



A REVIEW ON COSMECEUTICAL PRODUCT

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ABSTRACT

There is already a vast variety of cosmeceutical products on the market, however the literature frequently lacks data to support their usage. In particular, there is a lot of evidence for tretinoin's effectiveness in treating photoaging, but there is less proof for retinoid-based cosmetic products. The authors assess the most recent information about vitamin A-derived cosmeceutical products in the literature and draw their conclusions. that extensive randomised, controlled research have demonstrated that cosmeceuticals containing retinaldehyde have the most favourable impact on ageing skin.

INTRODUCTION

It is human nature to desire beauty. As such, the use of cosmetics and personal care products can be traced back to ancient times where ingredients such as milk, honey, lemon juice, clay, mud and even arsenic have been used in the name of beauty. In the present days, the cosmetics and personal care industry is a vital industry that contributes significantly to the world gross domestic product(GDP). Figure 1 shows the snapshot of the global market size for the cosmetics, toiletry and fragrance industry for 2010.

The term 'cosmeceutical' is becoming more commonplace in the world of natural organic skincare. The word describes a product that is a cross between a *cosmetic* and a *pharmaceutical*. A cosmeceutical is essentially a skincare product that contains a biologically active compound that is thought to have pharmaceutical effects on the skin.

In other words, you might think that that lavender extract in your skincare is just there to make it smell nice, but actually the manufacturer might have included it for some of its active chemical compounds that have anti-inflammatory or antibacterial properties.

This concept shouldn't come as any surprise. The huge booming global market for natural skincare has demonstrated that consumers are keen to move away from what they see as skincare filled with synthetic chemicals. Along with a growing interest in organic food, clothes and other wares, consumers are now also starting to seek out natural organic skincare. The concept of a cosmeceutical fits perfectly within this ethos.

However, this hot new concept hasn't made government bodies responsible for medicinal drugs very happy. Legally, the concept of a cosmeceutical has no leg to stand on. The US Food and Drug Administration does not recognise "any such category as 'cosmeceuticals'".

In the EU, cosmetics legislation envisages that a cosmetic product may have a secondary preventative (but not curative), purpose. Any skincare product that branded itself as a medicine would require authorisation and horrendously expensive testing in order to be sold anywhere in the world.

NEED FOR STUDY ON COSMECEUTIALS

Maintaining a youthful and healthy appearance. Ultimately as the population in the world of the Now a day it's not just the interest of people but certainly has become the need of the people median age increases there is rise in the demand of the cosmeceuticals. Over 560 million people in India are age group–18-35 years. As the median age increases, the market is going to boom, especially the growing number of women in the workforce feeling the hassle to maintain a youthful and vibrant appearance. This has resulted in rapid growth of cosmeceuticals in the natural personal care industry.

As there is constant growth in the global market, a lot of money is playing in the hands of people at the same time, and there is an increase in the population with higher qualifications and knowledge; thus, this class of population has become more beauty-conscious and is spending a large amount of their earnings in maintaining a youthful appearance, that is, in cosmeceuticals. Thus, the cosmeceutical market has become one of the fastest-growing markets worldwide. Developments in technology and the invention of new ingredients have further contributed to the progress in the commercialization of cosmeceutical products worldwide. The market that reached to the mark of US\$ 27.2 Billion in 2010 is likely to augment at a rapid pace in the coming years with anti-aging skin care taking the top spot in revenue patterns

