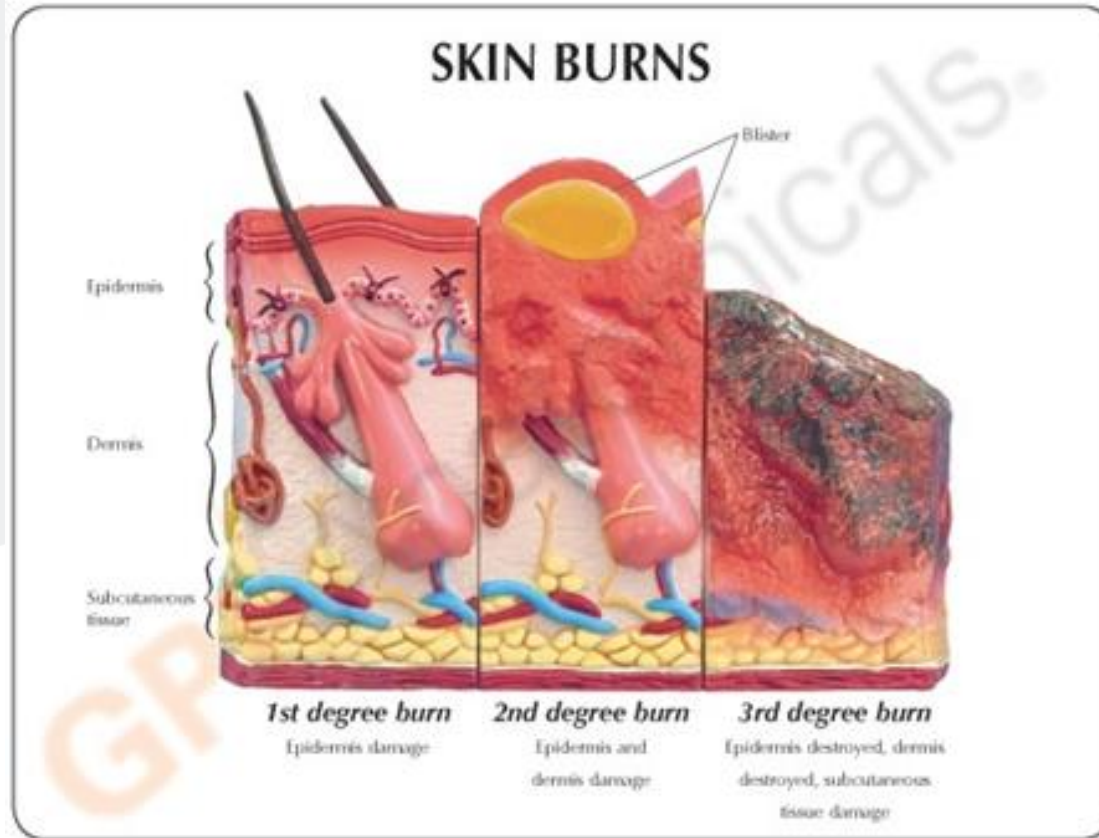
- First – degree : epidermis , erythema , no blister no medical care
- Second degree: dermal and beyond: superficial and deep:
- 3 rd degree



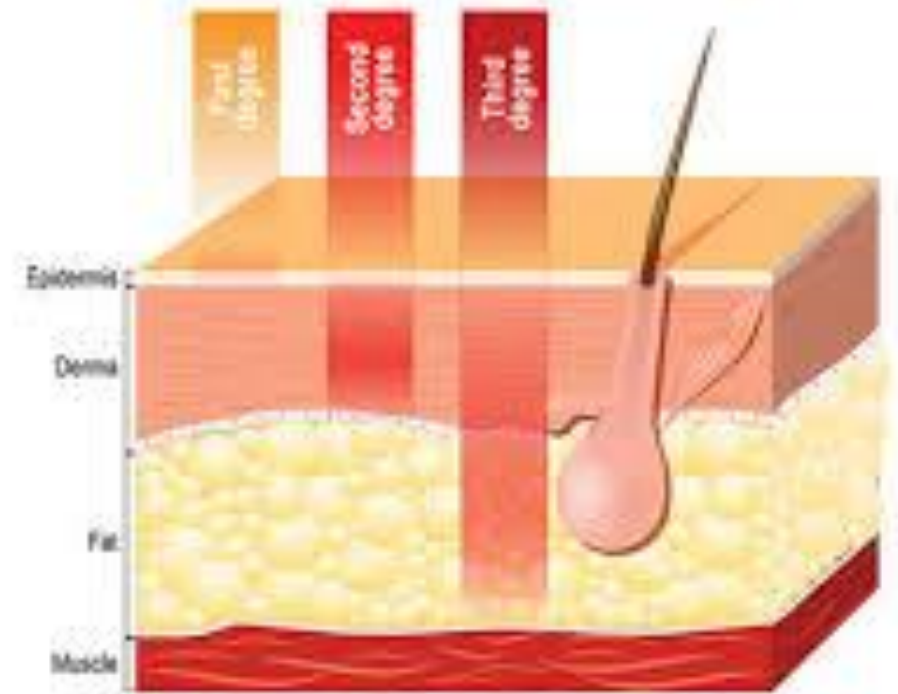
<https://nursinghelpline.blogspot.com/>



# Wound .....



# Degrees of Skin Burns



# Wound .....



## Burn Measurement



### EPIDERMIS



1st Degree Burns

### DERMIS



2nd Degree Burns

### HYPODERMIS



3rd Degree Burns

### MUSCLE

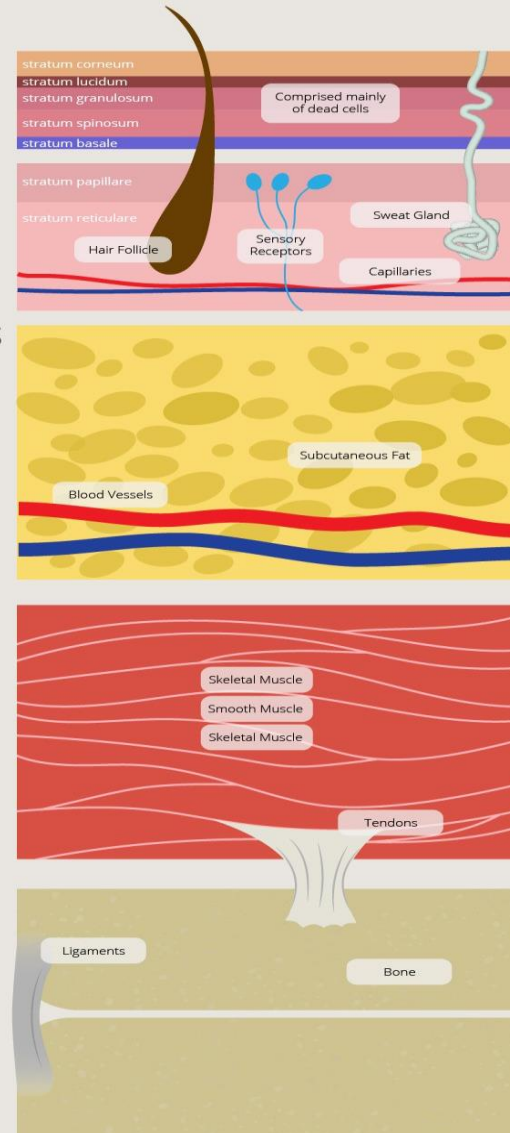


4th Degree Burns

### BONE

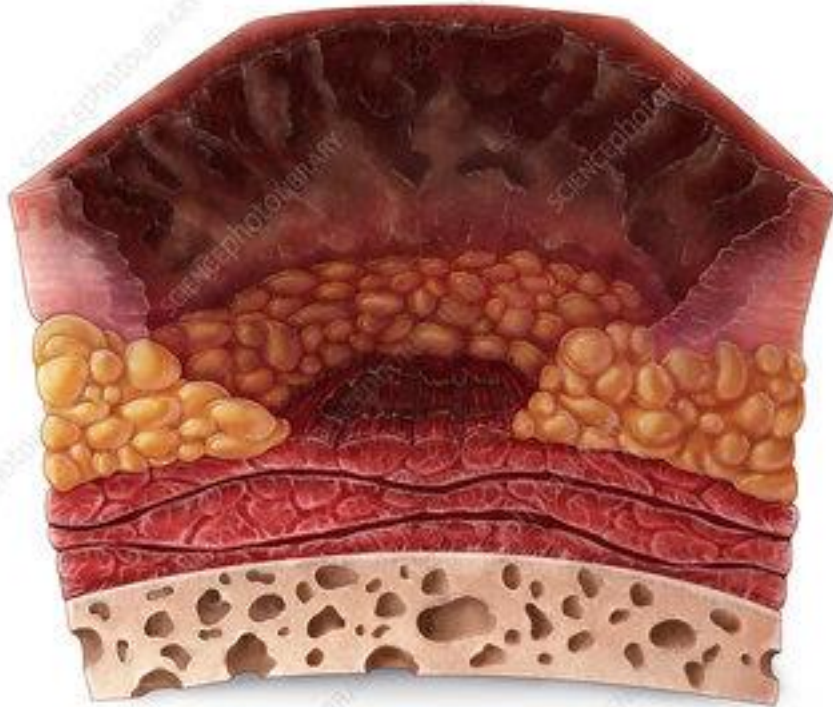


5th & 6th Degree Burns





# Wound ....



Epidermis  
Dermis  
Subcutaneous  
Muscle



Superficial  
(first degree)  
burn



Partial thickness  
(second degree)  
burn



Full thickness  
(third degree)  
burn





# Second degree burn



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A1MX70  
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## 4<sup>th</sup> degree burn



## 2<sup>nd</sup>



## 3<sup>rd</sup>



**Jainuheal** Natural Formula  
Each 100g contains: Honey - 40g  
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• Disinfects open wounds and prevents infection and superficial wounds  
• Stops inflammation after laser therapy  
• Avoid contact with eyes & other mucous membranes  
• Store below 10°C, protect from light & freezing  
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W W W . A R G A N O . I R



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# IN THE NAME OF GOD

# THE WOUND MANAGMENT

*Center for Research and Training in Skin Disease and Leprosy*

*Tehran University of Medical Sciences*

**Khadijah Tawakoni, MD.**



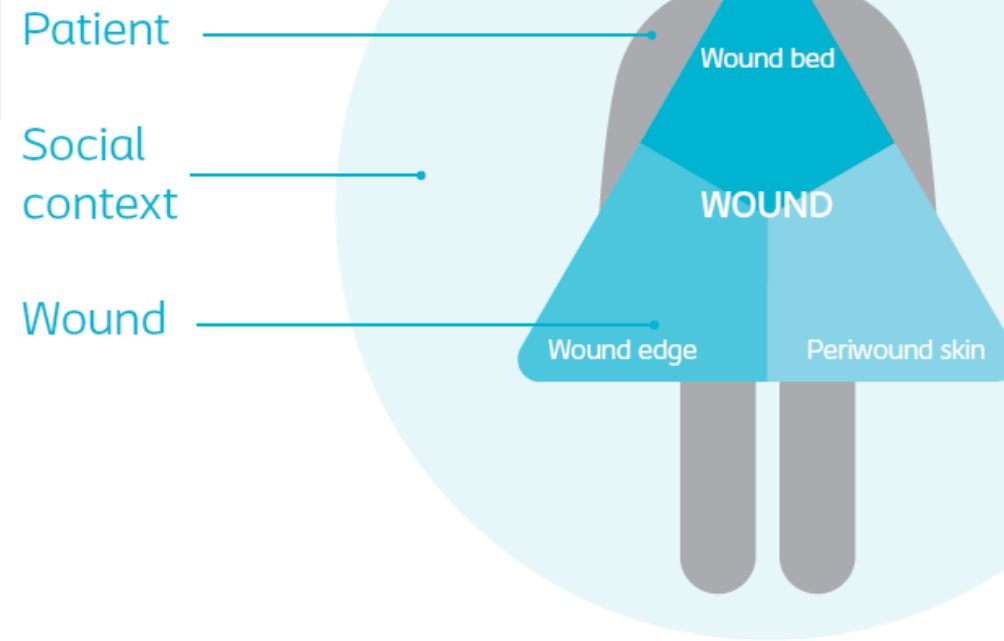
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# Holistic Framework





# Holistic Wound Assessment

- ❑ Optimal wound management starts with a holistic wound assessment. This will help to more efficiently set management goals, which will increase the potential for better treatment outcomes.



# Patient & Social context

## ☐ Information

- ✓ Age
- ✓ Gender
- ✓ Nutrition & Mobility
- ✓ Smoking & Alcohol
- ✓ Work & living arrangement

