Pharmaceutical and Cosmetic Preparations

3rd Stage

College of Pharmacy

Lecture: 6

- Sunscreens
- Anti-aging Skin Care Formulations

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Ph.D in Pharmaceutics

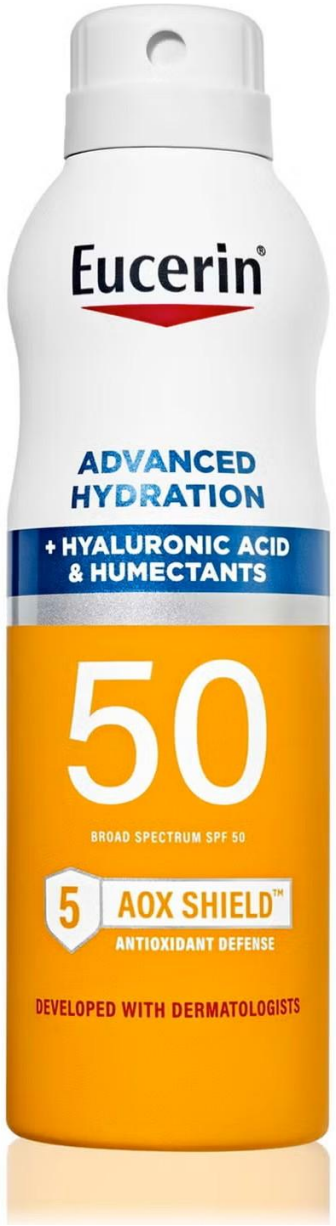
2025 -2026

Semester: 2nd

Sunscreens

Introduction to Sunscreens

- Sunlight contains **ultraviolet (UV) radiation**, and when the skin is exposed to UV without protection, **several biological effects occur**.
  - The most immediate and obvious effect is **sunburn**, which is a sign of skin damage.
  - **Long-term or lifetime exposure to UV radiation significantly increases the risk of skin cancer.**
- Sunlight also has beneficial effects, such as stimulating the production of **vitamin D** in the body.
  - Therefore, **healthcare professionals** recommend a **"safe sun" strategy**, which allows controlled exposure to sunlight while minimizing harmful effects.
- A major component of this strategy is the **use of sunscreens**.



Introduction to Sunscreens

- When UV radiation reaches the skin, its energy can be absorbed by molecules in the skin.
- This absorption may lead to the formation of **harmful chemical species** such as **60,40-DNA photoproducts and free radicals**, or dissipate the excess energy as **heat or phosphorescence** which can damage cells and contribute to **skin aging and skin cancer**.
- Sunscreens function (work) by **preventing UV radiation from interacting with these skin molecules (chromophores)**.
- Sunscreens are generally classified into **two main types**:
  - **Physical (inorganic) sunscreens** – These contain mineral particles that **reflect or scatter UV radiation** away from the skin.
  - **Chemical (organic) sunscreens** – undergo a chemical transformation, known as resonance delocalization, to **absorb UV radiation** and **transform it to heat**, thereby preventing damage to the skin.



Function of Sunscreen

- The main function of sunscreen products is to **reduce the amount of UV radiation that reaches the skin**. They achieve this by **absorbing, scattering, or reflecting UV rays**.
- This is accomplished through the use of a combination of :
  - **UV filters** (active ingredients that block or absorb UV radiation-(Table 1))
  - **A film-forming vehicle** (the base formulation that spreads on the skin and forms a protective layer)
- Whereas for most products, such as cosmetics or over-the-counter (OTC) drugs, it might be enough to simply include ingredients that have an established effect, for sunscreens, the protective effectiveness is communicated directly to consumers as the **Sun Protection Factor (SPF)**.
  - **SPF** mainly measures protection against **UVB radiation**, which has wavelengths approximately between **290–320 nm** and is responsible for **sunburn (erythema)**.
- However, protection against long-wavelength UV **UVA-I (340–400 nm), (340–400 nm)** is also important because UVA contributes to **skin aging and long-term skin damage**.
- For consumers, the most recognized and understood skin response to sunlight exposure is erythema or “sunburn” which is why SPF is based on the skin’s erythema response.