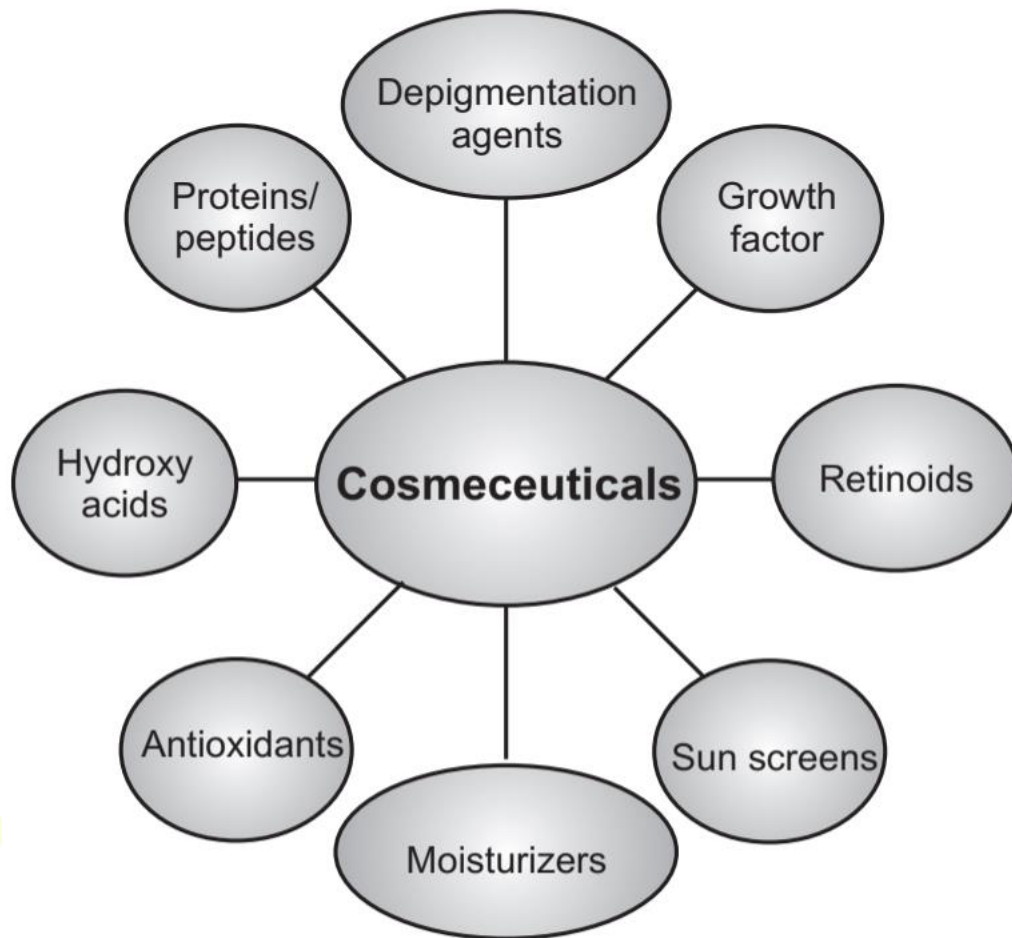
Effect of ROS (Reactive oxygen species) on skin

Ultraviolet (UV) radiation is a portion of the electromagnetic spectrum that lies between rays and visible light, that is, between 40-400 nm (30-3 eV).

The UV spectrum was divided into five spectra: Vacuum UV (40-190 nm), Far UV (190-220 nm), Ultraviolet C [UVC] (220–290 nm), Ultraviolet B [UVB] (290-320), and Ultraviolet A [UVA] (320-400 nm). UVA can be further divided into two subsections: UVA I (340-400 nm) and UVA. Solar UVR at the Earth's surface comprises roughly about 95-98% of UVA and 2-5% of UVB, and all UVC is absorbed by stratospheric ozone. The frequency of ultraviolet type B or UVB radiation is mainly responsible for the erythema of sunburn and suntan on the skin. Once the human skin is exposed to UVB, it is absorbed by the DNA of keratinocytes. Its high-energy radiation, which is dependent on its wavelength, causes not only sunburn but also skin aging and cancer. To avoid the harmful effects of repeated exposure to ultraviolet radiation, personal protection and personal measures are needed. The interaction of UVR with the skin surface causes biochemical changes in collagen, elastin, and connective tissues, resulting in the breakdown of collagen and elastin fibers of the skin by the enzymes collagenase and elastase, which are responsible for maintaining skin firmness and elasticity. Skin deterioration begins, and as the skin becomes less elastic, it gradually becomes drier and looks wrinkled.