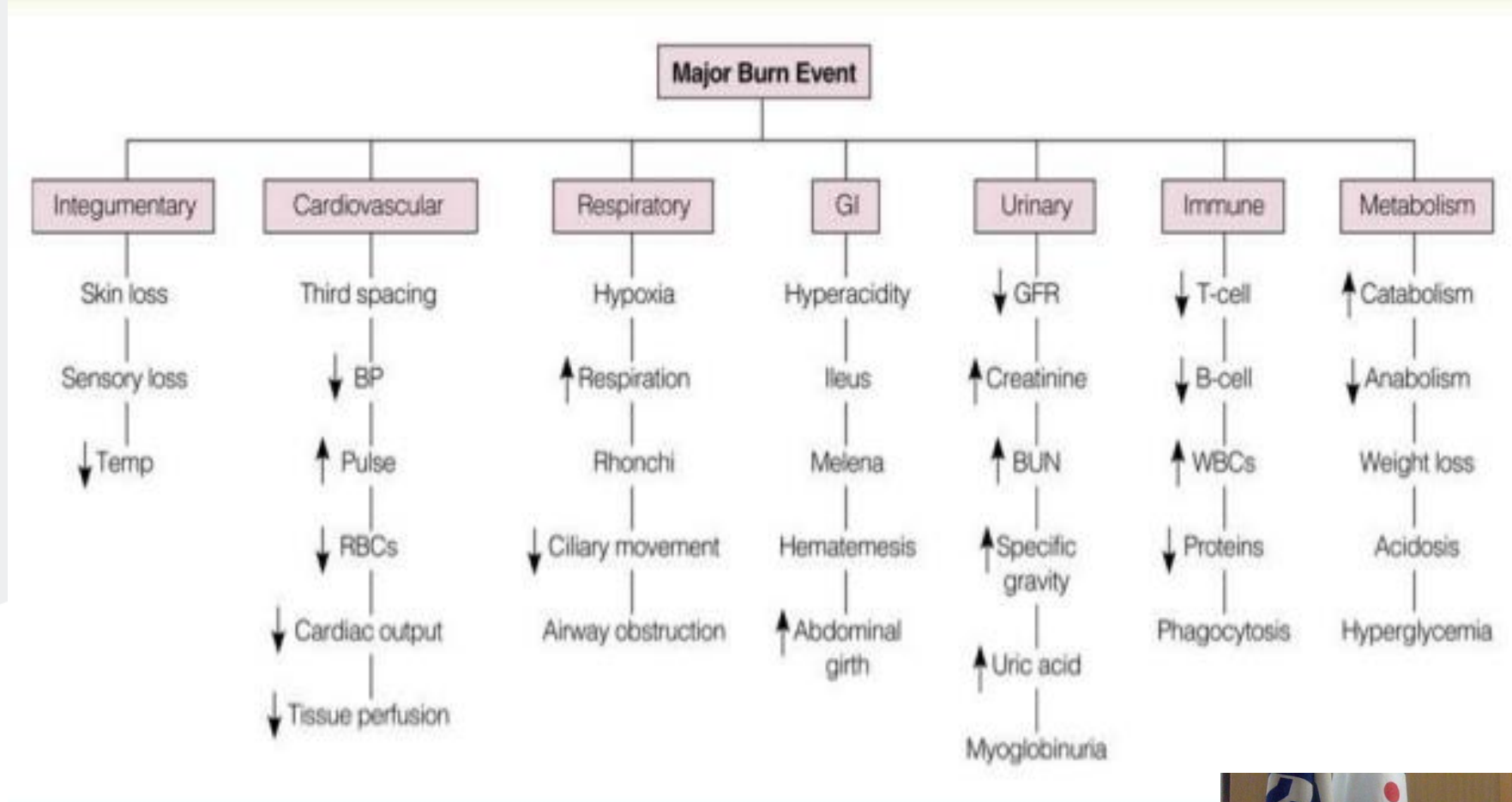
## ☐ Medical history

- ✓ Co-morbidities
- ✓ Medications

## ☐ Wound description

- ✓ Type/diagnosis
- ✓ Location & Duration
- ✓ Size
- ✓ Pain





# Holistic Wound Assessment

Assessment



Management Goals

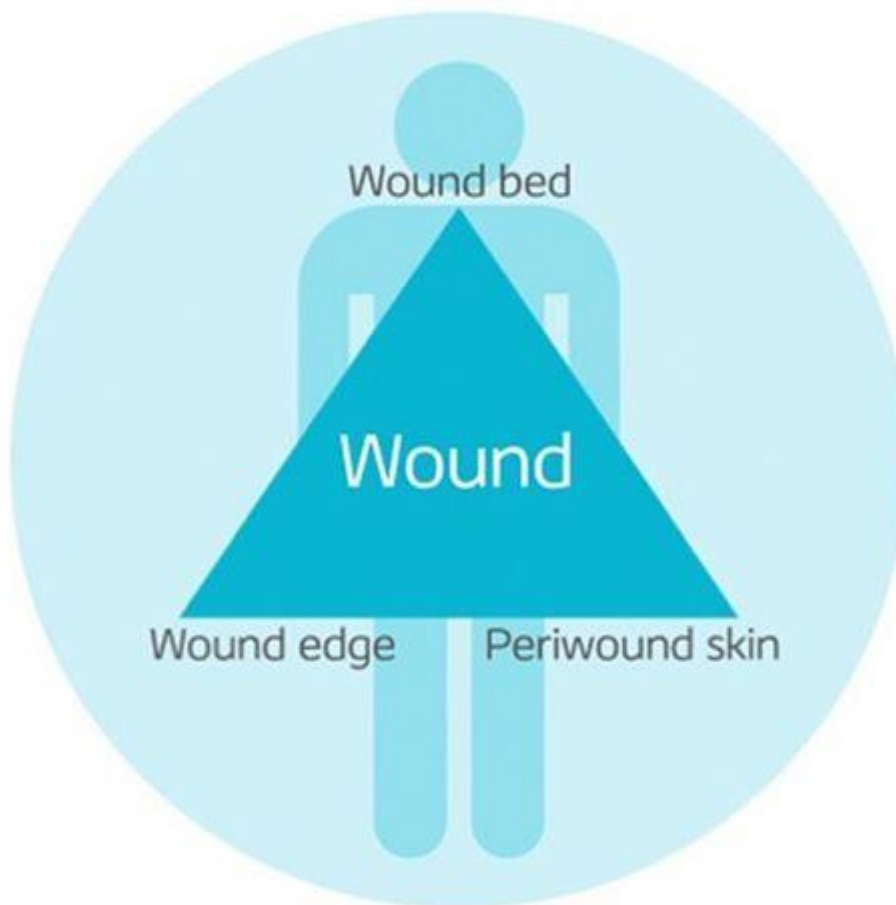


Treatment

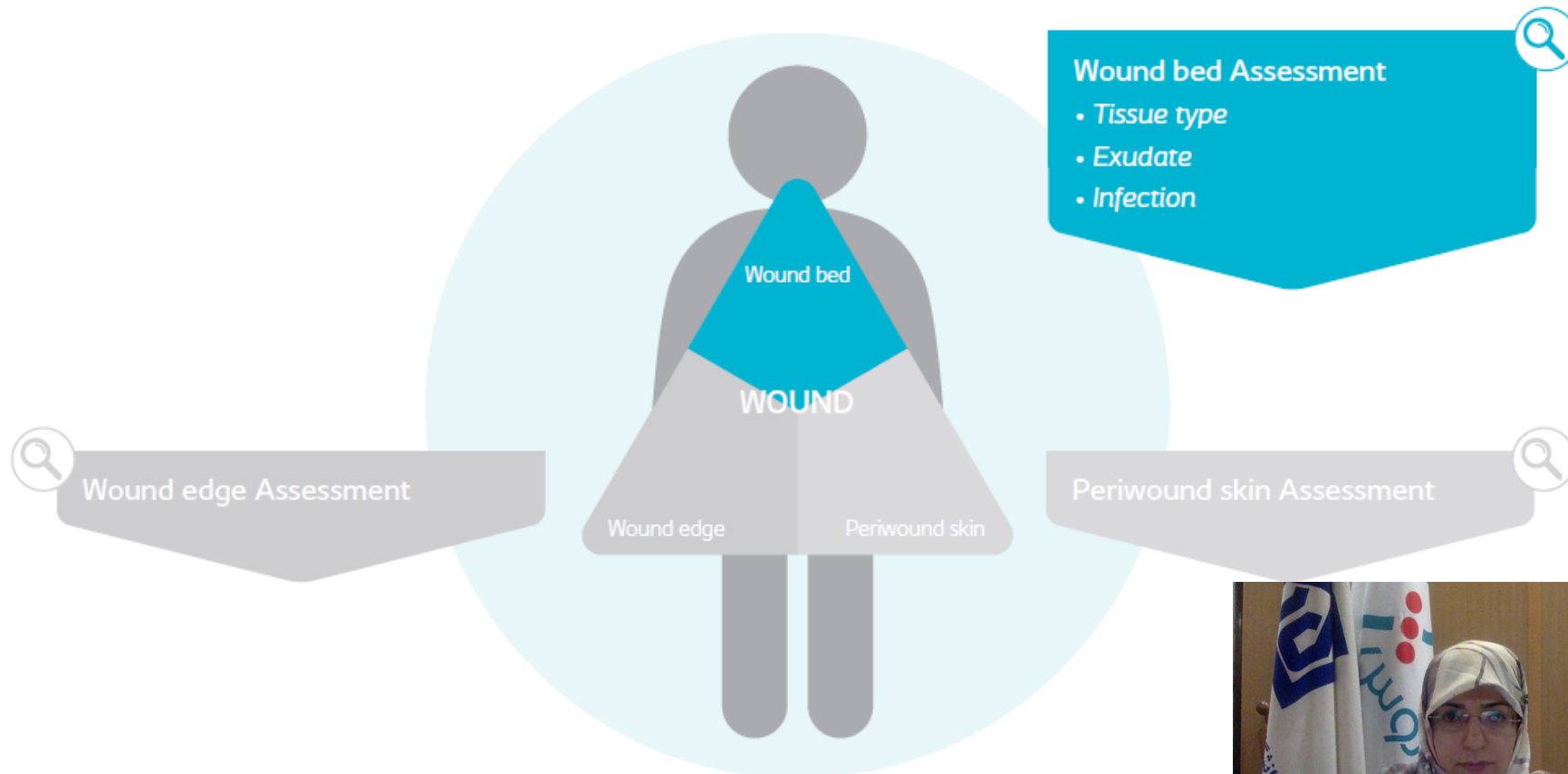




# The Triangle of Wound Assessment



# Wound Bed Assessment



# Tissue type



# Tissue type

## ☐ Necrotic

- ✓ Black, dead tissue, which contains dead cells and debris that are a consequence of the fragmentation of dying cells

## ☐ Sloughy

- ✓ Yellow, fibrinous tissue that consists of fibrin, pus, and proteinaceous material

## ☐ Granulating

- ✓ Red new connective tissue and microscopic blood vessels that form on the surfaces of a wound during the healing process

## ☐ Epithelializing

- ✓ Pink/white tissue in the final stage of healing where epithelial cells resurface the wound

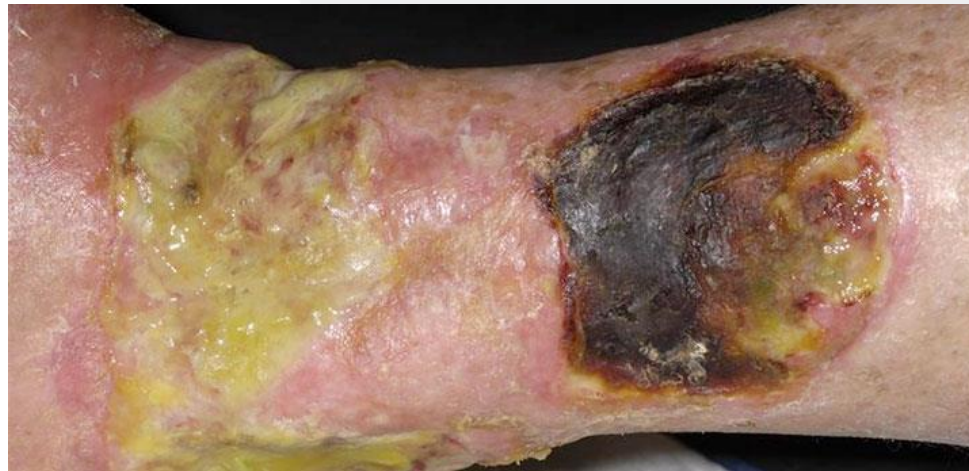




# Exudate

❑ Fluid from the wound

- ✓ In normal healing increases during inflammatory stage to cleanse the wound and provide a moist environment, which maximizes healing
- ✓ In chronic wounds, this fluid is biochemically different, which break down the protein framework in the wound causing further tissue break down

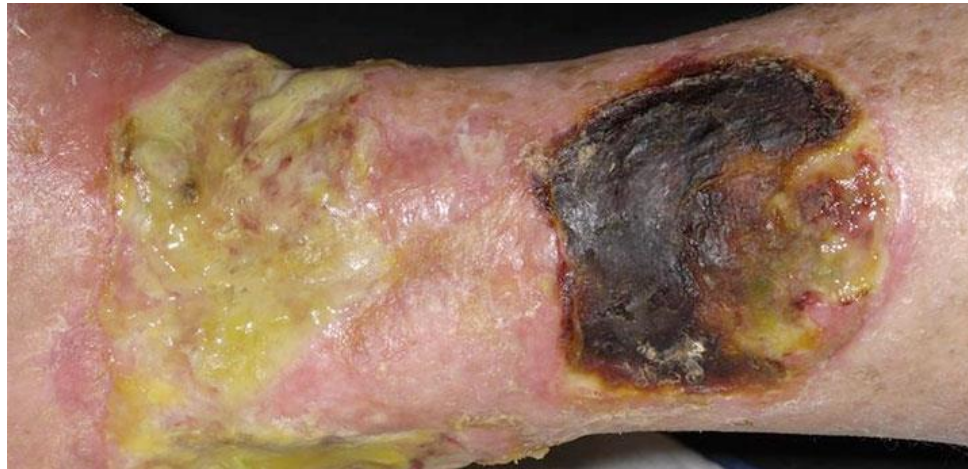


# Exudate

## Exudate

Level ☐ Dry ☐ Low ☐ Medium ☐ High

Type ☐ Thin/watery ☐ Cloudy ☐ Thick  
☐ Purulent ☐ Clear ☐ Pink/red



# Infection

- The presence of bacteria or other microorganisms in sufficient quantity to damage tissue or impair healing. Clinical signs of infection may not be present in patients who are immunocompromised, or those that have poor perfusion or a chronic wound



# Infection

## ☐ Local

- ✓ Increased pain
- ✓ Erythema
- ✓ Local warmth
- ✓ Oedema
- ✓ Increased exudate
- ✓ Delayed healing
- ✓ Friable granulation tissue
- ✓ Malodor
- ✓ Pocketing

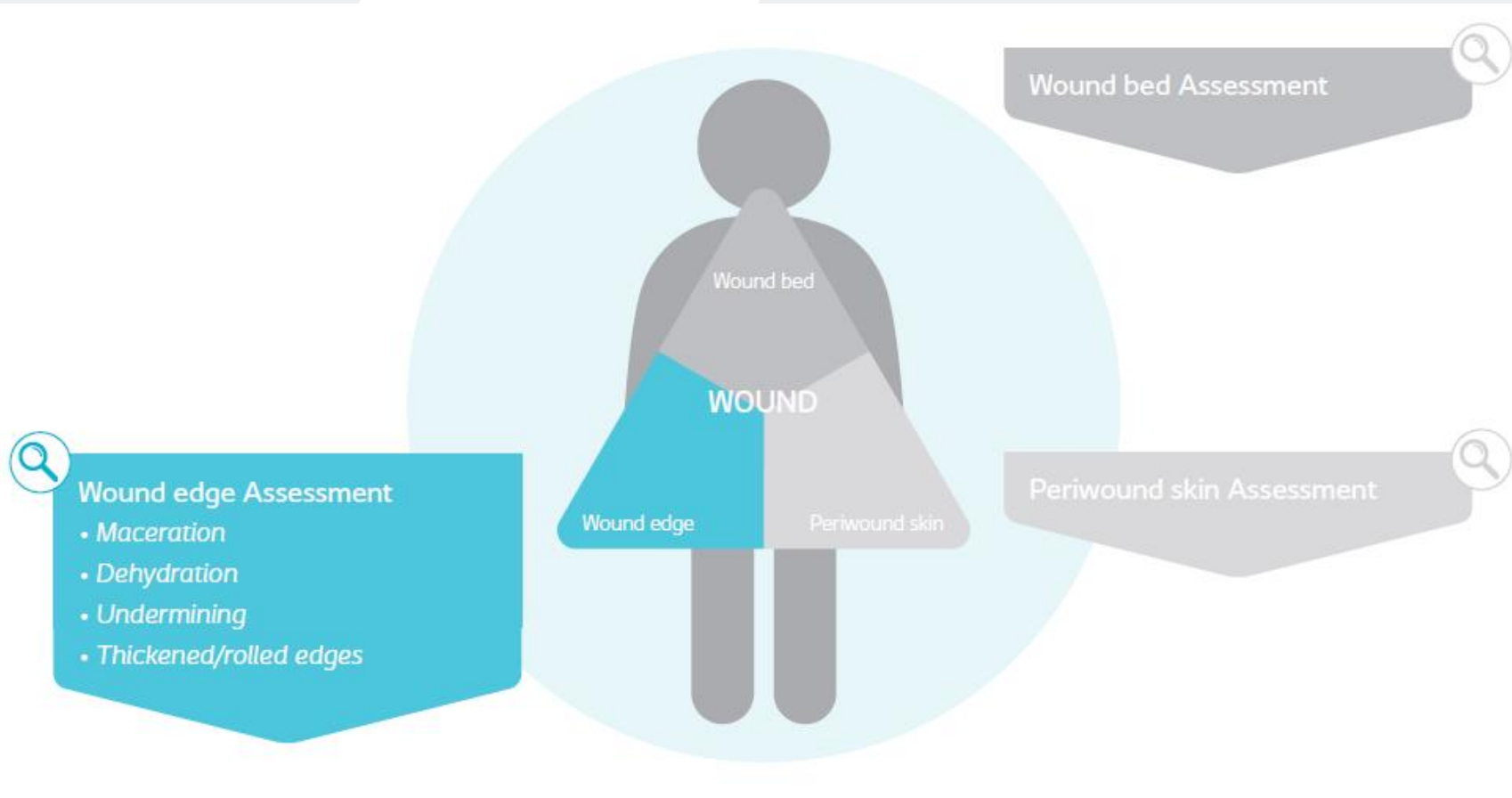
## ☐ Spreading/systemic

- ✓ Increased erythema
- ✓ Pyrexia
- ✓ Wound breakdown
- ✓ Abscess/pus
- ✓ Cellulitis
- ✓ General malaise
- ✓ Raised WBC count
- ✓ Lymphangitis





# Wound edge assessment



# Maceration

Softening and breaking down of wound edge resulting from prolonged exposure to moisture and wound exudate. Frequently appears white



# Dehydration

Low moisture impairing cellular development and migration needed for new tissue growth



# Undermining

The destruction of tissue or ulceration extending under the wound edge so that the ulcer is larger at its base than at the skin surface



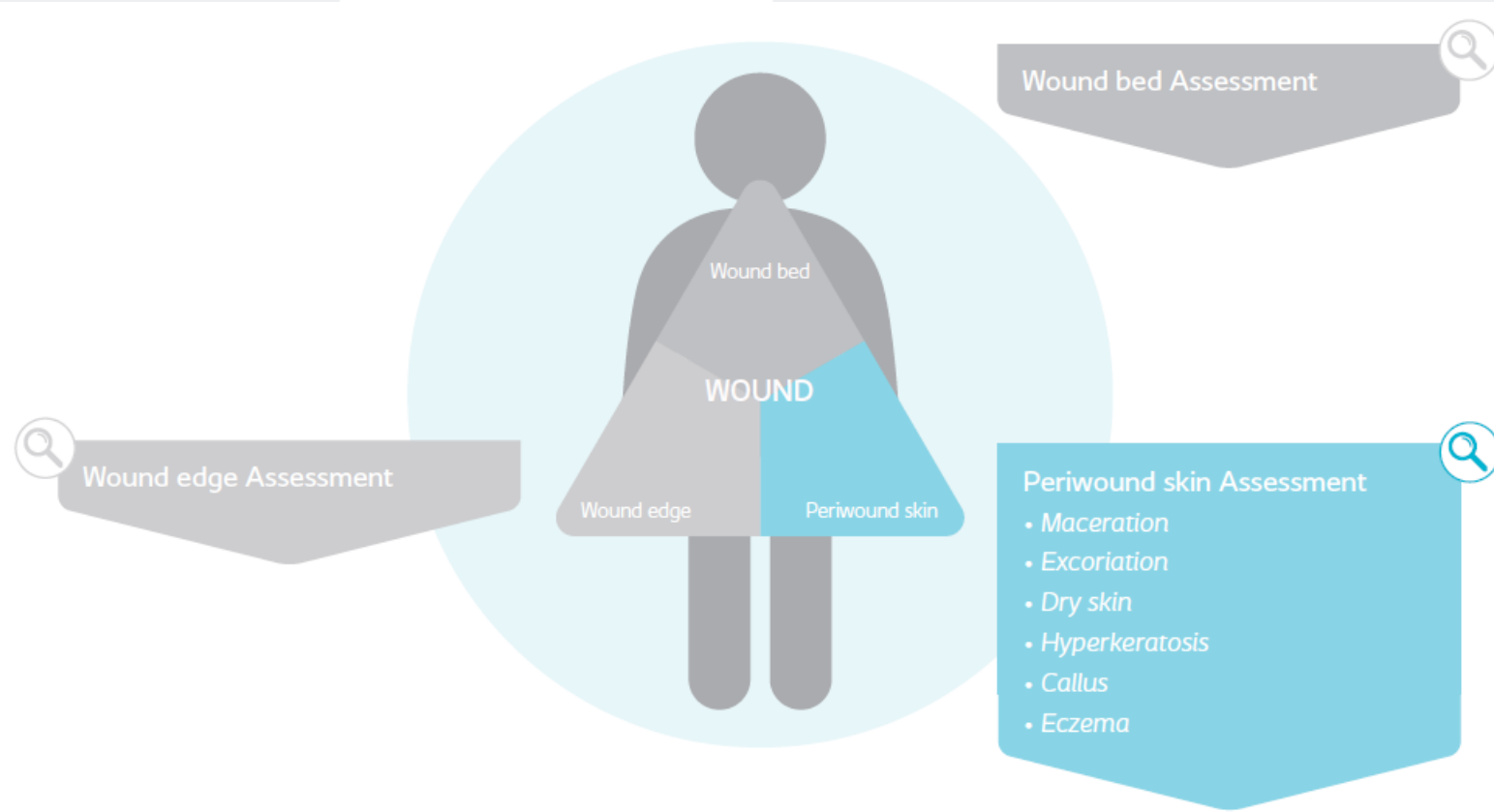


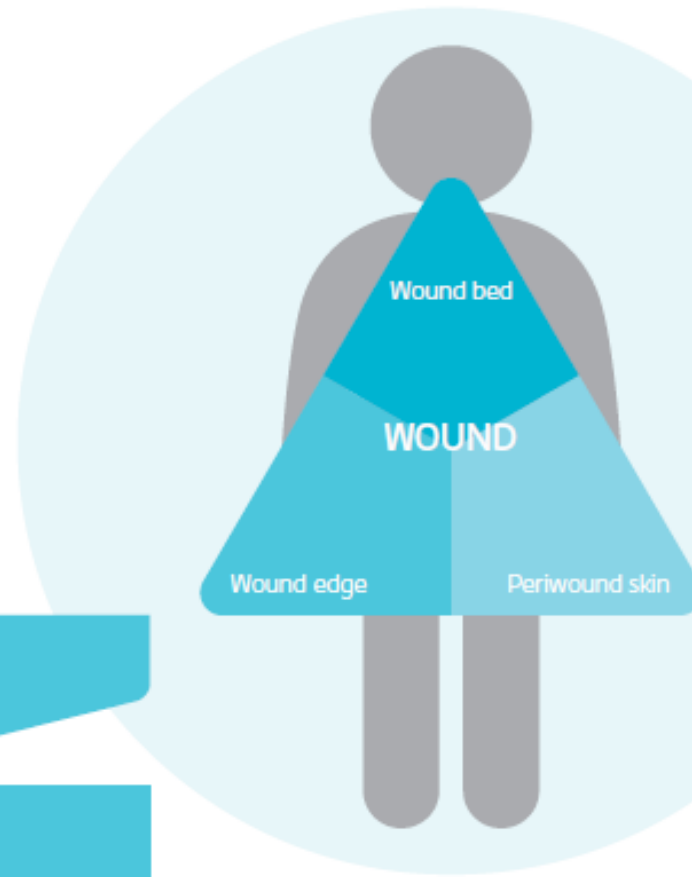
# Rolled edges

Epithelial tissue migrating down sides of the wound instead of across. Can present in wounds with inflammatory origin, including in cancer, and can result in poor healing outcomes if not addressed appropriately