Understanding SPF

- The **Sun Protection Factor (SPF)** is a numerical value that indicates how well a sunscreen protects the skin from UV radiation.
- Regulatory authorities such as the **U.S. Food and Drug Administration (FDA)** regularly evaluate sunscreen filters, and some ingredients may be removed if they are found to be unsafe or ineffective.
- SPF is defined as the **ratio between the UV dose needed to produce minimal redness (erythema) on protected skin compared to unprotected skin**.
- This redness threshold is called the **Minimum Erythema Dose (MED)**. It is the **smallest amount of UV radiation that produces visible redness on the skin**.

Mathematically:

$$SPF = \frac{MED\ on\ protected\ skin}{MED\ on\ unprotected\ skin}$$

- This redness is:
  - **Uniform** (even across the exposed area)
  - **Barely perceptible** (just noticeable, not severe sunburn)

Understanding SPF

- The SPF can be represented as a percent of erythemally-weighted UV transmitted, i.e., 1/SPF ×100, or **percentage of UV radiation blocked by the sunscreen**. i.e., 1-(1/SPF) ×100
- For example:
  - **SPF 15** blocks about **93.3% of UV radiation**
  - **SPF 30** blocks about **96.7% of UV radiation**
- This shows that although the SPF number doubles, the increase in protection is relatively small (only about **3% more UV blocked**).

Table 1: Approved UV filters

UV filter	Up to % concentration
Aminobenzoic acid or PABA	15
Avobenzone or butyl methoxydibenzoylmethane	3
Cinoxate	3
Dioxybenzone	3
Homosalate	15
Menthyl anthranilate or meradimate	5
Octocrylene	10
Octyl methoxycinnamate or octinoxate	7.5
Octyl salicylate or octisalate	5
Oxybenzone or benzophenone-3	6
Octyl dimethyl PABA or padimate O	8
Phenylbenzimidazole sulfonic acid or ensulizole	4
Sulisobenzone	10
Titanium dioxide or TiO_2	25
Trolamine salicylate	12
Zinc oxide or ZnO	25

- These filters are on regular check-up by the FDA, and accordingly, some of them could be removed.

Limitations of the SPF Test

- However, SPF has several important **limitations**:

I. SPF is measured under artificial conditions:

- The SPF test is done using:
  - an **artificial UV light source**
  - a **fixed dose of radiation**
  - a specific **endpoint: erythema (redness)**
- This means the results are obtained in **controlled laboratory conditions**, which may not perfectly represent **real sunlight exposure**.

II. SPF is a number that can be misleading

- SPF is a **numerical value**, but people often **over interpret small differences**.
- For example:
  - **SPF 12 vs SPF 17** looks very different numerically.
  - But **biologically, the protection may be almost the same**.
- Additionally, SPF values can change depending on:
  - the **type of light source used**
  - **testing conditions**
  - **natural sunlight vs solar simulator**

Limitations of the SPF Test

III. SPF does not increase linearly

- SPF values are **non-linear**.
- For example:
  - **SPF 30 does NOT give twice the protection of SPF 15**
  - Protection increases gradually but **not proportionally**.