Classification of Cosmeceutical Products :-

1. Retinoids
2. Sunscreens
3. Moisturizers
4. Antioxidants
5. Hydroxy acids
6. Topical Proteins and Peptides
7. Depigmentation agents
8. Growth factors



CLASSIFICATION OF COSMECEUTICALS

1. Retinoids Retinoids are premier evidence-based cosmeceuticals because they function through surface cell receptor interactions to produce a clinically defined effect. Other retinoids, such as pro-B vitamins (niacinamide and panthenol) function differently by physically enhancing the barrier properties of the stratum corneum. They are the most prevalent cosmeceuticals in the market. They consist of natural and synthetic derivatives of vitamin A, which reduce hyperpigmentation and inhibit enzymes from breaking down collagen. Many of their cosmeceutical claims are based on data derived from studies of tretinoin and other retinoid drug classes. Some key retinoids include retinoic acid (tretinoin), retinol, retinaldehyde.

Retinoic Acid (Tretinoin): There is extensive literature on the use of tretinoin, which is considered one of the most potent compounds for treating the signs of aging and/or photodamaged skin, including fine lines, hyperpigmented spots, and wrinkles. However, side effects such as burning and scaling have limited their acceptance. To minimize these side effects, various novel drug delivery systems have been developed.

Retinol (Vitamin A): Retinol is oxidized to retinaldehyde and then to retinoic acid, the biologically active form of vitamin A. In vivo studies have shown that topical retinol has only modest retinoid-like biological activity compared to topical retinaldehyde and retinoic acid. Two randomized controlled trials reported significant improvements in fine wrinkles after 12 and 24 weeks of treatment.

Retinaldehyde: Retinaldehyde is largely viewed as an intermediate form during the conversion of retinol to retinoic acid. Studies have shown that it is active in the human skin. Moreover, some studies have reported that this retinoid can produce significant clinical improvements in the appearance of fine and deep wrinkles.

2. Sunscreens Sunscreens are the single most important cosmeceuticals because they protect the skin against solar radiation, which is the most damaging environmental agent. As a result, they help to prevent signs of aging. To be effective, sunscreens should provide broad-spectrum coverage that includes both UVA- and UVB-blocking agents to inhibit photoaging and be part of a daily skincare regimen. UVA and UVB radiation contribute to disruption of the extracellular matrix, a vital phenomenon related to photoaging. Broad-spectrum UVA and UVB sunscreens are the cornerstone of photoaging therapy. Sunscreens contain active ingredients that act as ultraviolet filters. Enzophenones (dioxbenzone, oxybenzone, and sulisobenzene) provide protection in the UVB and UVA II ranges (320–340 nm). The recommended application is 2 mg/cm²; however, this is rarely achieved in real-life practice.

3. Moisturizers :-Moisturizers are the most useful product for the management of various skin conditions (e.g., atopic dermatitis, psoriasis, pruritus, and aging skin). These products include emollients, occlusives, and humectants. The majority of moisturizers enhance skin barrier function. Moisturizers claim to make the skin smoother, softer, more radiant, less wrinkled, and firmer. They improve the tactile properties of dry and aging skin, restore the normal barrier function of the skin, and reduce the release of inflammatory cytokines. Moisturizers based on materials such as petrolatum, silicon, mineral oil, and glycerin enhance

skin barrier functions. Moisturizers restore water content to the epidermis and provide a soothing protective film.

4. Antioxidants :-Topically applied antioxidants enhance the skin's natural antioxidant protection system. They reduce free-radical damage by blocking the oxidative processes in cells. These are used to protect skin from photodamage, cancer, and photoaging. Antioxidants inhibit inflammation that causes collagen depletion. They protect against photodamage and skin cancer. However, there is no completely satisfactory agent available for humans. Explanations for this could include the fact that:

Reactive oxygen species (ROS) affect different pathways in different situations and an antioxidant focused on one such pathway may be ineffective in a redundant pathway.

ROS pharmacokinetics in the target tissue may not relate to that of the antioxidant.

Bioavailability and target organ concentration of the antioxidant may be a limiting issue.

Common antioxidants include alpha-lipoic acid (ALA), L-ascorbic acid (vitamin C), niacinamide (vitamin B3), N-acetyl-glucosamine (NAG), α -tocopherol, and ubiquinone (CoQ10) that are described below.

