Pharmaceutical and Cosmetic Preparations

3rd Stage

College of Pharmacy

Lecture: 7

- Topical Exfoliation- Clinical Effects and Formulating Considerations
- Herbs in Cosmeceuticals: Are They Safe and Effective?

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Introduction

- **EXFOLIATION** by definition, to exfoliate is to remove the surface in scales or laminae. Therefore, **classical exfoliants** are those *agents that work at the skin's surface, causing the removal of skin in layers.*
- Exfoliation is characterized, based on its mechanism of action, into 3 categories:
  1. physical/manual (loofah or microdermabrasion)
  2. chemical/keratolytic agents (e.g., salicylic acid)
  3. natural/exuviation (e.g., alpha-hydroxy acids)
- **Manual or physical exfoliation** involves the use of **physically abrasive devices** such as **loofahs** and could also include instrumental techniques such as **microdermabrasion**.
- **Manual exfoliants** physically scrape and remove surface skin cells.
- Salicylic acid represents the **chemical/keratolytic** class of exfoliants.
  - Recent reviews of salicylic acid propose a change to the term "desmolytics" to more accurately reflect the action of these materials on the skin.
  - These agents dissolve the desmosomal bonds between cells, beginning at the uppermost skin layers, and provide exfoliative effects from the top of the skin downward in a nonspecific manner.





Introduction

- **Natural exfoliation**, also known as exuviation, is the naturally occurring process of epidermal turnover, which occurs approximately every 28 days.
- Compounds that **enhance the natural process of exuviation** include the **alphahydroxy acids (AHAs), polyhydroxy acids (PHAs), and bionic acids.**
  - These agents target the base of **the stratum corneum**, the layer identified as the stratum dysjunctum, and function by diminishing bonding strength between cells in a specific manner, leading to normalization of cell turnover and, thus, exfoliation.

Physical exfoliants: Scratching the surface

- Physical exfoliants involve the use of **manual implements** to erode away surface skin cells.
- Presumably, as rubbing is continued and additional force is exerted, skin cells will continue to forcibly desquamate in a non-specific manner.
- This can continue until the stratum corneum is removed and the “glistening” layer of the live epidermis is reached.
- A similar effect can be observed following repeated tape stripping, which could be thought of as a process of forced physical exfoliation.
- Common methods of **manual exfoliation** include the use of **physically abrasive materials** such as pumice, loofahs, and buff puffs. The repetitive action of shaving with a razor also serves to physically remove or exfoliate the stratum corneum.
- Newer methods of physical exfoliation, such as microdermabrasion, involve the use of sophisticated equipment that “**sandblasts**” the skin surface with particles.

Physical exfoliants: Scratching the surface

Bathing Devices

- **Buff puffs, loofahs, mesh poofs**, and, to a certain extent, **washcloths** are used by many people on a daily basis to provide varying degrees of exfoliation to the face and body.
- **The amount of exfoliation** is dependent on the force of application, the number of passes over the skin, and the abrasiveness of the material being used.

Shaving

- Shaving with a razor blade **removes hair** as well as the **stratum corneum**.
- As a result, there are many potential detrimental effects to skin, including increased risk of irritation from other topically applied products, such as antiperspirants .
- Moreover, while **shaving** seems at first to **make the skin smoother**, this process actually generates uplifting scales and increased dryness, as well as diminished barrier function in the stratum corneum and a pro-inflammatory environment in the epidermis.