IV. SPF does not guarantee protection against UVA

- This is one of the **most important limitations**.
- SPF mainly measures protection against **UVB**, but it does **not assure protection against UVA radiation (340–400 nm)**.
- UVA radiation:
  - penetrates deeper into the skin
  - contributes to **skin aging and skin cancer**
    - Because **in vivo UVA testing is difficult**, researchers often use **in vitro methods**, where sunscreen is applied to a surface and UV transmission is measured using spectrophotometry.
    - This allows scientists to calculate a **"metric" for UVA protection**, although it is not exactly the same as testing directly on human skin as such, cannot provide quantitative information regarding "protection."
    - Substrate spectrophotometric methods for measuring sunscreen absorption have several advantages. They are **cost-effective, reproducible**, and **do not require exposing human subjects to artificial filtered light**, whose potential health risks are uncertain.
    - In addition, **in vitro spectrophotometric results provide useful complementary data** to the **in vivo Sun Protection Factor (SPF) measurements**, helping to better evaluate sunscreen effectiveness.

Active Ingredients: UV Filters

- The **active ingredients in sunscreens are UV filters**. These substances protect the skin by:
  - **absorbing UV radiation**
  - **reflecting UV radiation**
  - **scattering UV radiation**
- Usually, sunscreens contain a **combination of UV filters** to achieve:
  - the desired **SPF**
  - **broad spectrum protection** (both UVA and UVB)

➢ **Wavelength coverage**

- To achieve **SPF 15**, filters must absorb UV light in the range: **290–340 nm (UVB region)**
- However, if we want **UVA protection (340–400 nm)**, fewer ingredients can do this effectively.
  - Specifically, one must select either:
    - **Avobenzone**
    - **Zinc oxide**
      - These are important for **long-wavelength UVA protection**.

Active Ingredients: UV Filters

- **Higher SPF requires more filters**
  - As the **SPF value increases**, the sunscreen usually contains:
    - **more UV filters**
    - **higher concentrations of UV filters**
  - Typical examples:
    - **SPF 15:** about **10–15% UV filters**
    - **SPF 45:** may require **30% or more**
  - So generally:
    - **Higher SPF = higher concentration of UV-filter ingredients**

Sunscreen Products and Formulation

- The goal when designing a sunscreen product is to achieve several things simultaneously:
  - the desired **SPF**
  - **broad spectrum protection** (UVA + UVB)
  - **water resistance**
  - **good skin feel and cosmetic acceptability**
  - **reasonable cost**
- From an ingredient standpoint, most sunscreen products are typically very similar to conventional lotions or creams, with the key difference being the addition **of 4% to 40% sunscreen actives**

Sunscreen Products and Formulation

➢ Types of UV filters used in formulations

- From a formulation perspective, the current list of UV filters can be categorized into one of four groups based on the **physical properties** of the active:

1. **Polar oils filters**
   - Examples: **Octinoxate**, **Octisalate**, **Homosalate**, **Octocrylene**
   - These dissolve in the **oil phase** of formulations
2. **Oil-soluble crystalline solids**
   - Examples: **Avobenzone**, **Benzophenones**
     - These are solids but dissolve in oils.
3. **Water-soluble salts**
   - Example: **Ensulizole**
     - These dissolve in the **water phase** of the product.
4. **Insoluble powders/particulates (mineral filters)**
   - Examples: **Zinc oxide**, T**itanium dioxide**
   - These work mainly by **scattering and reflecting UV radiation**.

Sunscreen Products and Formulation

- In sunscreen formulations, **UV filters can make up a very large portion of the product (sometimes up to 40% in high SPF sunscreens)**.
- Because they are present in such high amounts and have different **physical and chemical properties**, the **choice and combination of these UV filters become the most important factor in formulation**.
- The selected UV filters influence several key aspects of the product: **Cost, Skin compatibility, Aesthetics / skin feel**
- Therefore, formulators must carefully **select and combine different UV filters** to achieve the desired **SPF protection while maintaining acceptable cost, safety, and pleasant skin feel**.

Cost

- The higher the level of sunscreen actives in a formulation, the greater the formula cost, and hence the more marketers charge for the product.
- As a result, manufacturers try to balance:
  - The level of protection (SPF value)
  - The cost of the formulation

Skin Compatibility

- Along with fragrances and dyes, UV filters, particularly organic moieties, are known to elicit irritant responses in subjects predisposed to such skin reactions.
- It is generally desirable, therefore, to reduce to a **minimum the concentration and number of UV filters** present in a sunscreen product formulation to minimize the risk of these types of incompatibilities.