5. Hydroxy acids

These include α -hydroxy acids (AHAs; glycolic acid, lactic acid) and β -hydroxy acids (BHAs; salicylic acid). Hydroxy acids are used worldwide and most probably for centuries as active dermatological drugs and cosmetic ingredients. The exact mechanism of action of hydroxy acids remains unknown and is largely controversial. Some experts claim that AHAs increase the synthesis of glycosaminoglycans which improve the quality of elastic fibers, and increase the density of collagen; whereas BHAs have hemolytic properties and help in various xerotic and ichthyotic disorders. AHAs are also referred to as fruit acids and are a common ingredient of cosmeceutical products. Examples include citric acid, malic acid, glycolic acids, pyruvic acid, lactic acid, tartaric acid. AHAs improve skin texture and reduce the signs of aging by promoting cell shedding in the outer layers of the epidermis and by restoring hydration. The mechanism of action is not completely understood. One hypothesis suggests that AHAs reduce the calcium ion concentration in the epidermis and, through chelation, remove the ions from the cell adhesions, which are thereby disrupted, resulting in desquamation. This is enhanced by cleavage of the endogenous stratum corneum chymotryptic enzyme on the cadherins, which are otherwise protected from proteolysis by conjugation with calcium ions. The resulting reduction of the calcium ion levels tends to promote cell growth and slow cell differentiation, thus giving rise to younger-looking skin.

6. Topical Proteins and Peptides :-Cosmeceutical peptides have the potential to improve the appearance of aging skin. Topical peptides are regarded as cellular messengers that are formed from amino acids and are designed to mimic peptide fragments with endogenous biologic activity. These pentapeptides (e.g., KTTKS) are comprised of

a subfragment of type I collagen propeptide, and play a role in signaling fibroblasts to produce collagen in the skin, which can improve the appearance of wrinkles. One variation, the palmitoyl pentapeptide known as Pal-KKTKS (Matrixyl™, Sederma) was tested in a controlled, double-blind, left-right randomized, split-face study of 93 women between 35 and 55 years of age who had Fitzpatrick I-III type skin. Pal-KTTKS concentration was 3 ppm; both groups were treated twice daily for 12 weeks. Improvements in wrinkle appearance and length were observed.

There are various types of cosmeceutical peptides such as signal peptides, carrier peptides, and neurotransmitter inhibiting peptides. Overall cosmeceutical peptides trigger a wound-healing mechanism that activates fibroblasts in response to fragmented chains of elastin and collagen. Peptides increase collagen production to improve skin appearance, resulting in smoother skin.

7. Depigmentation agents :-popular. Common depigmenting ingredients include hydroquinone, ascorbic acid (vitamin C), kojic acid, and licorice extract (glabridin). inuation.

8. Growth factors:- Epidermal growth factor (EGF) stimulates epidermal growth and is used in the treatment of burns and excision wounds, where it accelerates re-epithelization. Transforming growth factor (TGF) stimulates normal skin growth and cellular growth and repair. TGF exerts positive regulatory effects on the accumulation of the body's extracellular matrix proteins. TGF is also a mediator

Formulation Considerations

Although some products claim for the active ingredients used in cosmeceutical formulations are evidence-based, consumers often place their confidence in the claims made by the manufacturer. Without testing to assess the efficacy of key active ingredients about overall product content, it is possible that at inadequate concentrations, any beneficial effect will become unapparent. Ensuring consistency of formulations is also an area that has been neglected and necessitates regulation. One of the most important parts of any cosmeceutical is the vehicle that carries the active ingredient into the skin. Vehicle delivery systems can:

- Augment the efficacy of the active ingredient
- Inactivate the active ingredient
- Improve the skin barrier
- Provoke allergic contact dermatitis.

In some skin conditions, the vehicle may be as good as the active preparation, and it may take three months or more to see a difference.

Categorization of Cosmeceuticals in Few International Markets

Japan :-Japan accommodates cosmeceuticals by calling them “quasi-drugs”. These are products that exert mild actions on the human body. The ingredients included in the quasi-drug must be pre-approved before being marketed in Japan. All products claiming to be cosmeceuticals are considered quasi-drugs and require pre-approval before selling in the market.