Physical exfoliants: Scratching the surface

Microdermabrasion

- The closed, self-contained procedure known as **microdermabrasion** was first developed in the mid-1980s by researchers in Italy to eliminate the risk of airborne blood generated during conventional dermabrasion treatments. Microdermabrasion was approved for use in the United States by FDA in 1997 and has become one of the most popular procedures used for aesthetic skin care.
- This novel exfoliation technique utilizes a stream of aluminium oxide, sodium bicarbonate, or sodium chloride crystals that functions by "sandblasting" skin under mild suction, which serves to collect the aerosolized crystals and skin particulates for disposal.
- Depending **on the power of the machine, the number of passes of the hand piece over the skin, and/or the speed of the hand piece over the skin**, microdermabrasion can cause superficial exfoliation of the uppermost layers of the epidermis or reach the dermis, as indicated by signs of bleeding.
- Microdermabrasion has been used to treat a variety of skin conditions, including **photoaged skin, acne, hyperpigmentation, striae distensa, actinic keratosis, and keratosis pilaris.**
- Adverse events are infrequent and include pigmentation irregularities, which occur mainly in darker skin and prolonged erythema lasting beyond 24 hours.
- Many microdermabrasion protocols suggest a series of superficial procedures on a monthly or half-monthly basis in order to achieve skin benefits while minimizing the likelihood of adverse events.
- Several publications support the safe and effective use of microdermabrasion, with both dermal and epidermal benefits.

Chemical exfoliation

- Chemical exfoliants are substances that **cause superficial skin cells to desquamate** at an increased rate as a result of their ability to disrupt intercellular bonding within the stratum corneum.
- This effect on skin occurs through several different mechanisms:

❑ Exuviating Compounds:

- **Alpha-hydroxy acids, polyhydroxy acids, and bionic acids**
  - The **alpha-hydroxy acid (AHAs), polyhydroxy acids (PHAs), and bionic acids** are exfoliating compounds that enhance desquamation and cell turnover.
  - Because of the differences in their molecular structures, these compounds provide some additional benefits to the skin as described below.
  - Alpha-Hydroxy Acids—**Anti-aging Plus Exfoliation** AHAs, such as glycolic acid, lactic acid, and mandelic acid, have many beneficial effects on skin, including **enhanced exfoliation as well as reversal of photoaging.**
  - Upon topical application, AHAs have been shown to have a profound effect on **desquamation and exuviation,** the natural process of epidermal cell turnover.
  - When applied to **severely hyperkeratotic skin**, such as **ichthyosis**, AHAs at cosmetic strengths [defined by the Cosmetic Ingredient Review panel as a concentration of 10% or less with a minimum pH of 3.5 cause separation of abnormally thick stratum corneum at the base of the stratum corneum, the layer known as the stratum compactum.

Chemical exfoliation

Exuviating Compounds:

- In severely hyperkeratotic skin, the thickened stratum corneum lifts off as a sheet.
- This observation **distinguishes** the effects of AHAs from traditional, nonspecific exfoliating agents, such as salicylic acid, which diminish corneocyte cohesion throughout the entire thickness of the stratum corneum.
- AHAs have been shown to **normalize the process of exuviation**. As a result, continued use of AHAs results in a normalized rate of desquamation, and skin shedding becomes clinically lessened or non-apparent to the product user after two to three weeks.
- The mechanism of action of AHAs in promoting desquamation is postulated to be due to **activation of the naturally-occurring enzyme steroid sulfatase to facilitate conversion of cholesterol-3-sulfate to cholesterol at the level of the stratum compactum.**
- **Exfoliation of normal, healthy skin** requires the biochemical conversion of cholesterol-3- sulfate to free cholesterol in skin.
- When present at elevated levels, the more ionic molecule, cholesterol-3-sulfate, increases desmosomal bonding strength between corneocytes, thus prolonging the desquamation process.
- X-linked ichthyosis is known to be deficient in this critical enzyme

Formulating factors for the hydroxyacids

- There are several factors to consider in the formulation process to optimally and safely deliver hydroxy acids to skin.
- The AHAs, PHAs, and bionic acids are **mild, organic acids** that are optimally absorbed into skin when present in the **free acid, non-ionized form**.
- As a result, **formulation pH is extremely important**.
  - At a defined pH, the concentration of the acid and its pKa determine the amount of free acid and, thus, bioavailability, provided by a formulation.
  - As the pH of a formulation is **reduced below the pKa of the acid**, there is a significant increase in the amount of free acid that is available for penetration.
  - As a result, **the potential** to cause **sensory irritation** and **erythema increases** and must be considered in the formulation process.
  - Formulation technologies exist to **facilitate the gradual penetration of free acid into skin**, thereby diminishing irritation potential and stinging without reducing skin benefits.
    - One such technology utilizes *amphoteric amino acids during formulation pH adjustment to temporarily complex free AHA molecules and allow a more gentle delivery of the AHA with reduced irritation and stinging.*