Effects on Skin Feel (Product Aesthetics)

- Each type of sunscreen active described above can have a **negative** impact on the sunscreen product **skin feel**, with higher levels having a corresponding larger effect.
- Specifically, the general skin-feel tradeoffs of the various types of sunscreen actives are:
  - Certain **polar UV filters** tend to make products feel **oily or greasy**, especially when used at high concentrations.
  - To dissolve some Oil-soluble crystalline solids sunscreen ingredients, formulators must add high levels of **olvents or emollients**. These ingredients can make the product **sticky on the skin**.
  - Some sunscreen ingredients contain **water-soluble salts**, which reduce the effectiveness of thickening agents. To compensate, formulators add **more polymer thickener**, which can make the product feel **heavy**.
  - **Insoluble powders** such as mineral UV filters can create a **dry or draggy sensation** when the product is spread on the skin. These powders can also produce the well-known **white cast** on the skin, which many consumers find undesirable.

Effects on Skin Feel (Product Aesthetics)

- Another important point is that sunscreens often leave a **film on the skin**.
  - In normal lotions and creams, the main ingredient is **volatile components** (such as water) which is **volatile** and evaporates after application. This leaves only a **thin layer of non-volatile ingredients** (such as moisturizers, emollients, and preservatives) on the skin, so the product feels **light**.
  - However, in **sunscreen formulations**, large amounts of **UV filters** are added to achieve protection levels such as **SPF 15 or SPF 30**. Because these UV filters are **non-volatile**, the amount of water in the product is reduced. After application, **more material remains on the skin**, creating a **thicker layer** that gives a **"coated" or heavy feeling**.
  - Even if technologies reduce **greasiness or stickiness**, the coated feeling can still occur because of the **high level of non-volatile ingredients**.
- Due to this discomfort, some people **apply less sunscreen or reapply less often**, which **reduces the effectiveness** of sun protection. Therefore, **cost, skin compatibility, and skin feel** are very important because they influence patient compliance and affect **how correctly and consistently people use sunscreen** either directly, viz amount of product applied and frequency of application/reapplication, or indirectly in decisions related to repurchasing the product

Formulation Challenges

- To overcome these issues, scientists have developed several **formulation strategies**.

❑ **Film-Forming Technologies**

- Special **film-forming agents** help sunscreen spread evenly across the skin.
- For example, the use of film formers, better wetting/spreading emollients, and shear thinning rheology modifiers allows sunscreen products to spread more evenly and form a uniform film on the skin.
- A **uniform film** ensures there are **no gaps or holes**, which improves UV protection.

❑ **Combination of UV Filters**

- Using a **combination of UV filters in both oil and water phases** of emulsions helps ensure **even distribution** and prevents unprotected areas.

❑ **Photostable UV Filters**

- Some UV filters **break down when exposed to sunlight**. Scientists try to develop **photostable sunscreen active combinations which allows lower concentrations of UV filters to be used to achieve a UV efficacy target** so that protection remains effective during sun exposure.
- If filters are not photostable, **higher concentrations must be used** to compensate for degradation.

Improving Sunscreen Product Aesthetics

- Several approaches are often utilized to manage the trade-offs of the various sunscreen feels on the skin. These include:
  - The use of **cosmetic powders** to reduce the **greasiness** of the oily UV filters or solvents. These powders can absorb oily materials and give the product a **drier skin feel**.
  - Adding oil-soluble film-forming polymers to **thicken the oily sunscreen** actives and solvents/emollients, thus reducing the slick/oily/greasy feel on the skin. Such polymers are also important as they increase the efficiency/efficacy of the sunscreen product by **improving uniform skin coverage or film.**
  - Incorporating silicone **emollients** to reduce the **draggy, dry skin feel** of zinc oxide and titanium dioxide sunscreen actives
  - Scientists also develop alternative product forms to minimize product skin feel negatives, such as using rub-free sprays

Regulatory Issues

Finally, sunscreens are subject to **strict regulations**.