# Peri wound skin assessment





## Wound bed Assessment

### Management goals

- Remove non-viable tissue
- Manage exudate
- Manage bacterial burden
- Rehydrate wound bed
- Protect granulation/epithelial tissue

## Wound edge Assessment

### Management goals

- Manage exudate
- Rehydrate wound edge
- Remove non-viable tissue
- Protect granulation/epithelial tissue

## Periwound skin Assessment

### Management goals

- Manage exudate
- Protect skin
- Rehydrate skin
- Remove non-viable tissue





## Wound bed

Assessment	Management goals	Treatment examples
<b>Tissue type</b> <ul style="list-style-type: none"> <li>• Necrotic</li> <li>• Sloughy</li> </ul>	<i>Remove non-viable tissue</i>	Debridement
<ul style="list-style-type: none"> <li>• Granulating</li> <li>• Epithelialising</li> </ul>	<i>Protect granulation/epithelial tissue</i>	Hydrocolloid
<b>Exudate</b> <ul style="list-style-type: none"> <li>• Dry</li> </ul>	<i>Rehydrate wound bed</i>	Hydrogel
<ul style="list-style-type: none"> <li>• Low</li> <li>• Medium</li> <li>• High</li> </ul>	<i>Manage exudate</i>	Appropriate dressing for exudate level (e.g. hydrocolloid for low, foam for high)
<b>Infection</b> <ul style="list-style-type: none"> <li>• Sign of infection</li> </ul>	<i>Manage bacterial burden</i>	Antimicrobial





# Barrier cream



# Film dressing





# Absorbent dressings





# Antimicrobial dressings



# Debridement Gels



# Hydrogel sheet



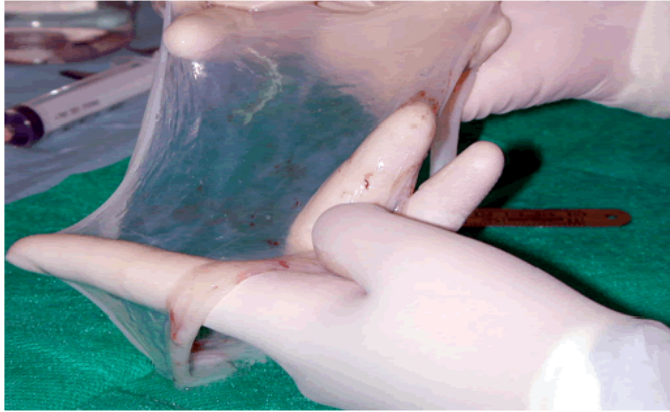
# Alginates





# Biologic dressings

## amniotic membrane



# Biosynthetic dressings

INTEGRA  
BIOBRANE





## Wound edge

Assessment	Management goals	Treatment examples
<ul style="list-style-type: none"><li>• Maceration</li></ul>	<i>Manage exudate</i>	Appropriate dressing for exudate level (e.g. hydrocolloid for low, foam for high)
<ul style="list-style-type: none"><li>• Dehydration</li></ul>	<i>Rehydrate wound edge</i>	Barrier cream
<ul style="list-style-type: none"><li>• Undermining</li><li>• Rolled edges</li></ul>	<i>Remove non-viable tissue + Protect granulation/epithelial tissue</i>	Debridement + Hydrocolloid





## Periwound skin

Assessment	Management goals	Treatment examples
<ul style="list-style-type: none"><li>• Maceration</li></ul>	<i>Manage exudate</i>	Appropriate dressing for exudate level (e.g. hydrocolloid for low, foam for high)
<ul style="list-style-type: none"><li>• Dry skin</li></ul>	<i>Rehydrate skin</i>	Barrier cream
<ul style="list-style-type: none"><li>• Excoriation</li><li>• Eczema</li></ul>	<i>Protect skin</i>	Barrier film
<ul style="list-style-type: none"><li>• Hyperkeratosis</li><li>• Callus</li></ul>	<i>Remove non-viable tissue</i>	Debridement



# Wound bed preparation: TIME in practice





# The TIME framework

- ❑ To assist with implementing the concept of wound bed preparation, the TIME acronym was developed in 2002 by a group of wound care experts, as a practical guide for use when managing patients with wounds (Schultz et al, 2003).
- ❑ The TIME summarizes the four main components of wound bed preparation:
  - ✓ Tissue management
  - ✓ Control of infection and inflammation
  - ✓ Moisture imbalance
  - ✓ Advancement of the epithelial edge of the wound.



# TIME is:

- **T** — for tissue: non-viable or deficient
- **I** — for infection/inflammation
- **M** — for moisture imbalance
- **E** — for edge, which is not advancing or undermining.





Thanks for your  
attention



# Potential use and side effects of plants in wound healing



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**assistant professor of dermatology**  
**Iran university of medical science**



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# INTRODUCTION

- Complementary and alternative medicine (CAM) represents a diverse set of healthcare systems, practices, and treatments that are grouped together because they are not considered part of conventional medicine.
- More specifically, “complementary medicine” can be defined as non-mainstream modalities or approaches used **in conjunction with** conventional medicine, while “alternative medicine” typically refers to the use of non-mainstream approaches **in place of** a conventional treatment.
- The overwhelming majority of CAM users in high-income countries, including those with dermatologic disorders, use CAM **to complement conventional medicine** rather than as a complete alternative.





- Interestingly, individuals with skin conditions are more likely to use CAM than the general population, making this topic particularly relevant to dermatologists.
- Many plants and their extracts have great potential for the management and treatment of wounds.
- Conventional dermatology uses many products of herbal origin, including podophyllin, psoralens, and pyrethrins.
- There is need for scientific standardization, validation and safety evaluation of plants of traditional medicine before these can be recommended for wound healing.



SELECTED TYPES OF COMPLEMENTARY AND ALTERNATIVE MEDICINE (CAM) WITH PROMISING EVIDENCE FOR TREATING DERMATOLOGIC DISEASES		
Skin disease	Type of CAM	Comments
Acne	• Tea tree oil (topical)	• Safe and effective; some risk for ACD or ICD
	• Dietary modification (avoiding dairy and high-glycemic foods)	• Probably decreases inflammation; adherence may be challenging
Atopic dermatitis	• Sunflower seed oil	• Enhances barrier function and may reduce pruritus
	• Coconut oil	• Antibacterial and moisturizing effects
	• Acupuncture/acupressure	• May modestly reduce pruritus; can be expensive to see practitioner
Psoriasis	• Indigo naturalis	• Anti-inflammatory effects on skin and nails; stains fabric
	• Curcumin (topical and oral)	• May have anti-inflammatory effects; color and odor can be offensive
Seborrheic dermatitis	• Tea tree oil (topical)	• Appears modestly effective; ACD or ICD may occur
Urticaria	• Vitamin D supplementation (oral)	• May help certain subset of population; safe
	• Acupuncture	• Multiple possible mechanisms; can be expensive to see practitioner
Verrucae	• Garlic (topical)	• Effective irritant and antiviral; unpleasant smell and ICD may deter its use
	• Zinc supplementation (oral)	• Results of clinical studies appear to be better than clinical experience; gastrointestinal upset fairly common
	• Propolis (oral)	• May be immunomodulatory; bee allergy is contraindication



- Herbal medicines have been used to accelerate wound healing since ancient times.
- Recently, scientists have been able to employ scientific methods to prove efficacy of many of these herbs and to get a better understanding of mechanisms of their actions.
- Preparations from traditional medicinal plants in wound management involve disinfection, debridement and the provision of suitable environment for natural healing process.



# MECHANISM OF WOUND HEALING

- The skin is among the largest and one of the most important organs in the human body.
- It represents the **first line of defence** of the body; provides protection from mechanical impacts of the environment, limits the influence of variations in the temperature, prevents entrance of chemicals and microorganisms and restricts radiation effect.
- Skin damage affects **all skin functions**; therefore, wounds can compromise patient's well-being, self-image, working capacity and independence.



- A wound can be defined as a **disruption** in the continuity of the epithelial lining of the skin or mucosa.
- Injury, due to surgery or accident, results in **destruction of tissue**, disruption of blood vessels and extravasations of blood constituents and **hypoxia**.
- Wound healing is a complex process that has three phases:
  - **inflammatory phase**
  - **proliferative phase**
  - **maturation phase**
- Wound healing is the result of interactions among cytokines, growth factors, blood and cellular elements, and the extracellular matrix.
- The cytokines promote healing by stimulating the production of components of the basement membrane, preventing dehydration, increasing inflammation and the formation of granulation tissue.





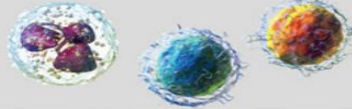
# Schematic depiction of distinct phases during wound healing

## Hemostasis



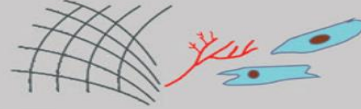
- \* Coagulation

## Inflammation



- \* Immune infiltration
- \* Debris clearance
- \* Pathogen killing

## Proliferation

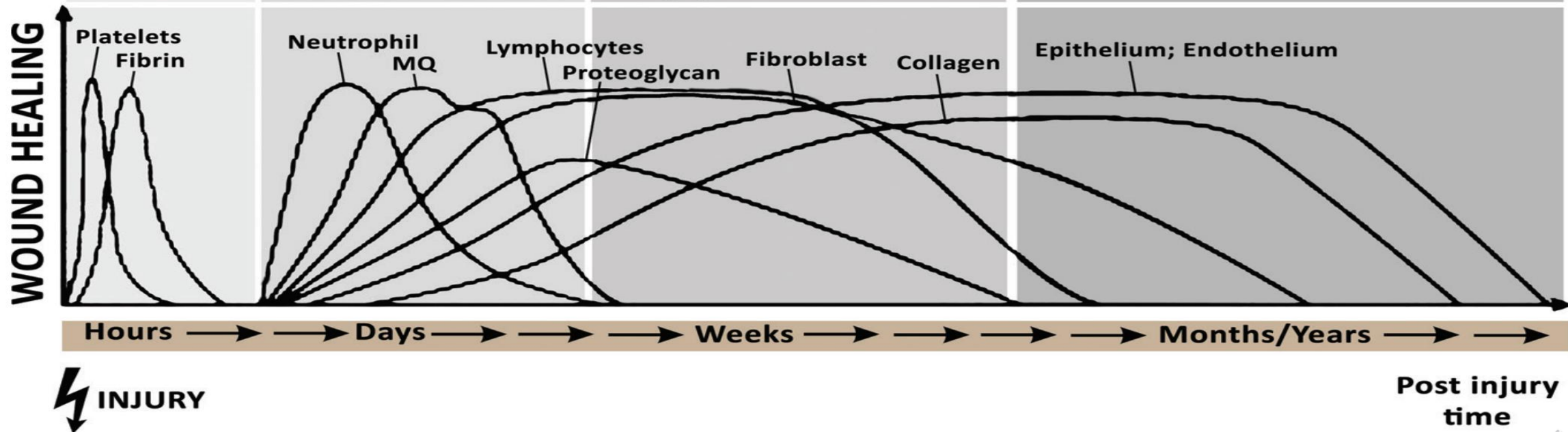


- \* Fibroblast proliferation
- \* Scar formation
- \* Collagen synthesis
- \* Angiogenesis

## Remodelling



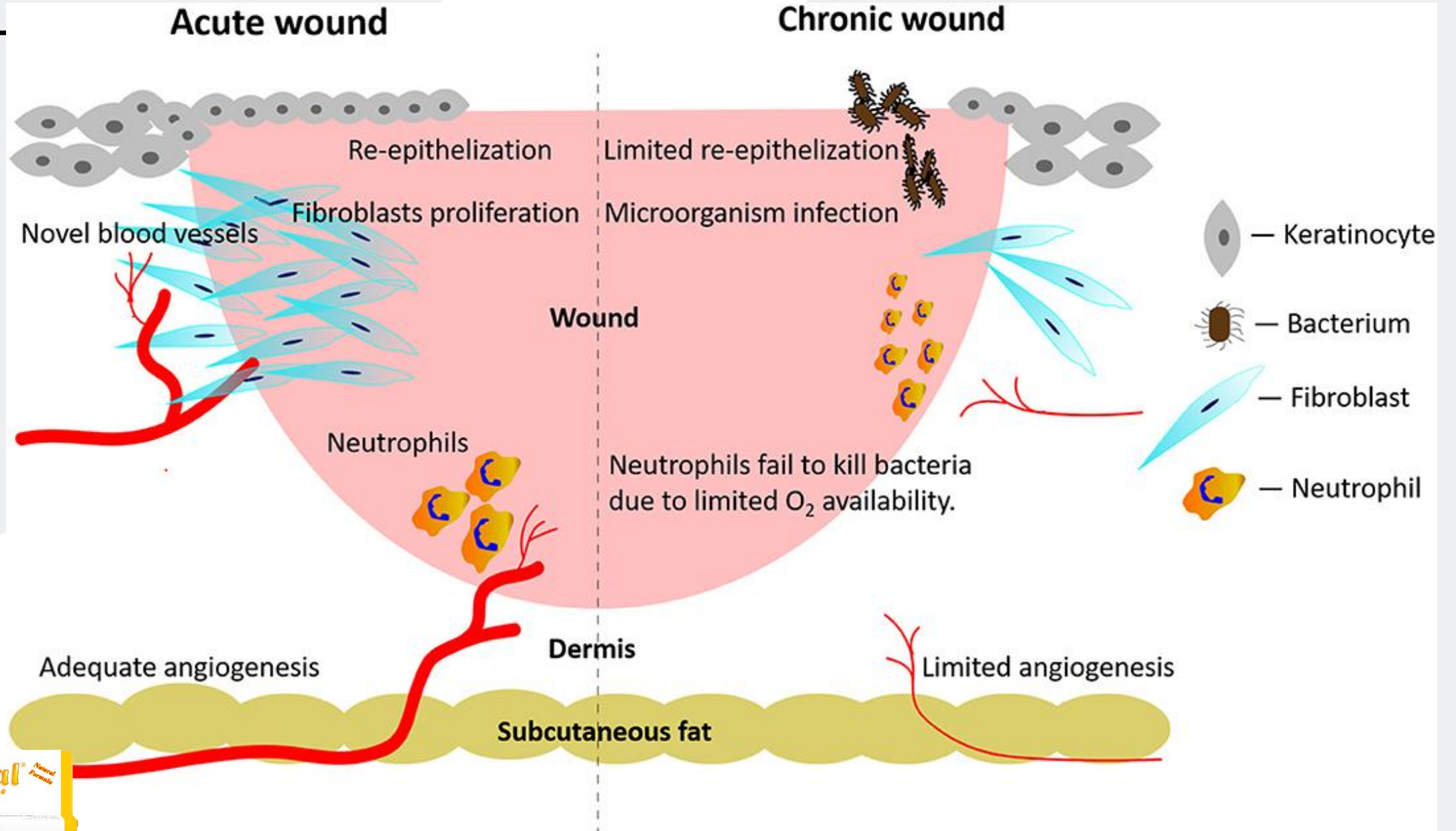
- \* Epithelization
- \* ECM remodelling
- \* Scar maturation/contraction
- \* Apoptosis





- Wounds can be broadly classified into acute and chronic wounds depending on their aetiology.
- **Acute wounds** occur most commonly due to accidents such as **trauma or burns** and should normally heal in a **short duration** provided the right treatment is given.
- **Chronic wounds** take a longer time to heal or sometimes even recur due to the underlying pathology.
- Hence, the **underlying problem** should first be identified and treated accordingly.
- When treating chronic wounds, it is important to note that **biofilms** (harbour various microorganisms) play an important role in the prevention of wound healing.