New Zealand :-New Zealand law provides a third category called “related products”. Related products are those having therapeutic use as a purpose secondary to the main use. Related products are to be labeled with an appropriate designation and trade name, the active ingredients to be disclosed quantitatively, the product's true nature, expiry date and batch number, a dose and its frequency, directions for use, and name and address of the manufacture.

Korea :-Korea Food and Drug Administration (KFDA) has classified cosmeceuticals or borderline products as “functional cosmetics” such as skin whitening, anti-aging, and sun care products. Functional cosmetics prevent

melanin pigmentation, spots, promote whitening of the skin, improve skin wrinkles, and block or diffuse UV rays to protect the skin. The KFDA is responsible for evaluating and improving the safety of functional cosmetics.

Thailand :-Under the current cosmetic regulation, cosmetics are classified as “controlled cosmetics” according to the ingredients used. The use of controlled ingredients as part of cosmetic products will require the notification of the products to FDA before being marketed in Thailand.

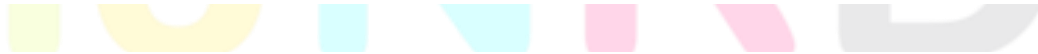
Australia :-In Australia the categorization of goods is based on two factors: (a) Claims made about the product and (b) The composition of the product. The products which are at the borderline are classified as therapeutic goods. These goods must use only approved ingredients. The goods must be included in the Australian Register of Therapeutic Goods. Safety and efficacy, and Good Manufacturing Practices data must be submitted to a regulatory authority. The National Coordinating Committee on Therapeutic Goods (NCCTG) guides acceptable and unacceptable cosmetic claims.

Canada :-In Canada cosmeceuticals are also called “dermo-cosmetics”. Canadian health authorities do not officially recognize cosmeceuticals as an independent cosmetics category. As several products fall into both categories of cosmetic and drug, Health Canada has identified category IV to accommodate these products. These products have fewer regulatory requirements because they have a low risk. The two key factors that are considered in the classification of a cosmetic versus drug are: the composition of the product and the proposed use of a product. AdvertisingStandards Canada, the Canadian Cosmetic, Toiletry and Fragrance Association, and the cosmetics division of Health Canada jointly have established the guidelines for cosmetic advertising and labeling claims. These guidelines help cosmetic manufacturers to use the wording of a claim on cosmetic products.

European Union :-Cosmetics in the EU are regulated under the Cosmetic Directive 76/768/EEC. To avoid the categorization of cosmeceuticals, the EU has clarified by establishing the “Illustrative list by category of Cosmetic Products”. EU has stringent laws where companies are required to submit proof of the claims made by the product. As borderline products are already classified as cosmetics, The EU doesn’t need a third category called cosmeceuticals.

United States of America

According to USFDA, there is no legal definition of cosmeceutical products. In the US, there are three categories such as drugs, cosmetics, and OTC drugs. USFDA states that a product can be both drug and cosmetic. USFDA classifies products depending upon the product claim. In the US, the classification of products is neat and simple. Some of the examples are:

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- A suntan product is cosmetic, but a sunscreen product is a drug.
 - A deodorant is cosmetic, but antiperspirant is a drug.
 - A skin exfoliant is cosmetic, but a skin peel is a drug.
 - A skin product to hide acne is cosmetic, but an anti-acne product is a drug.
 - A skin moisturizer is cosmetic, but a wrinkle remover is a drug.
 - An antibacterial deodorant soap is cosmetic, but an antibacterial anti-infective soap is a drug.
 - A lip softener is cosmetic, but a product for chapped lips is a drug.
 - A shampoo is cosmetic, but an antidandruff shampoo is a drug.
 - Toothpaste is a cosmetic, but anti-caries toothpaste is a drug.
 - A mouthwash is cosmetic, but an anti-gingivitis mouth wash is a drug.