- In the **United States**, sunscreens are regulated by the **Food and Drug Administration (FDA)**. They are classified as **Over-the-Counter (OTC) drugs** required to abide by the monograph regulating such products
- The OTC Drug Monographs establish conditions for safe and effective self-treatments
- These are regulatory standards for marketing of nonprescription drug products not covered by New Drug Applications (NDAs). Products marketed in accordance with the monograph do not require FDA approval.
- In **Iraq**, sunscreens are also classified as **OTC products**, meaning they can be sold **without prescription** and their distribution is not limited to community pharmacies.
- However, regulation is handled by the **Central Organization for Standardization and Quality Control**, rather than the Ministry of Health.

Anti-aging Skin Care Formulations

Anti-aging Skin Care Formulations

Introduction

- Many **cosmetic** materials are claimed **to have anti-aging effects when used topically**.
- **Anti-aging** is a very broad term used for methods that **slow down, prevent, or improve visible signs of aging**, especially on the skin. It generally covers two main approaches:
  - **Prevention** – actions taken early to **delay aging signs**, such as protecting the skin from damage.
  - **Improvement (correction)** – treatments or products that **reduce existing signs of aging**, such as wrinkles, sagging skin, uneven texture, dullness (sallowness), or hyperpigmentation.



Vitamin A

Forms

- Several forms of vitamin A are used cosmetically.
- The most widely utilized ones include **retinol, retinyl esters** (e.g., retinyl acetate, retinyl propionate, and retinyl palmitate), **and retinaldehyde**.
- Through endogenous enzymatic reactions, all of these are **converted** ultimately to **trans-retinoic acid** (trans-RA), which is the **active form of vitamin A in skin**.

Mechanisms

- Trans-RA is the active form of vitamin A in skin.
- Trans-RA works by entering skin cells and binding/interacts with **nuclear receptor** proteins described as RA receptors and retinoid X receptors, which can form heterodimer complexes.
- These **complexes** then interact with **specific DNA sequences** to affect transcription, they can increase or decrease the production of certain proteins and enzymes.
- Some specific changes induced by retinoid that are likely relevant to skin antiwrinkle benefits are those that result in thicker skin to diminish the appearance of fine lines and wrinkles.



Mechanisms

- Retinoids improve skin structure through several mechanisms:
  - **Increased epidermal proliferation and differentiation**
    Retinoids stimulate skin cells to **divide and mature faster**, which makes the **epidermis (outer skin layer) thicker** and healthier.
  - **Increased production of epidermal ground substance**
    They increase substances in the skin that **bind water** . This **improves skin hydration** and further **thickens the epidermis**.
  - **Increased dermal production of extracellular matrix components**
    Retinoids stimulate the dermis to produce more **collagen and other extracellular matrix components**, which **strengthen and thicken the dermis**.
    - **Result:** Thicker, more hydrated skin with increased collagen helps **reduce fine lines and wrinkles and improves overall skin texture**
  - In addition to stimulation of events in the skin, retinoids can also have an **inhibitory effect** on other tissue components. For example, retinoids are reported to **inhibit the production of collagenase**.

Efficacy

- Since retinoids are irritating to the skin, and is better tolerated by the skin than trans-RA.
- Since retinoids tend to be fairly potent, topical doses of less than 1% are generally sufficient to obtain significant effects.