## ❑ Moisture Balance

- Wounds require cellular growth to fill the skin defect.
- Cells require a moist aqueous environment and do not do well with dessication or the presence of excess wound fluid.
- Optimal moisture balance dressings include the absorbancy of foams and calcium alginates and the donation of moisture with a hydrogel.
- Many of the alternative medicines do not provide this moisture balance property except for those in a hydrogel type of preparation





➤ Always remember:

- The **cause of the wound** must be treated.
- Whether complementary alternative or conventional methods are used, if the cause is not addressed, the wound will not close.
- A **painful wound** is a signal to the patient and to the healthcare practitioner that something is wrong.

➤ Treating patient centered concerns as well as optimizing the initial components of local wound care, **debridement, moisture balance, infection, and inflammatory** control can go a long way to improving the lives of persons with chronic wounds.



# PLANTS WITH POTENTIAL USE IN WOUND HEALING

- Many plant-derived medicines (commonly called as **phytomedicines**) are affordable and cause minimal unwanted side effects.
- Nevertheless, increasing awareness of their potential activities, especially considering the possible combinations of various plant-derived molecules, which could induce **toxic effects** as well, points out the need for a systematic approach towards their evaluation before efficient introduction to wound care (or other fields of medicine).
- In recent years, extensive research has been carried out in the area of wound healing and management through plant-derived medicinal products.

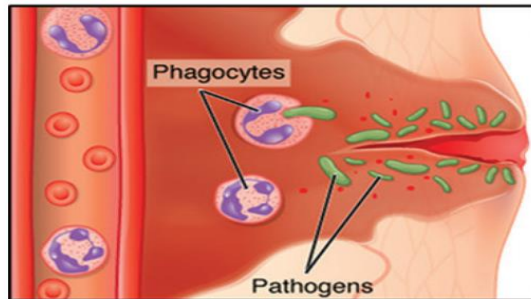




- Bioactive compounds in plants can be classified considering different criteria.
- The botanical approach on the other side considers the plant, from which they originate.
- The biochemical approach seems to be the most commonly used. The later is based on their classification according to the metabolic (biochemical) pathway, by which they are produced.
- Using this approach, groups are more clearly understandable to most readers with at least basic knowledge in chemistry.
- It is important to again note that it is not recommended the topical wound care use of any potentially toxic herbs or common topical irritants/allergens, including oil of clove, comfrey, Echinacea, garlic, goldenseal, horsebaum, or marshmallow.

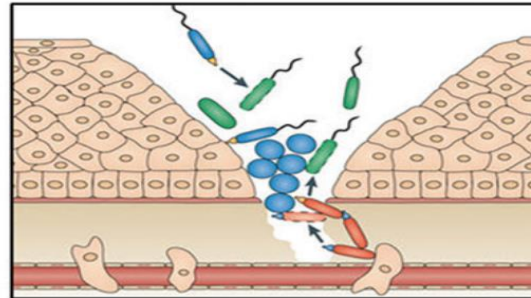


## ANTI-INFLAMMATORY



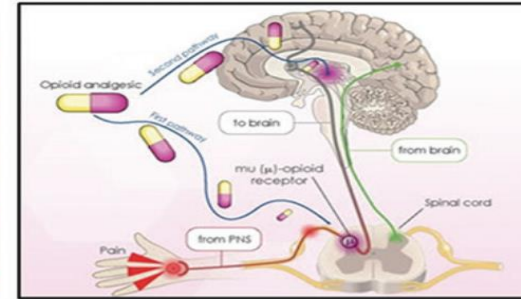
- ★ *Achillea* [28]
- ★ *Aloe vera* [29]
- Avena* [30]
- Azadirachta indica* [31]
- ★ *Calendula officinalis* [32]
- ★ *Cedrus deodara* [33]
- ★ *Chamomilla recutita* [34]
- ★ *Commiphora myrrha* [35]
- ★ *Curcuma longa* [36]
- Echinacea* [37]
- Euphorbia hirta* [38]
- Hypericum perforatum* [39]
- Rosmarinus officinalis* [40]

## ANTIMICROBIAL



- Achillea* [28]
- Angelica sinensis* [41]
- Azadirachta indica* [31]
- Calendula officinalis* [32]
- Cedrus deodara* [33]
- Chamomilla recutita* [34]
- Commiphora myrrha* [35]
- Curcuma longa* [36]
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- Hypericum perforatum* [43]

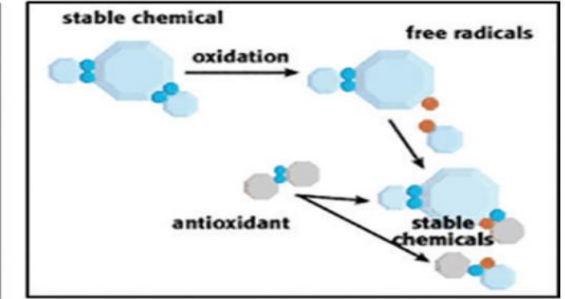
## ANALGESIC



- Angelica sinensis* [41]
- Commiphora myrrha* [44]
- Curcuma longa* [36]
- Euphorbia hirta* [38]
- Hypericum perforatum* [43]



## ANTIOXIDANT



- Chamomilla recutita* [34]
- Ginkgo biloba* [45]



## ❑ Essential oils

- The term essential has not an analogous meaning as in the case of essential amino acids or essential fatty acids.
- In the later cases, essential corresponds to a **lack of mechanism** for their respective synthesis in a specific organism, which also means that these have to be acquired by other means (e.g. diet).
- In general, essential oils are extracted by **distillation** (e.g. by steam).
- Due to their (often) **pleasant fragrance**, they are commonly used as components in perfumes, cosmetics, soaps and other products, for flavouring food and drink, and for other similar applications.
- There are several essential oils derived from plants with high potential to be used in wound treatment.



## Lavender oil

- Lavender (Lavandula) oil, derived from lavender flowers, is one of the most commonly used essential oils in various therapies.
- There are also reports describing its **anti-depressant activity**, as well as its effect on smooth muscles (acting as a **muscle relaxant**).
- Due to its **antibacterial and antifungal properties**, it has been used to treat **bites**.
- One study, conducted by Kane et al., reports about the significantly **reduced pain** intensity after aromatherapy using lavender oil during dressing changes in treatment of vascular wounds when compared with control therapies.





## Chamomile oil (Family: Asteraceae)

- Chamomile has been used for centuries as an antimicrobial, antioxidant, anti-inflammatory agent.
- It is traditionally used for dermatitis and may be applied topically or ingested as a tea.
- Chamomile contains terpenoids and flavonoids that inhibit cyclooxygenase and lipoxygenase as well as regulate T-helper-cell (Th2) activation and histamine release.
- Chamomile aids wound management also through increased granulation tissue weight, hydroxyproline content, rate of wound contraction and wound-breaking strength.
- Chamomile has the potential to induce allergic contact dermatitis, as well as contact urticaria.





## Tea Tree Oil

- Tea tree oil is an essential oil from the leaves of the native Australian tree, Melaleuca alternifolia.
- The indigenous people of Australia use tea tree oil from crushed leaves as a traditional remedy for coughs and colds as well as to treat wounds and skin infections.
- Tea tree oil is commonly used as a topical antimicrobial agent and has shown efficacy in treating acne and cutaneous fungal and bacterial infections.
- There are multiple reports of the antiseptic properties of tea tree oil, thought in part to be due to disruption of bacterial membranes.
- Tea tree oil can be very irritating and is a cause of allergic contact dermatitis; it may also produce gynecomastia



## ❑ Aloe vera (Family: Liliaceae).

- Aloe vera is applied topically to treat a number of afflictions including thermal burns, ulcers or chronic wounds, and mild cutaneous infections.
- Its gel has the ability to heal different kinds of wounds including ulcers and burns by forming a protective coating on the affected areas and speeding up the healing process.
- There have been anecdotal published reports suggesting aloe vera efficacy for acute frostbite, lichen planus, enhancement of postdermabrasion wound healing, psoriasis, and venous leg ulcers.
- Although generally well tolerated, aloe vera gel may cause an allergic contact dermatitis.



- The leaf gel has a hydrogel effect useful for autolytic debridement with a composition of up to 99% water with more than 75 other constituents, including vitamins A, C, and E and potentially some of the B group, enzymes, polysaccharides, amino acids, sugars, and minerals.
- 5 proposed primary mechanisms to explain the therapeutic effects of Aloe:
  - 1) Salicylate compounds block prostaglandin release.
  - 2) The molecular structure contains acetylated mannose– polysaccharide immunomodulating and anti-inflammatory agents.
  - 3) Magnesium lactate (mineral) inhibits histadine decarboxylase enzyme that controls conversion of histamine in mast cells.
  - 4) Carboxy-peptidase enzyme specifically inactivates bradykinin proinflammatory agent.
  - 5) Acemannan (polysaccharide) activates macrophages and tissue growth factor and inhibits thromboxane A2, thromboxane B2, and prostaglandin.



## ❑ Calendula officinalis (Marigold)

- In vitro pharmacological studies confirmed its **anti-viral, anti-genotoxic and anti-inflammatory properties.**
- Pot marigold was shown to possess also an antimicrobial activity against *Bacillus subtilis*, *Escherichia coli*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Candida albicans*, *Sarcina lutea*, *Klebsiella pneumoniae* and *Candida monosa*.
- Different preparations of pot marigold are known (e.g. suspensions or tinctures) for **topical use to reduce inflammation, as well as to control bleeding.**
- It was also shown to **improve the healing** of poorly healing wounds.



- Topically, marigold is most commonly used to treat dermatitis, wounds, ulcers, thermal burns, and herpes zoster.
- There is also evidence to support the use of calendula ointment to reduce radiation-induced skin toxicity.
- Calendula's active components include terpenoids (anti-inflammatory agents), carotenoids, polysaccharides (antibacterial agents), and flavonol glycosides.
- Calendula's anti-inflammatory effects in some cases exceed the effects of indomethacin.
- Calendula infused ointments in a beeswax base is preferred and may be applied directly to the wound base, onto the primary dressing, around the wound edge, and the periwound.
- There are rare reports of allergic contact dermatitis to Calendula, but it is generally well tolerated.





## ❑ Cedrus deodara (Family: Pinaceae)

- Deodar possesses **anti-inflammatory, anti-microbial, astringent** and **wound healing** activities and is therefore particularly useful in treatment of infected wounds.



## ❑ Curcuma longa (Family: Zingiberaceae)

- Turmeric is the ground root of Curcuma longa and its active compound is curcumin.
- Curcumin is the yellow pigment that gives turmeric, curry and yellow mustard their color, and it has been used for centuries in cooking and cosmetics.
- Turmeric possess anti-bacterial, anti-fungal, antioxidant, anticancer, analgesic and anti-inflammatory activities.
- Its anti-inflammatory properties, presence of vitamin A, as well as several proteins were shown to have a beneficial effect on the early formation of collagen fibres, which could be related to stimulation of fibroblastic activity.



- It **inhibits lipoxygenase and cyclooxygenase**, thereby reducing levels of leukotrienes, thromboxanes, and prostaglandins.
- Topical turmeric has been evaluated for **psoriasis** and **wound healing**, but color and odor limit its use.
- In a short-term study investigating the **anti-rheumatic** activity of turmeric, the effects were comparable with those of a nonsteroidal anti-inflammatory analgesic.
- Another study focusing on **postoperative inflammation** demonstrated that turmeric produced a better anti-inflammatory response than placebo in a small group of male patients following hernia operations.
- In North America, turmeric is generally taken orally; however, ayurvedic practitioners blend the powder into a paste or lotion for the treatment of superficial wounds, external inflammation, and arthritis.
- If used externally, the paste or lotion should be applied **only to intact skin.**



## ❑ Colloidal Oatmeal

- For decades, colloidal oatmeal has been used for its calming and soothing effects on the skin.
- Many over-the-counter products are derived from whole oat kernels ground into a fine powder and then combined with emollients to create various preparations from bath powders to moisturizing creams.
- Colloidal oatmeal is one of the few natural ingredients approved by the US Food and Drug Administration (FDA) for use as a treatment for skin conditions such as allergic contact dermatitis to poison ivy, irritant diaper dermatitis, and eczema.





➤ The therapeutic properties of oats :

- Firstly, oats have a high concentration of starches which explains their water-holding function.
- Secondly, high concentrations of phenols give oatmeal antioxidant and anti-inflammatory properties.
- Lastly, its cleansing activity is thought to be due to the saponins present in the grain.

➤ Products that contain colloidal oatmeal tend to have very low allergenicity.





## ❑ Feverfew

- Feverfew (*Tanacetum parthenium*) is a flowering plant from the daisy family.
- Originally named for its fever-reducing properties, it is also used to treat headaches, arthritis, and digestive disorders.
- Use of topical feverfew had been limited by the presence of irritating parthenolides in the plant, but an industry-patented process now allows for removal of these irritants.
- Feverfew possesses antioxidant and anti-inflammatory properties; it is thought to inhibit proinflammatory mediators released from macrophages and to reduce neutrophil chemotaxis.
- Dermatologic applications include treatment of **irritated sensitive skin, facial erythema, and tactile roughness**.



## ❑ Green Tea

- Green tea is made from unfermented tea leaves and can be ingested or applied topically.
- It contains the highest concentration of polyphenol antioxidants of any tea, save perhaps for white tea, which is the least processed of all teas.
- Epigallocatechin-3-gallate (EGCG) in green tea is the most potent of the polyphenols.
- Both topical and oral green tea can protect against inflammation, ultraviolet light induced photodamage, chemical carcinogenesis, and photocarcinogenesis.



## ❑ Honey

- Honey is a bee-derived substance composed primarily of fructose and glucose, but also contains numerous proteins, amino acids, vitamins, enzymes, and minerals.
- While honey is used to treat a wide variety of conditions including cutaneous infections and skin discoloration, it is most commonly applied to wounds to enhance healing. (burns, pressure ulcers, and infected wounds)
- The latter effect is thought to be due to its antimicrobial properties and the enzymatic release of hydrogen peroxide.
- Medical-grade honeys are now available by prescription, suggesting that honey may be entering the realm of conventional medicine.



- Honey has been used topically for centuries to accelerate wound healing along with other topical agents; **it is not a substitute for antimicrobials.**
- **Wound healing** properties of honey are thought to result from the **debriding** properties of the enzyme catalase, **absorption of edema** due to its hygroscopic properties, ability to promote **granulation and epithelialization** from the wound edges, and its **antimicrobial** properties.
- In general, honey is useful for increased **superficial bacterial burden**, especially when accompanied by a **hard eschar for autolytic debridement**.
- It is not useful in venous ulcers without increased bacterial burden or with **soft slough**.
- When honey becomes diluted with wound exudate, it may become **odiferous and even promote bacterial growth** if not changed at appropriate time intervals (depending on level of exudate).
- Patients need to be cautioned to use **only medically approved honey dressings**. Local or store-bought honey may contain bacteria and other contaminants.



## ❑ Licorice Root

- Licorice root has long been considered a natural remedy. (anti-irritant and anti-inflammatory properties)
- Licorice extract is produced by first boiling licorice root and then allowing the water to evaporate.
- It is used both topically and orally for rosacea and dermatitis and is typically found in preparations that target sensitive skin.
- Licorice also contains glycyrrhizin, a substance that, if ingested in high doses, can cause hypokalemia, arrhythmias, hypertension, congestive heart failure.





## ❑ Ginkgo biloba (Family: Ginkgoaceae)

- Ginkgo leaf extracts have been therapeutically used for hundreds of years.
- Its pharmacological activities include an increase in blood fluidity, anti-oxidative activity, membrane stabilization, improvement in cognition, and wound healing promotion.
- Various ginkgo preparations have been shown to improve granulation tissue breaking strength, as well as promote epithelization.
- Side effects of ginkgo biloba include:
  - Allergic skin reactions
  - Bleeding disorders
  - Constipation, Diarrhea, Nausea/vomiting
  - Dizziness, Headache, Restlessness, Seizures
  - Impaired fertility



## ❑ Rosmarinus officinalis (Family: Lamiaceae)

- Rosemary is used for wound treatment, hypertension, alopecia, and has antibacterial, antifungal, and antiviral activities.
- In wound healing, it reduces inflammation and enhances wound contraction, re-epithelization, and regeneration of granulation tissue, angiogenesis and collagen deposition.
- Side effects of rosemary include:
  - stomach and intestinal irritation, vomiting
  - Kidney damage
  - Seizures, coma
  - pulmonary edema
  - miscarriage



## ❑ Hypericum (st john's wort)

- It is well known for use in treating **depression**, and it has a history of topical use for **wounds, abrasions, and superficial burns**.
- Constituents of Hypericum also offer therapeutic effects: amentoflavone and hypericin have **anti-inflammatory** effects, whereas hyperforin inhibits the growth of **gram-positive bacteria**.
- In a randomized, double-blind clinical study, the healing of 144 women **post-cesarean** delivery using Hypericum demonstrated improved wound healing on day 10 and decreased scar formation on day 40 using the Vancouver Scar scale.







- Hypericum is an astringent (coagulates protein) and when prepared for external application is typically prepared by extracting the flower with olive oil or grape seed oil and mixed in an ointment for clinical use.
- The oily Hypericum preparation is thought to provide the anti-inflammatory action.
- Hypericum (usually seen with oral preparations) has been used for occasional skin irritation and photosensitivity.
- It is recommended that Hypericum be used on small wounds only to minimize risk of absorption.