Formulating factors for the hydroxyacids

- Another important factor in the hydroxy acid formulation process involves **selection of the specific AHA ingredient**.
- The relatively broad selection of ingredient options provides the formulator with the ability to **customize AHA solubility parameters and modify potential skin benefits**.
  - For example, the more common AHAs, including **glycolic acid and lactic acid**, are **readily soluble in water.**
  - In comparison, those with **lipophilic side** chains have **increased oil solubility** and the resultant increased potential to absorb into oily skin and pores.
    - Examples include mandelic acid (phenyl glycolic acid) and benzilic acid.

Salicylic Acid-A topical desmolytic

- Salicylic acid has been used as **a keratolytic** since the 1800s, when it was first derived from the bark of the willow tree.
- Its effects on skin are primarily limited to **enhanced shedding of the stratum corneum**, **with no increase in mitotic activity of the epidermis**.
- Salicylic acid reportedly functions by **decreasing corneocyte cohesiveness** over the entire thickness of the stratum corneum via disruption of desmosomal attachments and denaturing glycoproteins, thus the term "desmolytic."
- Aside from OTC formulations for acne, there are products designed for use in dermatologists' offices, including topical peels with concentrations of salicylic acid up to 30%.
- These products are primarily targeted for the **adjunctive treatment of acne** and are also used in **photoaging**.

Formulating factors for salicylic acid

- Salicylic acid is a somewhat **stronger acid** with **a lower pKa compared to most AHAs** due to the electron-withdrawing properties of the benzene ring.
- As a result, a lower pH should be considered to optimally formulate bioavailable products.
- However, as **pH is reduced** and **penetration is increased**, there is an **increased** likelihood of causing **irritation**.
- The concentration of use of salicylic acid in over the- counter (OTC) treatments of acne, dandruff, seborrheic dermatitis, psoriasis, and wart formulations is governed by the FDA, OTC monographs.
- These regulatory documents dictate product form, concentration, uses, directions, and warnings.
- Since these formulations are regulated as **OTC drugs**, the chemical stability of salicylic acid must be proven over the shelf-life of the formulation.
- Cosmetic formulations that make cosmetic claims, on the other hand, are **free to use varying strengths of salicylic acid**; however, the upper concentration may be limited by irritation potential.

N-acetylglucosamine: A non-acid chemical exfoliant for aging skin

- **N-acetylglucosamine (NAG)** is a water-soluble, neutral compound that can easily be incorporated into skin care formulations.
- It is found naturally occurring as a repeating unit of the abundantly available material known as **chitin** (e.g., shrimp shells).
- In human skin, it is a natural component of **GAGs, glycolipids, and membrane glycoproteins**.
- Along with glucuronic acid (a polyhydroxy acid), NAG is one of the repeating, alternating units in hyaluronic acid, the prominent GAG of skin.
- **NAG** represents a new class of **anti-aging and exfoliation compounds**.
- It's reported beneficial effects on **exfoliation occur as a result of its interaction with CD44 receptors** on corneocytes, which prevents cross-linking between cells.
- Topical application of NAG has been shown to **induce desquamation and epidermal cell turnover**, as well as increase epidermal differentiation.
- As a component molecule in **hyaluronic acid** and a potential precursor to its synthesis, **NAG** has been shown to **stimulate the synthesis of hyaluronan in fibroblasts and keratinocytes**.

N-acetylglucosamine: A non-acid chemical exfoliant for aging skin

- **Oral supplementation of NAG** (1 g orally per day vs. placebo for 60 days) reportedly reduced skin dryness and roughness, and increased moisturization.
- **Topical evaluation** of 8% NAG was shown to provide significant, clinically-assessed improvements on mild to moderate photo damage with substantial improvements in skin firmness and skin thickness.
- The latter effect is thought to be due to an increase in the production of GAGs, which increases skin volume through water binding and plumping.
- In addition to its desirable cosmetic effects, NAG was shown to be well-tolerated on skin and therefore represents a desirable new class of compounds in the growing exfoliation and anti-aging ingredient technology market.