Product/Formulation Challenges

- There are two primary challenges in working with retinoids:
  1. **induce skin irritation** negatively affects skin barrier properties
     - Retinoids can irritate the skin and weaken the skin barrier, especially at high concentrations. Although higher doses improve anti-aging effects, irritation limits how much can be used.
     - To reduce irritation, may be managed to some extent with appropriate formulation to meter delivery into the skin:
       - Use **retinyl esters** (milder forms of retinoids)
       - inclusion of other ingredients (e.g., those **with anti-inflammatory activity**) to calm the skin.
  2. Instability, especially to oxygen and light.
     - Thus, to ensure stability of retinoid in the finished product:
       - formulation and packaging must be done in an **environment that minimizes exposure to oxygen and light.**
       - The final product packaging also ideally needs to be **opaque and oxygen impermeable**, including the use of a small package orifice to reduce oxygen exposure once the container is opened.
       - In addition, a variety of other strategies can be employed, e.g., encapsulation of the retinoid and inclusion of stabilizing antioxidants.

Vitamin B3

Forms

- Three primary forms of vitamin B3 have found effective in skin care products:
  - niacinamide (aka nicotinamide)
  - nicotinic acid
  - nicotinate esters (e.g., myristoyl nicotinate, benzyl nicotinate).

Mechanisms

- Vitamin B3 serves as a **precursor** to a group of **endogenous enzyme cofactors**, specifically nicotinamide adenine dinucleotide (NAD), its phosphorylated derivative, and their reduced forms, which have antioxidant properties.

Efficacy

- Topical niacinamide improves other aspects of aging skin, such **as reduction in sebaceous lipids** (oil control) and **pore size**, which likely contribute at least in part to improved skin texture.
- Additionally, niacinamide **improves skin's elastic properties** as demonstrated for two parameters of skin elasticity.
- Beyond these effects, there is also **improvement in the appearance of skin color** (reduction in hyper pigmented spots and reduced skin yellowing) as noted above.
- Fairly high doses (2–5%) of vitamin B3 have been used to achieve desired benefits. However, since there is a very high tolerance of the skin to niacinamide, even with chronic usage, **high doses can be used acceptably**

Product/Formulation Challenges

- The main challenge when formulating products with **niacinamide or nicotinate esters** is preventing their **conversion (hydrolysis) into nicotinic acid**.
  - **Nicotinic acid** can cause **skin flushing** (redness, warmth, and irritation), even at very low concentrations.
    - To reduce this risk, products should be formulated at a **pH between 5 and 7**, where **hydrolysis is less likely**.
- For **nicotinate esters**:
  - Many types break down quickly into nicotinic acid on the skin, causing **rapid flushing within seconds or minutes**, even at about **1% concentration**.
  - **Longer-chain esters** (such as **myristoyl nicotinate**) are **more stable** and break down more slowly, so they are **better suited for topical skincare products**.
- The formulation must prevent formation of **nicotinic acid** to avoid skin redness, mainly by **controlling pH and choosing more stable ester forms**.



Vitamin C

Forms

- Vitamin C is used in different forms in cosmetic products, including:
  - **Ascorbic acid** (pure vitamin C)
  - **Ascorbyl phosphate** (magnesium or sodium salts)
  - Other ascorbate derivatives such as **ascorbyl palmitate** and **ascorbyl glucoside**.