GENUS FAMILY	<i>Achillea millefolium</i> Asteraceae	<i>Angelica sinensis</i> Apiaceae	<i>Aloe vera</i> Liliaceae	<i>Avena sativa</i> Poaceae
BIOLOGICAL ACTIVITY	 <p data-bbox="486 882 901 943">Antibacterial activity. Anti-inflammatory activity.</p>	 <p data-bbox="945 882 1421 982">Stimulation of wound healing. Increasing the strength of skin in healed wounds.</p>	 <p data-bbox="1454 882 1931 1053">Formation of a protective coating on the affected areas. Stimulation and speeding up of a wound healing process. Anti-inflammatory activity.</p>	 <p data-bbox="1964 882 2440 943">Anti-inflammatory activity. Facilitation of wound healing.</p>







GENUS FAMILY	<i>Azardica indica</i> Meliaceae	<i>Calendula officinalis</i> Asteraceae	<i>Cedrus deodara</i> Pinaceae	<i>Centella asiatica</i> Mackinlayaceae
BIOLOGICAL ACTIVITY	 <p>Anti-bacterial activity. Anti-fungal activity. Anti-viral activity. Anti-inflammatory activity. Help in collagen forming. Promotion of wound healing.</p>	 <p>Anti-viral properties. Anti-inflammatory activity. Antimicrobial activity. Facilitation of healing of poorly healing wound.</p>	 <p>Anti-inflammatory activity. Anti-microbial activity. Astringent activity.</p>	 <p>Increasing content of collagen and thickness of the epithelium. Increasing cellular proliferation. Promotion of collagen synthesis.</p>





**GENUS  
FAMILY**

***Chamomilla recutita***  
**Asteraceae**



**BIOLOGICAL  
ACTIVITY**

Antimicrobial activity.  
Antioxidant properties.  
Anti-inflammatory activity.  
Mild astringent properties.  
Acceleration of  
epithelization.

***Chromolaena odorata***  
**Asteraceae**



Enhancement of hemostatic  
activity.  
Inhibition of wound  
contraction.  
Stimulation of granulation  
tissue synthesis and re-  
epithelization processes.

***Commiphora myrrha***  
**Burseraceae**



Antibacterial and antifungal  
effects.  
Anti-inflammatory activity.  
Local anesthetic and  
analgesic activity.





***Curcuma longa***  
**Zingiberaceae**



Antibacterial and antifungal  
effects.  
Anti-inflammatory activity.  
Analgesic activity.  
Facilitation of collagen  
synthesis.




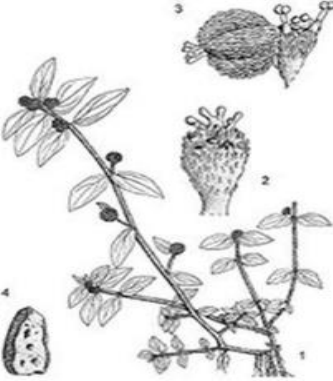




GENUS FAMILY	<i>Hypericum perforatum</i> Hypericaceae	<i>Hydnocarpus wightiana</i> Achariaceae	<i>Jasminum auriculatum</i> Oleaceae	<i>Pterocarpus santalinus</i> Fabaceae
BIOLOGICAL ACTIVITY	 <p>Anti-inflammatory activity. Antiseptic properties. Analgesic activity. Astringent activity. Antibacterial activity.</p>	 <p>Promotion of epithelization. Help in collagenization. Improvement of strength of scar tissue.</p>	 <p>Improvement of tensile strength in the early phase of wound healing. Acceleration of mucopolysaccharide accumulation.</p>	 <p>Increasing the rate of wound contraction, collagenization, skin breaking strength, granulation tissue dry weight, and hydroxyproline content.</p>









GENUS FAMILY	<i>Echinacea sp.</i> Asteraceae	<i>Euphorbia hirta</i> Euphorbiaceae	<i>Ginkgo biloba</i> Ginkgoaceae	<i>Helianthus annuus</i> Asteraceae
BIOLOGICAL ACTIVITY	 Antimicrobial activity. Anti-inflammatory activity.	 Analgesic activity. Anti-inflammatory activity. Inhibition of platelet aggregation.	 Antioxidant properties. Pro-healing activity: increase in blood fluidity, membrane stabilizing, improvement in cognition.	 Anti-inflammatory activity.





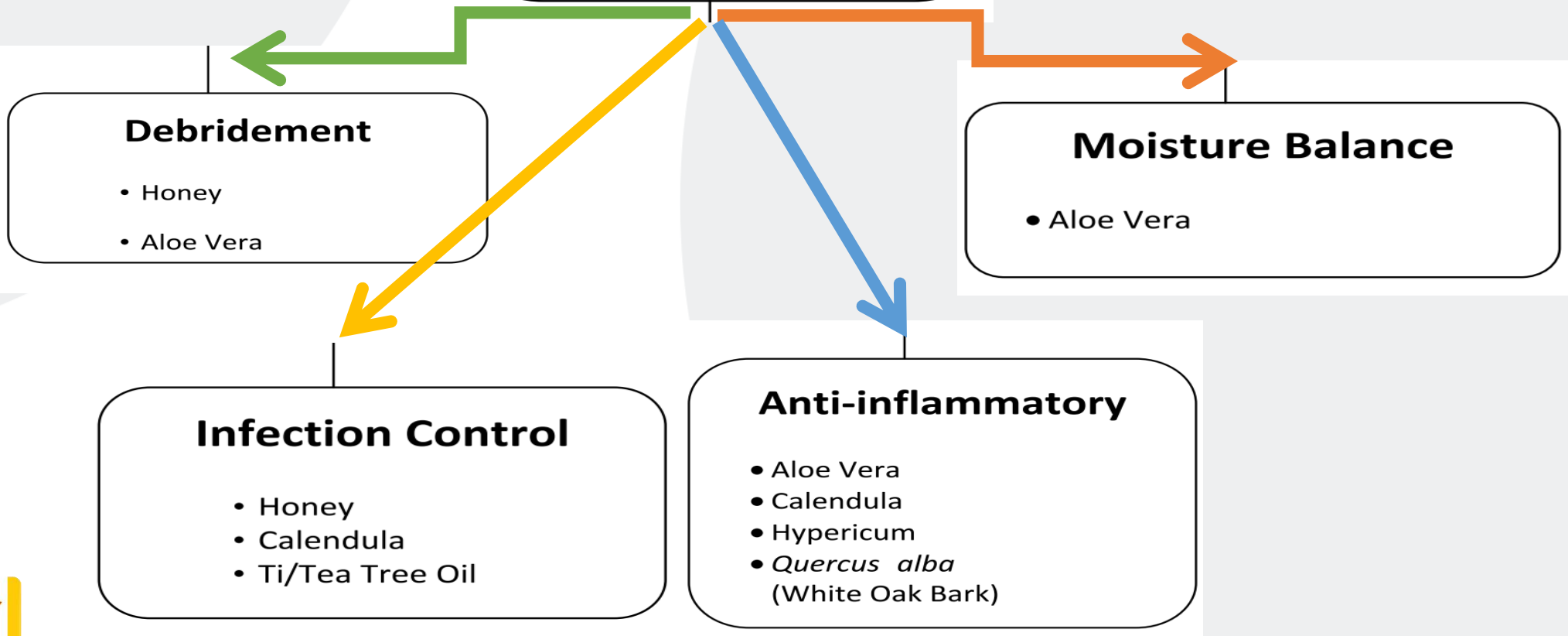
GENUS FAMILY	<i>Rosmarinus officinalis</i> <i>Lamiaceae</i>	<i>Tridax procumbens</i> <i>Asteraceae</i>
		
BIOLOGICAL ACTIVITY	Anti-inflammatory activity. Enhancement of wound contraction, re-epithelization, regeneration of granulation tissue, angiogenesis and collagen deposition.	Enhancement of epithelization and collagenization.







# Local Wound Care (Topical Therapy)



## CAM TOPICAL PRODUCTS

### Local Wound Care: Topical Products Proposed Mechanisms of Action as Listed in Categories

	Debridement	Antibacterial	Anti-inflammatory	Moisture Balance	Comment
<i>Aloe vera</i> gel (Aloaceae family)	X	X	X	X	<ul style="list-style-type: none"> <li>• Antipruritic</li> <li>• Pure extract contains 95% <i>Aloe</i> gel</li> <li>• Commercial products may contain alcohol</li> <li>• Contact allergic dermatitis occasionally occurs</li> <li>• Used for stalled chronic wounds</li> </ul>
<i>Calendula officinalis</i> (marigold)		X	X		<ul style="list-style-type: none"> <li>• Triterpenes are a main anti-inflammatory (anti-infective component)</li> <li>• Contact allergic dermatitis may occur</li> </ul>
Essential oils: chamomile, lavender, ti tree/tea tree		X	X		<ul style="list-style-type: none"> <li>• Not to be used on leg ulcers due to sensitization</li> <li>• Contact allergic dermatitis</li> <li>• May cross-react with ragweed group of plants</li> </ul>
Honey (propolis)	X	X		X	<ul style="list-style-type: none"> <li>• May cross-react with balsam of Peru</li> <li>• May become allergen with increased topical use</li> </ul>
<i>Hypericum</i> ( <i>St John's wort</i> )		X	X		<ul style="list-style-type: none"> <li>• Not to be used on large wounds (may cause increase in thyroid-stimulating hormone)</li> </ul>
<i>Quercus alba</i> (white oak bark)			X		<ul style="list-style-type: none"> <li>• Cross-reaction in patients allergic to aspirin</li> <li>• Use caution in individuals with renal/hepatic dysfunction, pregnancy</li> </ul>



# Specific side effects

- **Evening primrose oil** which has several Side effects like nausea (may decrease if taken with food), skin rashes and acne.
- **Comfrey** that is widely used for a variety of conditions particularly as a wound healing agent topically will be unsafe for internal use and perhaps, topically for deep wounds because it contains hepatotoxic alkaloids.
- **Aloe vera's gel** may inhibit bradykinin and hinders the formation of thromboxan. It should not be used in deep vertical cuts because it may delay healing. In some people it causes allergic dermatitis.
- **Henna** causes severe allergic reactions, even some case reports of systemic anaphylaxis were reported.
- **Chamomile** with several anti-fungal and anti-microbial properties may induce hypersensitivity cross-reactions to ragweed, Chrysanthemums (Compositae family).



# Conclusions

- Various plants produce secondary metabolites and other products that have beneficial effects on wound healing and other fields of medicine.



- Finally, the combination of traditional and modern knowledge seems to be the best approach to produce novel effective therapeutic interventions for wound healing with a significantly improved treatment efficacy, lowered side effects and costs.



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# معرفی داروی طبیعی موضعی به عنوان ترمیم کننده زخم و سوختگی

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# عسل



- اثر آنتی باکتریال بر روی گونه های گرم مثبت و گرم منفی ، هوازی و غیر هوازی و ...
- تسکین دهنده در ناحیه سوختگی و زخم
- در بیماریهای لثه و gingivitis
- در بیماری سرخک : در مراحل اولیه تا محو شدن کامل spot ها از عسل جهت مالیدن بر روی پوست استفاده میشود
- از خود عسل به تنهایی جهت ترمیم زخم، در درمان سرفه و گلودرد، به عنوان آنتی سپتیک موضعی، بیماری های چشمی، به عنوان ملین استفاده می شده.
- وجود مواد مغذی، آنتی اکسیدان، آنزیم و ترکیبات بهبود دهنده زخم در عسل باعث شده است که در درمان بیماری های پوستی کاربرد گسترده ای داشته باشد



# ترکیبات تشکیل دهنده عسل



- قند : (۳۲-۳۸ درصد) فروکتوز، (۲۸-۳۱ درصد) گلوکز،
- (۴-۵ درصد) فروکتوالیگوساکارید
- مینرال : کلسیم، منیزیم، پتاسیم، روی، آهن، گوگرد
- مجموعه ویتامین های ب
- پروتئین (۰,۱-۰,۵ درصد) و ...

- عسل سرشار از آنتی اکسیدانهایی است که به کاهش چین و چروک و مقابله با پیری پوست کمک می-کند. اثر آنتی اکسیدانی عسل به مقادیر total phenolic آن بستگی دارد و هر چه عسل تیره تر باشد درصد فنول آن بالاتر بوده و آنتی اکسیدان بهتری است.



# مکانیسم اثر آنتی باکتریال عسل



- با افزایش ویسکوزیته مایع زخم از رشد باکتری بر روی زخم جلوگیری می کند.
- غلظت بالای قند در عسل موجب مهار رشد میکروب می شود
- pH عسل در محدوده ۳/۲-۴/۵ و اسیدی است. اسیدی بودن عسل موجب مهار رشد میکروارگانیسم میشود.
- مطالعات نشان دادند عسل در برابر ۱۸ گونه استافیلوکوک اورئوس مقاوم به متی سیلین- ۷ گونه انتروکوک حساس به ونکومايسين و ۲۰ گونه انتروکوک مقاوم به ونکومايسين اثرات مهارکننده خوبی داشته است. مکانیسم اثر ضد میکروبی عسل به دلیل تولید **هیدروژن پراکسید توسط آنزیم گلوکز اکسیداز** عسل در محل زخم است.

Inhib که از غدد زنبور در عسل ترشح می شود به هیدروژن پراکسید و گلوکونیک اسید تبدیل می شود به ترتیب اثر ضد عفونی کننده و ضد میکروبی دارند.







- عسل، بافت را از آسیب های ناشی از رادیکال های آزاد که از سلول های التهابی آزاد می شود، محافظت می کند.
- حضور انواع ویتامین ها و آمینو اسید ها و .. یک منبع غذایی خوب برای regeneration بافت است.
- به دلیل خاصیت اسیدی، غلظت بالای شکر و up regulate کردن سیتوکین های التهابی نظیر اینترلوکین ۱ و ۶ بهبود زخم را تسریع می کند.
- در مطالعاتی که توسط Bansal و همکاران جهت مقایسه ی اثربخشی پماد عسل با silver انجام شد، اثربخشی بهتر و سرعت بهبودی بیشتری با استفاده از پماد عسل حاصل



بر اساس مطالعات انجام شده تنها تعداد کمی از روغن های گیاهی موجود به طور  
مستقیم و قطعی در فرایند ترمیم زخم موثر هستند:

• روغن زیتون

• روغن دانه انگور

• روغن بادام

• روغن آووکادو



# آووکادو



- آووکادو میوه چرب است و دارای اسیدهای آمینه مختلف مانند سیستین تریپتوفان و تیروزین میباشد.

- در تحقیقات جدیدی که انجام شده وجود **چند نوع آنتی بیوتیک** در آووکادو ثابت شده است.

قدرار کمی (در حدود ۲ درصد) روغن است.





# روغن آووکادو



- روغن آووکادو از پالپ میوه آووکادو استخراج می شود.

- غنی از اسید لینولئیک، لینولنیک اسید و اسید اولئیک (۵۰٪) است.

- حاوی  $\beta$ -sitosterol،  $\beta$ -کاروتن، لسیتین، مواد معدنی، اسیدهای چرب،

- امگا ۳ و ۶ و ویتامین A، C، D و E بوده که یک منبع غنی سازی برای

- پوست های خشک و آسیب دیده به شمار می رود.

- اثرات مرطوب کنندگی، آنتی اکسیدان، ضدالتهاب، ترمیم کنندگی و تقویت کنندگی نیز دارد.

- تجویز موضعی عصاره میوه ای آووکادو بر روی زخم باعث تسریع اپیتلیاسیزاسیون و افزایش مقدار

- هیدروکسی پرولین در زخم می شود.

- روغن آووکادو همچنین کلاژن سازی را افزایش داده و تعداد سلول های التهابی را در طول پروسه ترمیم

- زخم را کاهش می دهد.



# آوو کادو



- تحریک ساخت کلاژن: کلاژن پروتئین اصلی در ساختار پوست است که در انعطاف و استحکام پوست نقش دارد.

روغن آوو کادو حاوی **اسیدهای چرب غیراشباع و استروئیدهای طبیعی** به نام **استرولین** است که موجب لطافت و نرمی پوست شده و با افزایش ساخت کلاژن سبب **جوان سازی** و نوسازی سلولهای پوستی می شود

- اثر مرطوب کنندگی: با حفظ رطوبت پوست باعث کاهش خشکی، خارش، درد و التهاب می شود
- ترمیم زخم: مطالعات نشان داده است روغن آوو کادو در بهبود زخم، بریدگی و اسکار به دلیل افزایش ساخت کلاژن و کاهش تعداد سلول های التهابی به سرعت سبب بهبودی می گردد.





# آوو کادو



- پیشگیری از پیری زودرس: روغن آوو کادو حاوی آنتی اکسیدان **کارتنوئید** است.

از پوست در برابر آسیب های ناشی از **رادیکالهای آزاد** محافظت می کند. مصرف موضعی این روغن روی پوست موجب کاهش خطوط و چین و چروک صورت می شود و با بهبود ظاهر پوست از پیری زودرس جلوگیری می کند.

- درمان آفتاب سوختگی: روغن آوو کادو با داشتن **خواص آنتی اکسیدانی و ترکیبات پلی فنلی**، نقش موثری در پیشگیری از عوارض ناشی از اشعه خورشید روی پوست دارد.

- بهبود الاستیسیته پوست - درمان پسوریازیس - درمان آگزما - پاک کننده آرایش - مناسب برای ناخن های خشک و شکننده

✓ در یک مطالعه حیوانی با مصرف موضعی و یا خوراکی 300mg/kg/day روغن آوو کادو به مدت ۱۴ روز

**بهبودی کامل زخم حاصل شد.** این اپیتلیزاسیون و بهبودی کامل را می توان به مقدار بالای **هیدروکسی**

**پرولین** در روغن آوو کادو نسبت داد.



# مواد مسدود کننده

- مواد مسدود کننده همان طور که از نامشان پیداست، **لایه روغنی محافظ و مسدود کننده ای** را بر روی پوست ایجاد می کنند و **از تبخیر آب پوست جلوگیری به عمل** می آورند. موادی مانند پارافین، لانولین، اوسرین و روغن های گیاهی مثل روغن زیتون و روغن کنجد از این گروه هستند.
- با نرم نمودن موضع زخم از ایجاد تحریک و حساسیت موضع زخم جلوگیری می کنند.