The categorizations of borderline or similar products are discussed in Table.2 with some examples in major markets

Evaluation

The evaluation of the biological characteristics of the active ingredients in cosmeceuticals, especially for organic sources like marine extracts, depends on the selection of an appropriate EXTRACTION process. The quality of the end product depends majorly on a properly conceived and executed extraction technique. Of course, other factors that are of vital importance in determining the end product include various physicochemical properties of the source material, the type, and concentration of the extracting solvent, the ambient pH, temperature, and pressure conditions of the extraction methodology amongst others.

The extraction techniques divide into conventional or classical, and the novel or modern approaches.

CONVENTIONAL EXTRACTION METHODS :

- (1) Hydro-distillation
- (2) Soxhlet extraction
- (3) Maceration
- (4) Percolation
- (5) Infusion
- (6) Decoction
- (7) Hot continuous extraction

Of the above, Soxhlet extraction has been the conventional methodology, especially for plant/marine-derived sources. However, the need for pre-digestion by acids with consequent time consumption is a major limiting factor. Other limitations of the above-mentioned conventional extraction techniques include the requirement of high purity solvents, low extraction yield, decomposition of thermolabile ingredients, and long extraction periods. The novel non-conventional (modern) extraction techniques were developed to overcome some/most of these limitations. Further, since modern technologies comply with the U.S. Environmental Protection Agency (EPA) standards, they are considered eco-friendly or 'green.' A detailed discussion of each of the modern technologies and evaluation methodologies for individual cosmeceuticals is beyond the scope of this CME chapter. Thus interested readers are advised to refer to comprehensive articles authored on this subject.

EVALUATION OF COSMECEUTICALS

The father of 'cosmeceuticals,' Dr. Albert Kligman, suggested three crucial questions to be answered to ascertain the claimed physiological/biological/therapeutic effect of a cosmeceutical product.

1. Is the active ingredient able to penetrate the stratum corneum (SC) and be deliverable in sufficient concentrations to its intended skin target over a time course consistent with its mechanism of action?
2. Does the active ingredient possess a known specific biochemical mechanism of action in the target cell or tissue in human skin?
3. Are there published, double-blind, peer-reviewed, placebo-controlled, statistically significant, clinical trials to substantiate the efficacy claims?

PENETRATION ACROSS STRATUM CORNEUM(SC):

Penetration of ingredients across the SC, a robust barrier to prevent transepidermal water loss (TEWL), is the first hurdle to be overcome. Proteins, peptides, sugars, and nucleic acids with molecular weights >1000kDa and highly charged molecules find it difficult to penetrate an intact SC. The penetrating behavior of an active ingredient can undergo evaluation:

- (1) *in vitro*
- (2) *ex vivo*, and
- (3) *in vivo*

Basic Principle - The published human stratum corneum permeability coefficient (Kp, often expressed as log Kp) has been used for ages by investigators to develop models to predict skin permeability. The most commonly used device for *in vitro* diffusion and for determining penetration through skin consists of the Franz-type diffusion cell or its modifications. For *in vitro* studies, this barrier can consist of an artificial skin construct (ASC). *Ex vivo* studies employ either animal skin, human cadaver skin, or bovine udder skin (BUS) as the barrier.

For human *in vivo* penetration studies, tape stripping, or advanced spectroscopic methods, e.g., ATR (attenuated total reflection) spectroscopy is an option. A more advanced *in vivo* technique is microdialysis. Some newer approaches include - principal components analysis (PCA), probabilistic analyses, fuzzy modeling, artificial neural network (ANN) modeling, and biopartitioning micellar chromatography, amongst others. The development of newer carrier systems and techniques with nanoparticulation, ionto- and electroporation, liposomes, etc. have not only revolutionized the approach to enhance smooth percutaneous absorption of desirable ingredients but have correspondingly lead to the development of more sophisticated evaluation techniques.