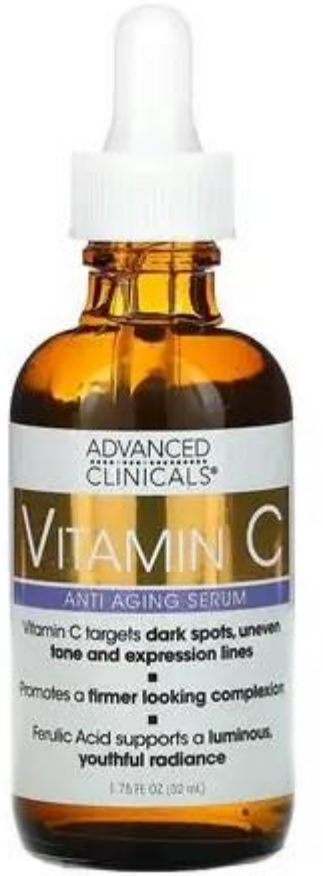
Mechanisms

- Vitamin C benefits the skin by:
  - Vitamin C is well known as an **antioxidant protects** skin from oxidative damage
  - Vitamin C has been utilized as a **skin lightener** (e.g., via tyrosinase inhibition and/or its antioxidant **effect an enzyme involved in melanin production**)
  - Providing **antiinflammatory properties** since it reduces the erythema associated with post-operative laser resurfacing.
  - In addition also serves as an essential **cofactor for the enzymes lysyl hydroxylase and prolyl hydroxylase**, both of which are required for collagen (Types I and III) biosynthesis, increasing the production of collagen and hence **wrinkle reduction**.

Vitamin C

Efficacy

- The reported **doses of vitamin C** tested are **fairly high.**
- Vitamin C, especially ascorbic acid, is **unstable and easily oxidizes** in formulations.
- In oil-in-water emulsions, about 50% may **degrade within a month**.
- Using **oxygen-impermeable pac**kaging (e.g., aluminum tubes) can **improve stability and reduce vitamin C loss** to less than 10%.



Vitamin C

Product/Formulation Challenges

1. The key challenge with vitamin C compounds in general is **stability** (oxygen sensitivity), particularly with ascorbic acid. Not only does oxidation lead to loss of the active material, but there is also **rapid product yellowing** (an aesthetic negative for the consumer).
   - Various stabilization strategies can be attempted to address the issue, such as **exclusion of oxygen during formulation, oxygen impermeable packaging, encapsulation, low pH, minimization of water, and inclusion of other antioxidants.**
   - Despite all those approaches, in general, ascorbate stability remains a challenge, and some of these approaches (e.g., very low pH) can lead to **unwanted aesthetic skin effects** as noted above.
2. **High Salt Content in Derivatives** :
   - For the **ascorbyl phosphates** (Mg and Na salts), the resulting **high content of salt in the product** can dramatically **impact the thickener system**, requiring increased use of thickener ingredients. These ascorbate derivatives are also considerably **more expensive** than other ascorbate compounds.
3. **Poor Skin Penetration** Another challenge is skin delivery.
   - Ascorbic acid's **penetration across skin is, in general, poor** (typically less than 1% of the topical dose entering skin).
   - For the phosphate derivatives of ascorbate, skin penetration can be an even greater challenge due to the **negative charges** on the phosphate moiety.
   - ➢ Therefore, **penetration enhancers** or special delivery systems are often needed.

Peptides

Forms

- There is a limitless array of possible peptides, based on amino acid sequence, number of amino acid residues, and use of derivatives/isomers of these residues.
- Among them are a few that have received particular focus in the cosmetic industry.
- They are palmitoyl-lysine-threonine-threonine-lysine-serine (pal-KTTKS; Matrixylw), acetyl-glutamate-glutamate-methionine-glutamine-arginine-arginine (Ac-EEMQRR; Argirelinew), and the tripeptide copper glycine-histidine-lysine (Cu-GHK).



Mechanisms

- Both KTTKS and GHK are fragments of dermal collagen and have been shown to stimulate the production of collagen and thus have been discussed in regard to wound healing. Incorporation of long-chain lipophilic residues such as palmitoyl onto peptides can dramatically improve their delivery into skin, e.g., the observed five- to six-fold increase in delivery of palmitoyl peptides versus their underivatized versions. Thus, pal-KTTKS was synthesized specifically for the topical use of this peptide.

Ac-EEMQRR is described as a mimic of botulinum neurotoxin (Botox), which functions by inhibiting neurotransmitter release, thus “relaxing” the muscles involved in defining facial wrinkles (53).