# لانولین



• لانولین به عنوان موم متشکل از استرها، دی استرها، استرهای هیدروکسیل

با وزن مولکولی بالا

• لانولین از ترشحات غدد چربی گوسفند حاصل می شود. این ماده به نام چربی پشم نیز شناخته می شود.

• لانولین و بسیاری از مشتقات آن در برای درمان و زیبایی پوست انسان استفاده می شود.

• عوامل مرطوب کننده طبیعی

• لانولین با حفظ رطوبت پوست باعث کاهش مرگ سلول، افزایش رگ زایی و کاهش درد میشود.



# ترکیبات موجود در موم پشم خالص و لانولین دارویی

ترکیبات موجود	موم پشم خالص (درصد وزنی)	لانولین دارویی (درصد وزنی)
استر های موم	75-90	97
الکل های آزاد	6-12	2.5
اسیدهای چرب آزاد	1-8	0.3
آب	1-5	0.05
اجزای نامحلول	0.1-2	ناچیز
نمک های محلول در چربی	0.2-2	ناچیز
نمک های محلول در آب	0.1-0.2	ناچیز
بقایای مواد شوینده	0.1-1	0.02
مقدار پراکسید	قابل اندازه گیری نیست	12meq/kg
رنگ	متغیر	زرد تیره
بو	متغیر	بدون بو

مقدار پراکسید	قابل اندازه گیری نیست	12meq/kg
رنگ	متغیر	زرد تیره
بو	متغیر	بدون بو



# لانولین در ترمیم زخم

- **آبرسانی** نقش مهمی را در ترمیم زخم ایفا می کند. به واسطه آب رسانی ترمیم زخم در **اثر رشد اپی تلیوم** بر روی سطح برهنه پوست ترمیم زخم اتفاق می افتد.
- ترمیم پوستی و آنژیوژنز در محیط مرطوب سریع تر اتفاق می افتد.
- در واقع زخم در محیط مرطوب سریع تر ترمیم یافته و همچنین احتمال ایجاد هر گونه اسکاب و اسکاری در محیط مرطوب نسبت به محیط خشک کاهش بیشتری می یابد.
- در مطالعات قبلی انجام شده، اثبات شده است که کرم حاوی لانولین **سرعت ترمیم زخم و بازسازی پوست** را تا **۳۵٪** افزایش می دهد. این گروه همچنین شامل ویژگی های ترمیم کنندگی لانولین که قابل مقایسه با پترولاتوم است در حالی که پترولاتوم نقشی در ترمیم زخم ندارد.





# Zinc oxide



- Zinc is an essential element for **tissue repair** and may **accelerate wound healing**.
- Zinc is an **antimicrobial and anti-inflammatory agent**
- Antioxidant role in **protecting against free radical-induced oxidative damage**. Zinc **protects against UV radiation, enhances wound healing**, contributes to immune, and **decreases** the relative **risk of cancer and cardiovascular** disease.
- All body tissues contain zinc; in skin, it is **five to six times more** concentrated in the **epidermis than the dermis**.
- Zinc confers resistance to **epithelial apoptosis** through cytoprotection against **reactive oxygen species and bacterial toxins** possibly through **antioxidant activity**.
- Zinc oxide in paste bandages **protects and soothes inflamed peri-ulcer skin**.
- Clinical evidence emphasizes its importance in **autodebridement, anti-infective action, and promotion of epithelialization**.





- In **diabetic foot ulcers**, a zinc oxide-medicated occlusive dressing was **significantly more effective** in **debridement**.
- topical zinc **reduced oral antibiotic consumption** significantly compared with placebo treatment.
- **Staphylococcus aureus** was cultured significantly less frequently from zinc oxide-treated than from placebo-treated wounds, substantiating its **antiseptic property**.
- Zinc-containing products available for topical application in wound management include **paste bandages**, **occlusive adhesive dressings**, and **zinc-saline dressings**



**Table 1.** Nonexhaustive list of commercial zinc-containing wound care products

Product	Manufacturer	Zinc content and other ingredients	Documentation
Zinc paste bandages (Unna boot) <sup>192</sup>			
Calaband <sup>®2, 193</sup>	Mölnlycke Health Care, Göteborg, Sweden	Zinc oxide (9.25%) Calamine (5.75%) Phenosept	Venous leg ulcers <sup>195</sup>
Gelocast <sup>®</sup>	Smith & Nephew, Hull, UK	Zinc oxide (10%)	
Steripaste <sup>®194</sup>	Mölnlycke	Zinc oxide (15%)	
Varolast <sup>®</sup>	Hartmann, Heidenheim, Germany	Zinc oxide (15%) Methyl and propyl <i>p</i> -hydroxybenzoates	
Viscopaste <sup>®</sup> PB7 <sup>194</sup>	Smith & Nephew	Zinc oxide (10%) Cetearyl alcohol, methyl and propyl <i>p</i> -hydroxybenzoates	
Zincaband <sup>®2,193</sup>	Mölnlycke	Zinc oxide (15%) Propyl <i>p</i> -hydroxybenzoate	Venous leg ulcers <sup>195,196</sup>
Zipzoc <sup>®</sup> (stocking)	Smith & Nephew	Zinc oxide (20%)	
Other zinc-supplemented dressings			
Curasorb <sup>®</sup> Zn	Tyco, Mansfield, MA	Zinc-impregnated (0.18%*) calcium alginate	Chronic skin ulcers of different etiologies <sup>197</sup> Diabetic foot ulcers <sup>114</sup> Burns <sup>115</sup> Venous and arterial leg ulcers <sup>165</sup> Medium to heavy exudating secondary healing wounds <sup>198</sup>
Dermagran <sup>®</sup> Hydrophilic	Dermascience, Princeton, NJ	Zinc ointment (0.05%*) in nonwoven swab Zinc-saline formulation in gauze	
Mezinc <sup>®</sup>	Abigo Medical, Askim, Sweden	Zinc oxide (25%) and zinc resins in an adhesive mass	
Trionic <sup>®</sup>	Johnson & Johnson Wound Management, Norderstedt, Germany	Zinc (0.03%*), calcium and manganese supplemented alginate	







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## **Case Report**

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# **Successful Treatment of Ulcers with Honey-Based Topical Preparation: Five Case Reports**



# Methods

## Materials and Methods

Before-and-after design of study was conducted at the Skin Diseases & Leprosy, Research & Training Center of Tehran University of Medical Sciences from June to September 2017 to find out the effect of honey ointment on poor healing wounds. The patients provided informed consent to have their photographs published. All clinical cases are described in (Table 1). Before application of honey ointment on the wound on the first day, the wound was cleaned with normal saline; honey ointment was applied directly or on sterile cotton gauze, and the wound was dressed daily in the morning and evening.





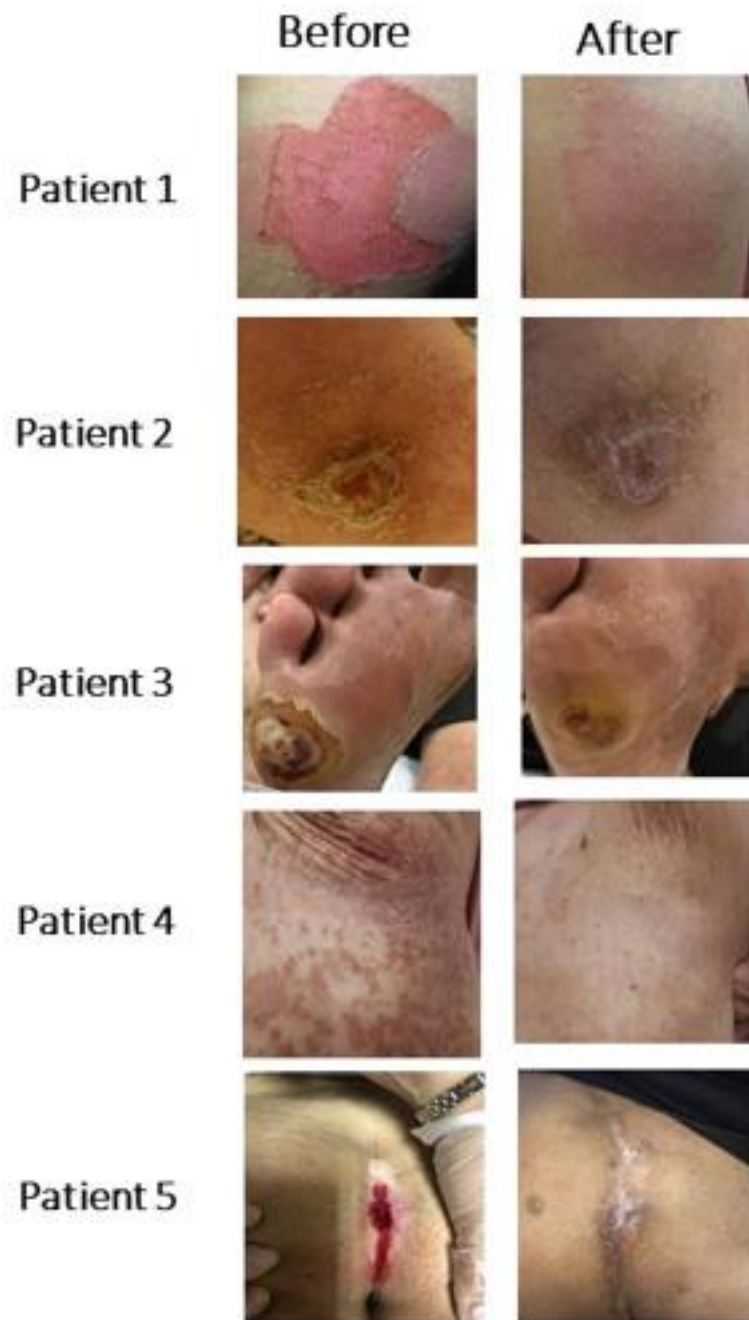
# Results

- There was significant improvement in the healing process as formulation possesses antibacterial, wound cleansing, and wound healing properties. All patients showed significant improvement after 2-3 weeks with honey ointment.
- A combination of honey and lanolin may be effective in the treatment of low to moderate wounds.

**Table 1:** Description of five clinical cases.

Case	Age/sex	Disorder	Application	Duration	Result
Patient 1	12/male	chemical burning	wound was washed with normal saline, and then covered with sterile gauze dressing twice a day	7 days	Controlled infection and edema, reduce the size of wound
Patient 2	50/male	diabetic foot ulcer	wound was washed with normal saline, and then covered with sterile gauze dressing three times a day	10 days	reduced the swelling and infection associated with wound, soothed healing
Patient 3	40/male	diabetic foot ulcer	wound was washed with normal saline, and then covered with sterile gauze dressing 3 times a day	14 days	Partial clinical resolution of the foot ulcer and infection disappeared
Patient 4	32/female	burn caused by hot water steam	wound was washed with normal saline, and then covered with sterile gauze dressing twice a day	3 days	Improve healing process and reducing pain and inflammation.
Patient 5	25/male	malodourous and deterioration wound on his buttock	wound was washed with normal saline, and then covered with sterile gauze dressing three times a day	21 days	Significant improvement was noted and the wound was almost healed.







# موارد مصرف فراورده های موضعی حاوی عسل و روغن های گیاهی

- انواع زخم و سوختگی های درجه ۱ و ۲ به منظور ترمیم و بازسازی آسیب های پوستی
- زخم پای دیابتی
- زخم جراحی
- زخم های عفونی
- زخم تروما (زخم های حادثه ای)
- التهابات پوستی





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# THANK YOU FOR YOUR ATTENTION



W W W . A R G A N O . I R



TEHRAN UNIVERSITY  
OF  
MEDICAL SCIENCES



# Emerging treatments for superficial burn and wounds

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M.D. Dermatologist

Center for Research and Training in Skin diseases and Leprosy



TEHRAN UNIVERSITY  
OF  
MEDICAL SCIENCES



# Wound care strategies

- Classical Approach:

- Wound debridement
- Topical Treatment (antimicrobial agents and etc. )
- Wound dressing
- Skin grafts

- Emerging strategies:

- A more integrated approach
- Enzymatic debridement
- Cytokines and growth factors as topical
- Biologic skin substitutes that act as both wound dressing and re-epithelializing agent



**Tissue**

**Infection/Inflammation**

**Moisture**

**Epithelial Edge of Wound**

Mechanical Debridement

Sharp  
Hydro-powered  
Ultrasonic

Chemical Debriding  
Agents

Bromelain

Antimicrobial agents

Bacitracin  
Polysporin  
Mupirocin  
Silver nitrate  
Silver sulfadiazine  
Cerium nitrate  
Povidone iodine

Dressings

Silicone  
Chitin  
Alginate  
Hydro-polymers  
Polyurethane foam  
Hyaluronic acid  
Artificial dermis

Biologics

Allografts  
CEA/A  
dHACM  
hAM



# Topical agents

- Growth Factors and Cytokines,
- PRP and PRF
- Herbal medicine
- Vitamins







# Growth factors and cytokines



# Growth factors and cytokines

- Clinical efficacy proved:
  - Platelet derived growth factor (PDGF)
  - Fibroblast growth factor (bFGF)
  - Recombinant human epidermal growth factor (EGF)
  - Granulocyte-macrophage colony-stimulating factor (rhGM-CSF)
  - Vascular endothelial growth factor (VEGF)
- FDA approval: PDGF and EGF
- Best effects on Diabetic ulcers



# Growth factors and cytokines, PDGF

- Regulate cell growth and division, chemoattractant for mesenchymal cells, angiogenesis.
- PDGF- BB most effective isoform in wound repair.
- The first recombinant growth factor approved by FDA in the for topical administration.
- Significantly effective in **diabetic foot ulcers**.
- Less effective in **pressure ulcers** and **venous ulcers** due to decreased penetrance.
- Effective in **partial thickness burns** in animal studies.



# Growth factors and cytokines, FGF

- FGF-2, known as basic FGF (bFGF), is the best studied and has a confirmed role in the proliferation of epithelial and mesenchymal cells as well as a possible role in angiogenesis.
- FGF-2 significantly effective in **pressure ulcers**.
- FGF-2 showed clinical efficacy in treatment of **partial burns**. Accelerated healing, reduced scarring, and improved color.
- FGF-1 (acidic FGF or aFGF) also effective in **partial burn** with increased rate of fully healed lesions and shorter healing time.
- FGF-10 effective in **venous ulcers**.
- No clear benefit in **diabetic foot ulcers**.



Trafermin  
Fiblast® Spray



# Growth factors and cytokines, KGF

- KGF also known as FGF-7 recruits fibroblasts in order to accelerate granulation tissue formation.
- Clinical application in pretreatment of mucositis associated with chemotherapy and radiotherapy.
- Protective effects also documented for urothelial and pulmonary tissue.
- Lacks overall efficacy in skin wound repair.



## Palifermin





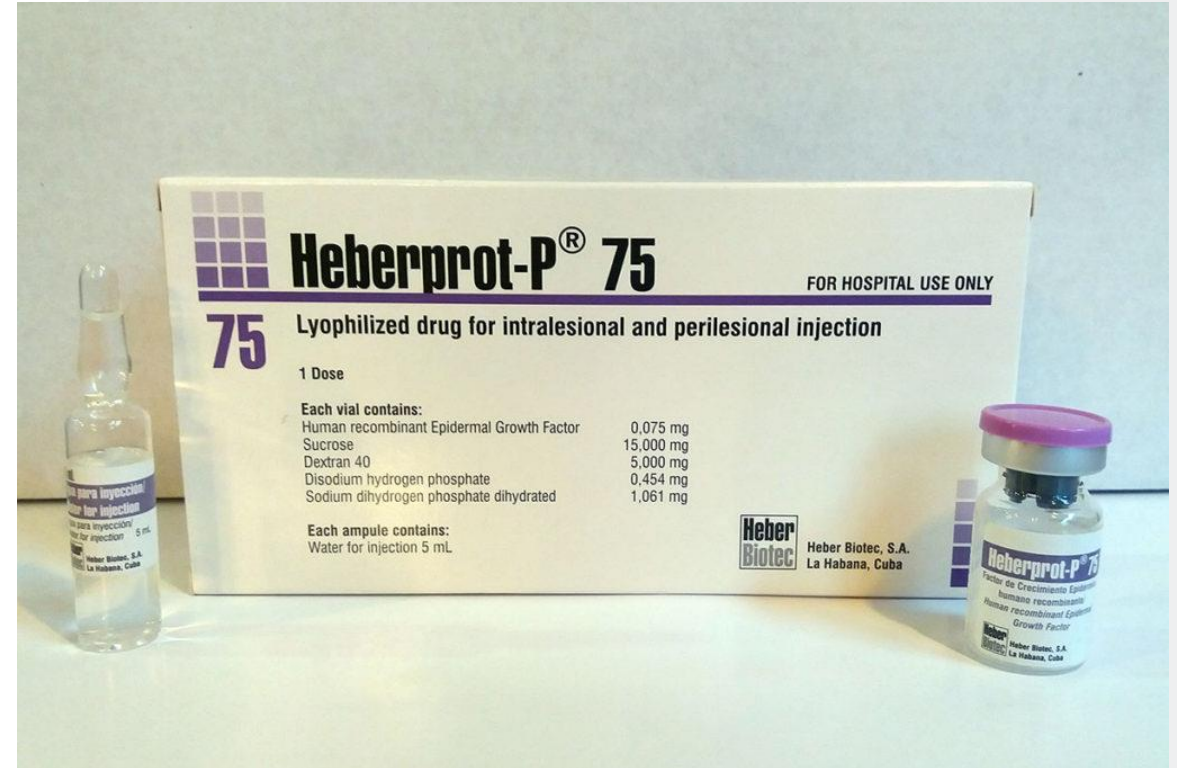
# Growth factors and cytokines, EGF

- Facilitates re-epithelialization by stimulating the proliferation and migration of keratinocytes.
- Also increases the tensile strength of new skin.
- Three commercially available forms
- EGF significantly effective in partial burn wounds, non-healing ulcers, and diabetic foot ulcers.