BIOENGINEERING TESTS FOR DRUG TARGET IDENTIFICATION

Various bioengineering techniques have been employed to determine the specific drug target within the skin. Some of these include:

- (1) Evaporimetry - for measurement of cosmeceutical impact on reducing TEWL
- (2) Corneometry - conductivity of skin to a low electric current to evaluate skin water content
- (3) Profilometry - to evaluate skin texture and improvement in skin elasticity and fine wrinkles
- (4) Laser Doppler flowmetry - to evaluate erythema indices using the Doppler effect to measure the cutaneous blood flow
- (5) A-scan ultrasound imaging - to ascertain the 'skin thickening' claims of cosmeceuticals

CLINICAL TRIALS FOR SUBSTANTIATION OF CLAIMS

This is perhaps the most important aspect of evaluation, but it is not an entity in isolation, rather an amalgamation of basic, translational, and clinical trial data on a cosmeceutical. Ideally, clinical trials should prefer noninvasive instruments to measure parameters such as TEWL, corneometry, skin elasticity, colorimetry, profilometry, and other techniques to approve or disprove efficacy claims. Pre-treatment and post-treatment photography is essential but not adequate in isolation owing to pitfalls in standardized clinical photography. Further, the study design should include a large cohort as feasible, be controllable through a placebo, or another entity with well-established effects. Randomization, statistical analyses, and well-defined objective outcome measures are also criteria.

The traditional way of histology to demonstrate the effects of a product is ideal but suffers from logistic issues. In contrast, dermoscopy and/or confocal microscopy are novel and validated tools for better assessment than gross photography and are preferred over histology by study subjects and/or volunteers owing to their non-invasive trait.

BENEFITS OF USING COSMECEUTICALS

One of the biggest benefit is that cosmeceutical products can significantly improve your skin's appearance and behavior of your skin cells without a trip to the doctor for a prescription. They contain stronger concentrations of medical-grade ingredients that have been tried and tested by science allowing for higher-quality results. Though they can be more expensive, many clients consider them to be a better value. With higher quality ingredients, you can expect better results that last longer than over-the-counter products. However, it is important to note that they will not produce results similar to that of cosmetic procedures such as botox or injectable fillers.

ADVANTAGES

There Are 5 Advantages of Cosmeceutical Skin Care Products:

- 1. There are more key ingredients in cosmeceuticals.** Cosmeceuticals that you buy at a medical office have higher concentrations of [active ingredients](#). Most retail lines have lower amounts.
- 2. Cosmeceuticals use more advanced formulas.** Often they have the most promising new ingredients or the latest generation of more established ingredients. Sometimes these ingredients may not work in a retail product because of irritation; BUT in a medical setting, with professional follow-up, they work extremely well. Although a product label lists the product's ingredients, it does not list the recipe (the amount of ingredients and order they were added, the pH, and other things that determine a product's final chemistry). Ingredients like [vitamin C](#) are expensive when formulated properly. Many brands will use the same ingredients - *but their recipe is different* - resulting in an end product that is also different.
- 3. Cosmeceutical skin care products are more likely to penetrate your skin.** Scientists use the 500 Dalton Rule for Skin Penetration to ensure the molecules of key ingredients can get into the skin. Essentially, if the molecules are too large, the product may not work.
- 4. Cosmeceuticals offer a better value because they work.** Often patients buy retail skin care products that are not based on good science – and then are disappointed when they fail. Cosmeceuticals are sold in medical offices by skin care professionals who tailor a regimen and order of application specifically for you. The order in which the ingredients are applied to your skin is very important because some ingredients affect skin penetration – making other ingredients more or less effective.
- 5. Cosmeceuticals ensure your product is effective.** Many skin care ingredients break down when exposed to light and air. The best manufacturing and packaging ensures your skincare ingredients don't lose their potency.

DISADVANTAGES

- 1, skin diseases and reaction
- 2,allergies
- 3,harmful for eyes
- 4,damage to nails if using nail polish

5,cancer and other chronic diseases

6, aging

7, danger to reproductive organs

8,hair problems

9,headaches

10,unwanted dependency on cosmetics

CONCLUSION

Helping patients understand the degree of improvement that can realistically be achieved as well as potential side effects remains the primary responsibility of the physician with regard to these products. Many of the new cosmeceuticals in development sound very exciting, but the physician's concern is to help patients choose the best products available today.

As technology advances and cosmeceuticals continue to become more sophisticated and more widely used, the medical profession must continue to take an active role in familiarizing themselves with these products and in educating patients about the benefits and risks of cosmeceuticals.

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