Peptides

Efficacy

- The peptide pal-KTTKS is quite potent clinically, providing effects from very low topical doses, and it does not induce skin irritation responses (no redness, dryness, burn, sting, or itch responses). In contrast to the potency of pal-KTTKS, the reported effects of other peptides require much higher doses, such as 2% for Cu-GHK and as high as 10% for Ac- EEMQRR.

Product/Formulation Challenges

- An important challenge is delivery into the skin since peptides are poorly penetrating, especially as the number of amino acid residues increases. An approach to that problem is the addition of a lipophilic chain (e.g., palmitate), which in the case of KTTKS increased skin penetration several-fold over the underivatized peptide.
- An additional challenge is the cost. As the number of amino acid residues increases, the cost of the peptide can increase dramatically. The consequences are that only low levels of peptide can be used in the product (which is acceptable if the peptide is potent, as in the case of pal-KTTKS) or the finished product cost to the consumer must be very high

Dimethylaminoethanol (DMAE)

Mechanism

- DMAE (also known as deanol) is a precursor to acetylcholine, a neurotransmitter involved in increased muscle tone. There could be firming of the skin via effects on the facial musculature. In addition, acetylcholine may affect the keratinocytes (specifically their proliferation, adhesion, and motility), leading to “epidermal contractility,” leading to a firming/tightening effect on the skin. DMAE also has antioxidant properties, which may contribute to its anti-aging effects.

Product/Formulation Challenge

- DMAE, a base, has historically been used as a formula pH-adjusting agent. Its pH is approximately 10. Thus, pH adjustment to the desired value appears to be sufficient.

Kinetin (N6-Furfuryladenine)

Mechanisms

- Kinetin is a plant hormone. It is a powerful natural antioxidant with effects in protecting DNA and protein from oxidative damage. Even very low levels (ppm) delay the onset of changes associated with cell aging, e.g., appearance of lipofuscin, appearance of multinucleate cells, and microtubule disorganization.

Efficacy

- Topical 0.1% kinetin was reported to improve several aging skin problems, such as wrinkling, poor texture, and hyperpigmentation. The 0.1% dose is well tolerated by the skin, with no significant irritation issues described.

Product/Formulation Challenge

- The limitation with kinetin is its fairly low solubility in formulation. This restricts the upper dose to approximately 0.1% for an aesthetically elegant formulation. This also impacts delivery into skin, although even from this Relatively low dose, sufficient material does enter skin to provide clinical effects.

Triterpenoids

Forms

- There are numerous plant-derived triterpenoid compounds and derivatives of them, with a few receiving attention in the cosmetic area, e.g., asiatic acid, ursolic acid, medacassic acid, oleanolic acid, betulinic acid, and boswellic acid. There are also naturally occurring saccharide esters of these, such as asiaticoside, which is the ester of asiatic acid.

Mechanisms

- There are many reported mechanisms for triterpenoids, for example, antioxidant, anti-inflammatory, elastase inhibition, wound healing, and promotion of collagen and ceramide production. Since triterpenoids share some structural similarity to steroidal compounds such as hydrocortisone, they may also share some of the mechanistic properties and potency of such compounds (e.g., anti-inflammatory effects).

Product/Formulation Challenge

- The key issue with triterpenoids is poor solubility, which also results in limited skin delivery. Formulation in liposomes has been employed to improve both delivery and formula solubility, although the resulting increase in oil content of the formulations may negatively impact the aesthetics.

Ubiquinone (co-enzyme Q10)

Mechanism

- Ubiquinone is an endogenous antioxidant present throughout the body, including the skin. The levels decrease with age. Topical ubiquinone replenishes the skin.

Efficacy

- The skin care benefits of topical ubiquinone address only the antioxidant properties of this ingredient.

Product/Formulation Challenge

- Ubiquinone is yellow-orange in color. Thus, only low doses (1%) can be used in topical cosmetic skin care products to avoid aesthetic color concerns. This low dose likely limits the benefit potential of this ingredient.