# Growth factors and cytokines, EGF

- Heberprot-P<sup>®</sup> contains 75 µg of freeze-dried EGF
- Intralesional
- Three times per week



# Growth factors and cytokines, EGF

- Regen-D™ 150 is a gel containing 150 µg/g EGF
- Topical
- Twice daily



# Growth factors and cytokines, EGF

- Easyef® is a dermal solution spray indicated for diabetic foot ulcers.



# Growth factors and cytokines, VEGF

- VEGF-A is the best studied and has a notable role in initiating angiogenesis through the proliferation and migration of endothelial cells
- recombinant human-VEGF (rh-VEGF) showed clinical efficacy in treatment of **diabetic foot ulcer**.
- In animal models, the use of a protease-resistant VEGF-A has been proposed for use in the protease-rich microenvironment of chronic wounds.
- Clinical studies are limited.





# Growth factors and cytokines, GM-CSF

- GM-CSF recruits Langerhans cells, stimulates local recruitment of inflammatory cells, advances myofibroblast differentiation to facilitate wound contraction, and mediates proliferation of the epidermis.
- Administration of GM-CSF to **non-healing wounds** and **venous ulcers** increases wound rapier rate, reduces the average healing period, and the rate of re-ulceration.



# Growth factors and cytokines, TGF- $\beta$

- TGF- $\beta$  is involved in almost all stages of the wound healing and a pivotal role in myofibroblast differentiation and subsequent scar formation.
- The scar-less and the regenerative ability of the human fetus with the abundance of the TGF- $\beta$ 3 isoform in fetal wound healing, has lead researchers to identify either TGF- $\beta$ 3 as a therapeutic target to upregulate or TGF- $\beta$ 1/ $\beta$ 2 as targets to suppress for scar-less wound healing.



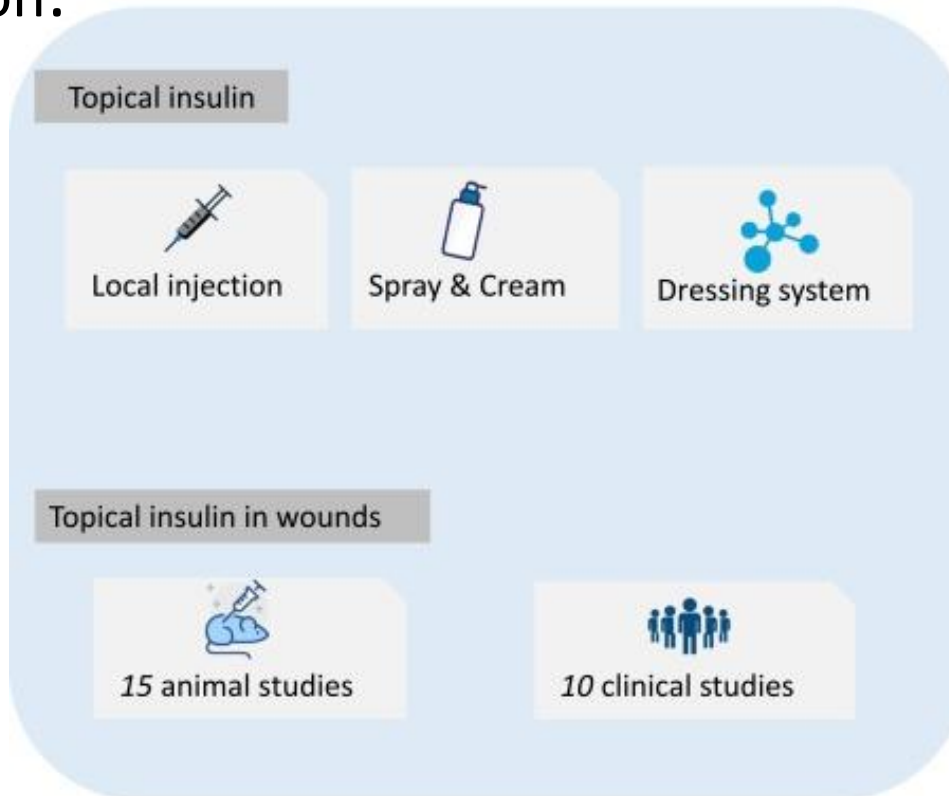
# Growth factors and cytokines, TGF- $\beta$

- Despite strong pre-clinical outcomes, current TGF- $\beta$  clinical trials have had disappointing results.
- Juvista (recombinant TGF-  $\beta$ 3) showed promise in early phase efficacy trials but failed to meet primary endpoints in a Phase III trial.
- Juvidex (inhibitor of TGF- $\beta$ 1/TGF- $\beta$ 2) also failed to meet the main study goals in a Phase II trial
- TGF- $\beta$  therapy could potentially have confounding results due to its dual importance in both normal wound healing but also in excessive fibro-proliferation.
- while blocking TGF- $\beta$  expression seems to prevent fibrosis, it can also lead to chronic, non-healing wounds.



# Growth factors and cytokines, Insulin

- Antioxidant
- Exerts anti-inflammatory effect by increasing IL-10 levels.
- Enhances keratinocyte and macrophage migration.
- Increases fibroblastic reaction.
- Clinically effective in:
  - Diabetic ulcer
  - Decubitus ulcer
  - Chronic wounds



## Efficacy



### Outcomes

- Improve wound closure
- Reduce wound healing time
- Improve wound remodeling



### Mechanisms

- Modify inflammation
- Accelerate epithelialization
- Accelerate neovascularization

## Safety



### No adverse systemic effects

- Hypoglycemia
- Hypokalemia
- Hypoaminoacidemia



### No adverse local effects

- Infection
- Pain
- Allergenicity



ORIGINAL ARTICLE

# Growth factor therapy in patients with partial-thickness burns: a systematic review and meta-analysis

Yi Zhang, Tao Wang, Jinguang He & Jiasheng Dong

Shanghai Ninth People's Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China

**Key words**

Growth factor; Partial-thickness burn;  
Wound healing

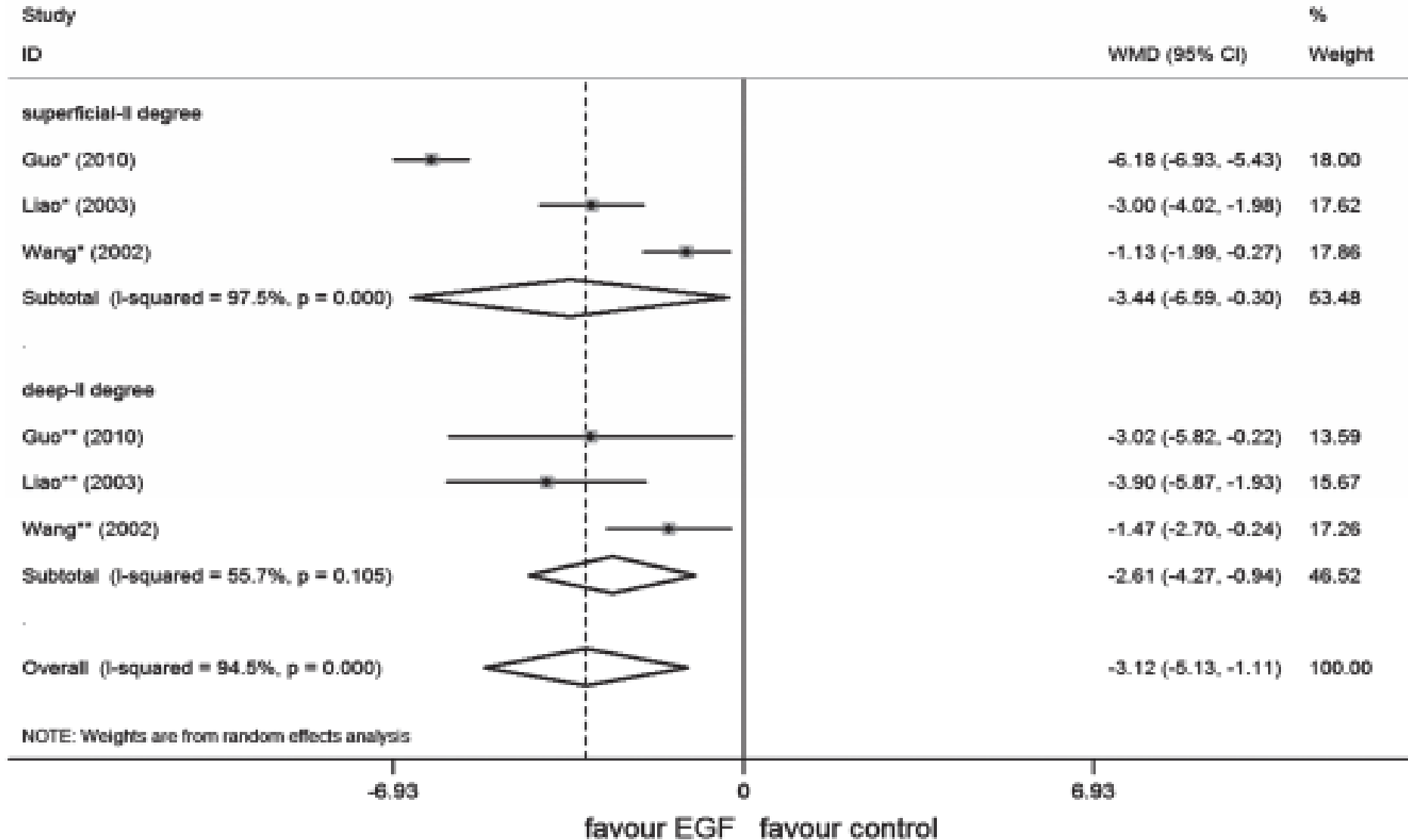
Zhang Y, Wang T, He J, Dong J. Growth factor therapy in patients with partial-thickness burns: a systematic review and meta-analysis. Int Wound J 2014; doi: 10.1111/iwj.12313



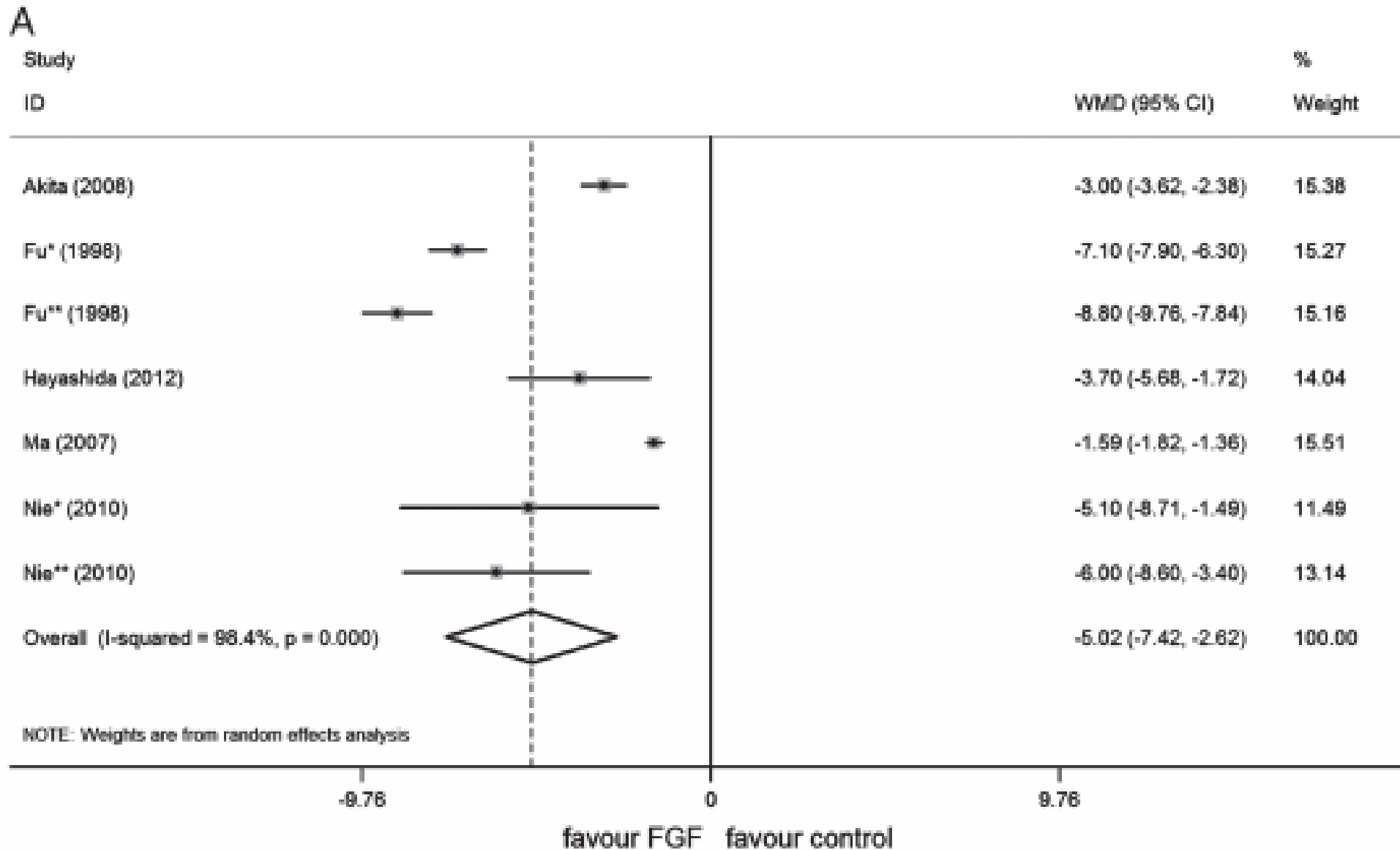


# Forest plot depicting the meta-analysis of wound healing time between growth factors (GFs) versus control group.

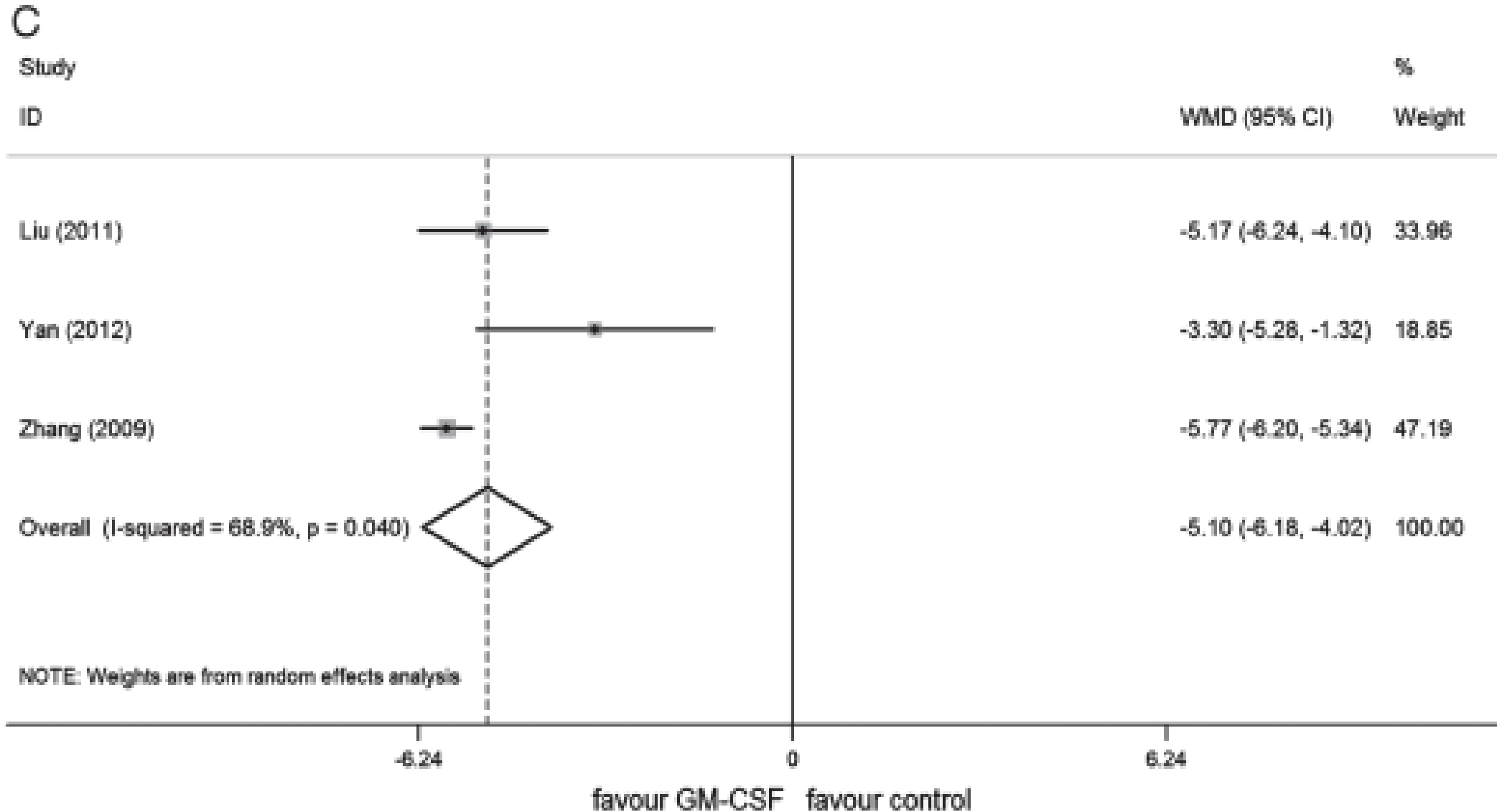
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# Forest plot depicting the meta-analysis of wound healing time between growth factors (GFs) versus control group.



# Forest plot depicting the meta-analysis of wound healing time between growth factors (GFs) versus control group.





# PRP, PRF

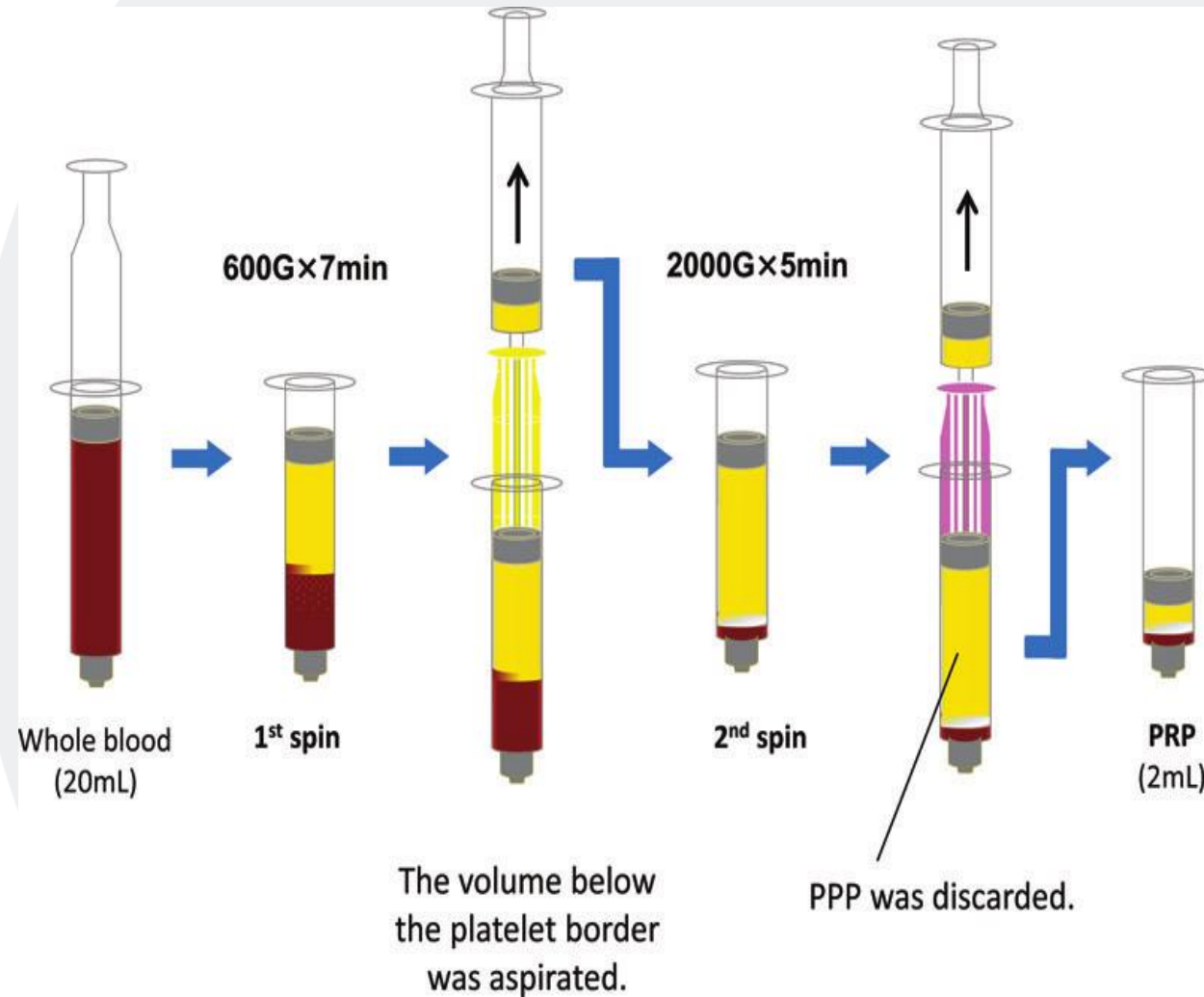


# Growth factors and cytokines, PRP

- PRP is a portion of autologous blood that contains an increased concentration of platelets (600,000 platelets/ $\mu\text{L}$ )



- Platelets releasing alpha granules that contain an abundance of growth factors such as PDGF- $\alpha\alpha$ , PDGF- $\alpha\beta$ , PDGF- $\beta\beta$ , TGF- $\beta$ , EGF, and VEGF.





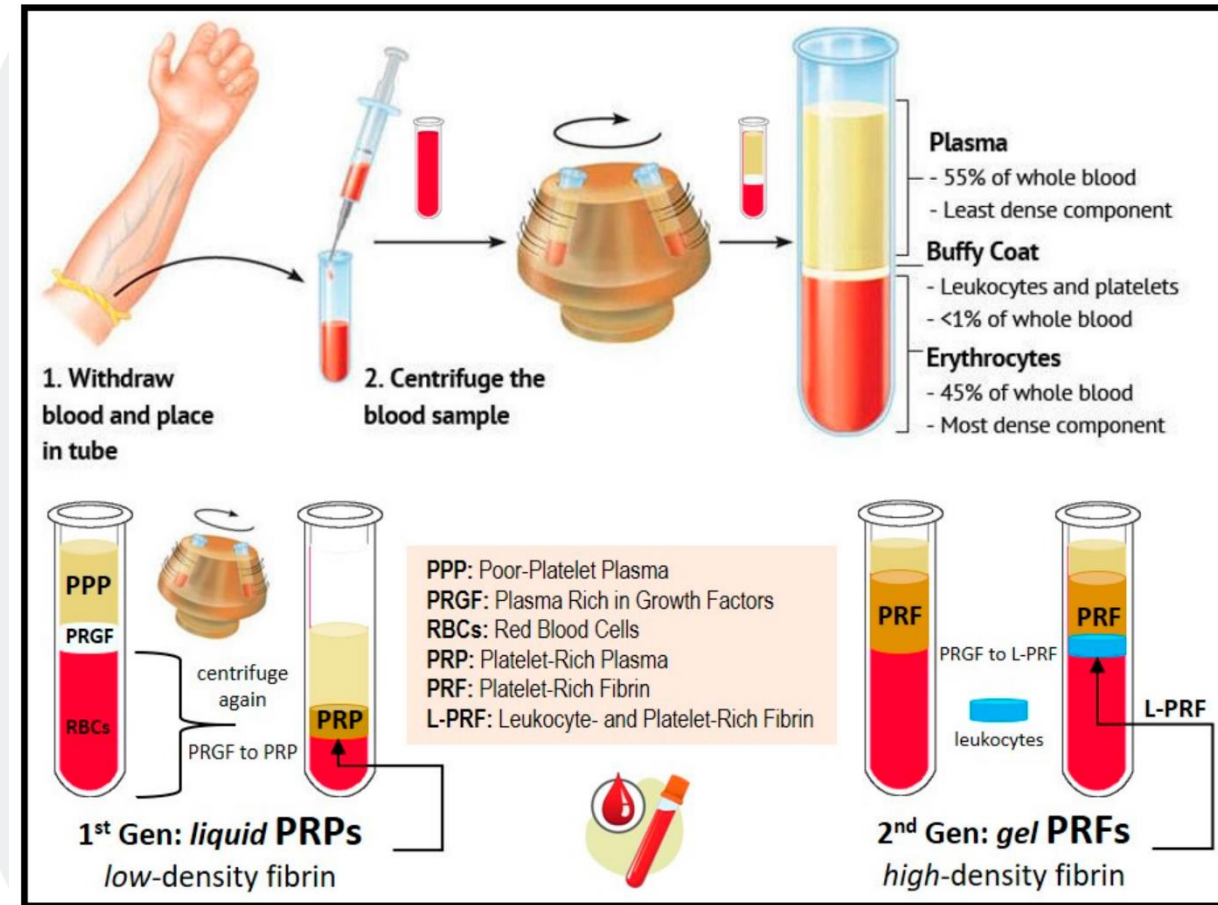
# Growth factors and cytokines, PRP

- First described by Ferrari in 1987, where it was used to seal incisions made during open-heart surgery.
- PRP is the most frequently employed growth factor product during surgery.
- PRP is effective in wound healing of mucosal surfaces, bone, and skin.
- PRP appears to improve the rate of **wound healing in healthy and diabetic** patients.
- Wounds treated with PRP exhibited accelerated wound closure and increased cellularity.



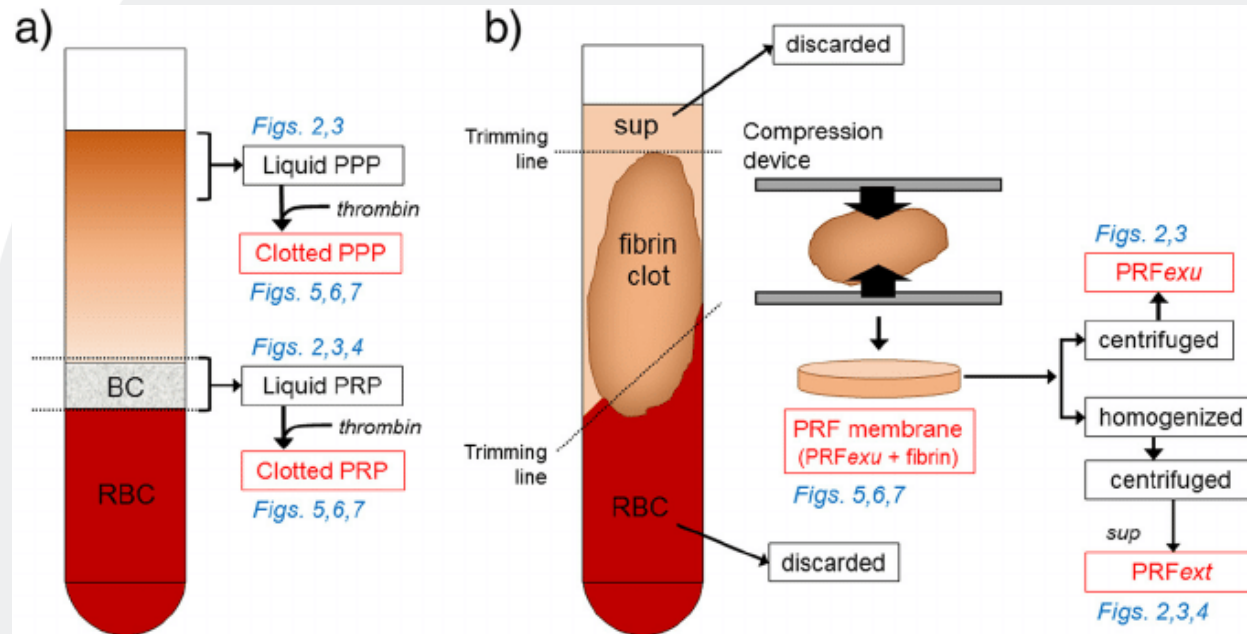
# Growth factors and cytokines, PRF

- Platelet-rich fibrin (PRF) is generated nearly identical to that of PRP.
- The main difference is that no anticoagulant or activator is used in the production of PRF.
- The final result is a platelet-charged fibrin clot that can be administered directly to the surgical site to stimulate wound healing and closure..



# Growth factors and cytokines, PRF

- Promotes hemostasis
- Promotes the secretion of growth factors
- Act as a three-dimensional scaffold to direct migration, proliferation, angiogenesis, and chemotaxis of inflammatory cells.
- Clinical application:
  - Oral and maxillofacial surgery
  - Ophthalmology
  - Dermatology (wound closure, graft survival)

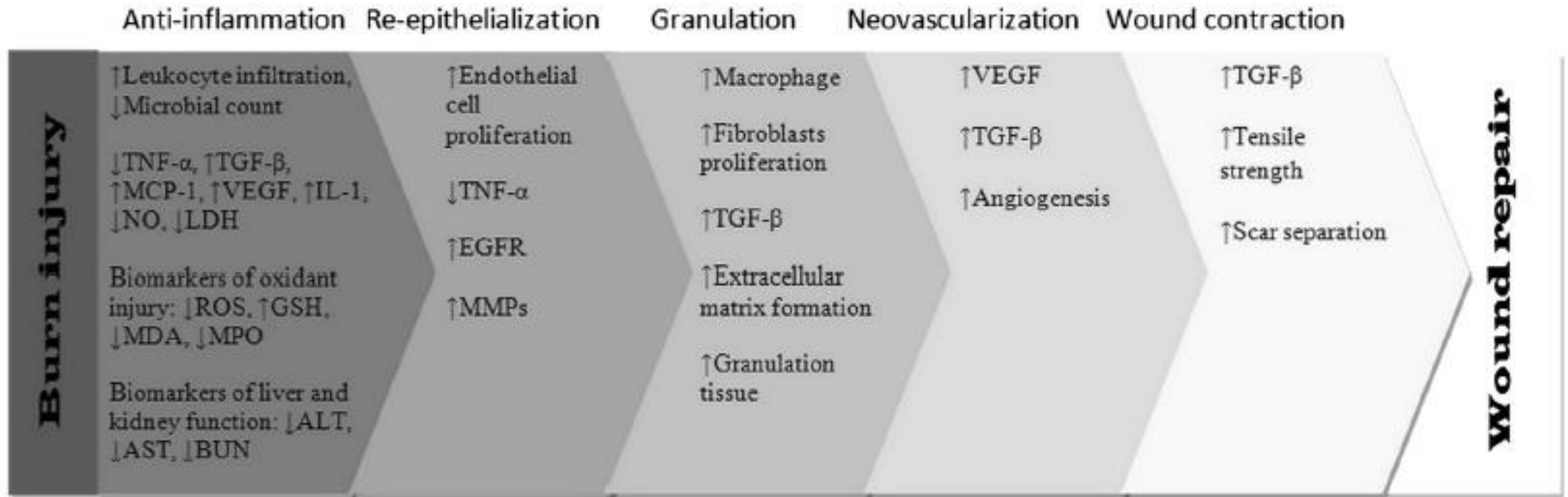




# Herbal medicine (Phytochemical)



# Herbal medicine (Phytochemical)





# Herbal medicine

Single herbal preparations with the best burn wound healing activity:

- Aloe vera
- Marigold (*Calendula officinalis*)
- St. John's Wort (*Hypericum perforatum*)
- Melilotus Officinalis (yellow sweet clover)
- Allium sativum (Garlic)
- Centella asiatica (Indian pennywort, Asiatic pennywort)
- Hippophae rhamnoides (sea-buckthorn)



# Aloe vera

- The leaf gel is either apply fresh directly to the affected area, or extracted in hot water and topically applied.
- 100% aloe being considered most effective and anything less than 50% showing little or no effect in some studies



# Aloe vera

- The gel demonstrated burn wound healing potential by anti-inflammatory effect and increasing re-epithelialization and microcirculation.
- Decreases TNF-a, IL-6 and leukocyte adhesion.
- It also showed antibacterial effect against some bacteria.
- Best effect on **superficial burn** wounds.



# Marigold (Calendula officinalis)

- The inflorescence is soaked in oil to in order to extract its essence.
- Antimicrobial, antiviral, anti-inflammatory, antioedematous, immunomodulatory effects.
- Increased levels of the chemokine IL-8 and significant decrease in collagenase activity.





# Marigold (*Calendula officinalis*)

- Clinical efficacy documented for:
  - Diabetic ulcer
  - Superficial burn
- Contraindication in those allergic to member of the daisy family (Asteraceae; Compositae).





# St. John's Wort (Hypericum perforatum)

- The common name of “St. John’s Wort” derives from the date of ritual harvest in Europe – June 23rd, the eve of the festival that celebrates John the Baptist.
- H. perforatum is made by taking dried flowering aerial parts and steeping them in vegetable oil.
- Antibacterial, antiviral, antioxidant, anti-inflammatory, and keratinocyte differentiation effects.



# St. John's Wort (*Hypericum perforatum*)

- Clinical efficacy documented for:
  - Decubitus ulcer
  - Surgical wound
- Phototoxic skin reactions if ingested or exposed to the skin, especially in fair skinned individuals.
- UV-activated hypericin exhibits necrotic and apoptotic effects on human keratinocytes and melanocytes



# Melilotus Officinalis

- Clinical efficacy documented in treatment of diabetic ulcer and burns.
- Anti oxidative and anti-inflammatory properties.





# Centella asiatica (pennywort)

- All types of pennywort extracts have positive effect on wound healing by increasing re-epithelialization and keratinization.
- The most potent one is the ethylacetate extract.



# Hippophae rhamnoides (sea-buckthorn)

- Oral and topical administration of H. rhamnoides seed oil resulted in increase in tissue regeneration, GSH, MMP-2 and 9, VEGF, collagen type-III in the granulation tissues, as well as decrease in reactive oxygen species and edema.
- Omega 3/6, fatty acids, tocopherols and carotenoids are probable active components.







# Vitamins



# Vitamin E

- Vitamin E acts as a reducing agent by scavenging free-radicals to prevent oxidative reaction that can cause tissue damage.
- Vitamin E has been demonstrated to act synergistically with antibiotics (tigecycline or daptomycin).
- Effective in post surgical wounds and diabetic ulcer.



# Other vitamins

- **Vitamin A** stimulates epithelial growth, fibroblasts, granulation tissue, angiogenesis, collagen synthesis, epithelialization, and fibroplasia. Local (topical) and systemic supplementation with vitamin A has been proven to increase dermal collagen deposition.
- **Vitamin C** directly activates the transcription of collagen synthesis and inhibits NFkB, which is responsible for the activation of a number of pro-inflammatory cytokines



# THANK YOU FOR YOUR ATTENTION



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