What are they?

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Skincare products can be divided into cosmetics, to improve the appearance of skin, and drugs, used to treat skin diseases; drugs are distinguished as having a biological effect on living tissue. The term ‘cosmeceutical’ was first coined by a leading dermatologist by combining the words cosmetic with ‘pharmaceutical’. However, in most countries, this term is not recognized by regulatory bodies as a separate product class, thus it is not clear what type of products are considered to be cosmeceuticals.

These days, consumers are increasingly tantalized by many skincare options, ranging from the basic, for example moisturizers, to the more ‘extreme’ offered only through dermatologists, for example injectables, such as Botox and Zyderm (collagen), and ultimately plastic surgery. Additionally, there is a global media trend for TV programmes and magazine stories featuring the extraordinary improvements which can now be made in personal appearance. Along with a demographic of an aging society, people are increasingly fascinated by what is possible from the application of today’s scientific advances to skincare and are therefore demanding more and more efficacy from skincare products.

Skincare products can include soaps, cosmetics, colour cosmetics, cosmeceuticals and topical drugs. A basic dictionary definition of ‘cosmetic’ includes phrases such as “purporting to improve beauty, especially that of the complexion; correcting defects of the face, etc”, and “preparations for this purpose”. In fact, a skincare cosmetic needs to balance the requirement to provide a specific solution for a skincare need with meeting a variety of other formulation needs, such as being stable for the duration of its shelf life, being able to resist microbial contamination during consumer use, as well as smelling good and giving a good feeling when used by the consumer. For consumers, a cosmetic is not just about providing a benefit, it is also about meeting a complex number of their expectations when they use the product; often these are designed to give the user a wonderful experience so as to look, feel and smell good. Thus the challenge facing the cosmetic formulator is to provide all these sensory benefits from a product as well as staying true to the technical innovation which provides a benefit.

The term ‘cosmeceutical’ was invented by dermatologist Albert Kligman of the University of Pennsylvania by joining cosme(tic) to (pharma)ceutical. Kligman is credited with showing the effectiveness of all-trans-retinoic acid (ATRA) in improving the appearance of aged skin,
especially in reducing the appearance of fine lines and wrinkles, when applied topically. This was probably the first time that a profound benefit on one's appearance from using a compound applied topically had been documented, and Kligman coined the term cosmeceutical to describe those products containing ‘biologically active ingredients’ such as AHAs (α-hydroxy acids) or vitamin A (retinol) derivatives, and claiming to have a specific skin benefit, in this case anti-aging properties. One could say that a cosmeceutical product is usually one that produces an improvement in appearance, for, e.g., in wrinkles, compared with a drug which is used to treat a specific disease condition. Frequently, the data supporting an active compound used in a cosmeceutical product have been gathered using in vitro models, for example on skin cells or on skin models. It is not necessary to prove that the cosmeceutical provides a benefit in vivo, although many cosmetic companies may choose to test the product using a panel of consumers which often assesses a number of aspects of the product, including the perfume and how the product feels when it is applied to the skin.

Although the term cosmeceutical is frequently used in the cosmetic industry, it is not recognized or regulated as a separate category by regulatory groups and thus there is no standard definition. Unlike the clear distinction between cosmetics and drugs, there is less clarity around the definition of a cosmeceutical. For example, the US FDA (Food and Drug Administration) does not recognize the term, nor provide a definition for what is considered a cosmeceutical. Drugs, on the other hand, are subject to a detailed review and approval process by FDA. If a product has drug properties, it must go through a lengthy approval process requiring rigorous safety and clinical efficacy testing, but there are no such requirements for cosmeceuticals in the US. More stringent testing is required for drugs, since these are frequently new compounds which are taken into the body in amounts that can produce a biological effect. The formulation is designed specifically to achieve this, and needs to undergo rigorous safety testing.

The word cosmeceutical is also not recognized by the European Union, but, in some countries in the East, the word ‘quasi-drug’ is used instead. In Japan, for a product to considered a quasi-drug, the manufacturer must obtain a licence from the Ministry of Health, Labour and Welfare. Such products are characterized as having a ‘mild’ effect on the human body, and medicated cosmetics and soaps fall into this category. In Japan, the purposes for which quasi-drugs may be invented and sold are prevention of nausea and body odour, prevention of prickly heat, prevention of loss of hair or promotion of hair growth, eradication of fleas, etc.

**Topical retinoids as cosmeceuticals**

As mentioned, Kligman discovered the effectiveness of ATRA in providing skin benefits. ATRA (also called ‘tretinoin’) is widely used as a topical drug treatment for a number of skin diseases, including acne and some pre-cancerous lesions. Use of retinoic acid for these medical conditions often also produces skin irritation in many patients. Although it had been used for the treatment of acne since 1962, the first study of the effects of ATRA on facial wrinkles was published in 1983, and Kligman’s group subsequently showed, in 1986, that 0.1% ATRA cream used once daily could significantly improve the fine facial wrinkling resulting from chronic sun exposure. In some countries, ATRA is now available on prescription as ‘Renova’, although usage needs to be closely supervised as it can lead to irritation. However, it is classed as a drug, not a cosmetic.

Although some products claim to restore collagen, the mechanism of action for this effect is not all that clear. The mechanism of action for the reduction of wrinkle size is thought to be caused by the process of collagen synthesis and deposition. However, this effect is not clear and cannot be attributed to the reduction of wrinkles. The mechanism by which wrinkle reduction is achieved is not clearly understood. At the cellular level, ATRA acts with nuclear receptors to cause changes in gene transcription, and treatment of skin cells in culture provides evidence that it inhibits keratinocyte differentiation and stimulates epidermal hyperplasia.

Cosmetic companies have used the effect of ATRA on skin to provide alternatives which do not irritate and can be formulated into aesthetically pleasing products. The use of ATRA in products is tightly controlled, but in cosmetic products, there is a variety of retinoid derivatives which are safer when used for cosmetic purposes. Retinol (rather than retinoic acid) is also reported to reduce the appearance of fine lines in aging skin. A recent randomized, double-blind, vehicle-controlled study from John Voorhees’ group in the University of Michigan Department of Dermatology at Ann Arbor reported that the application of topical 0.4% retinol lotion to the skin of 36 elderly (i.e. mean age 87 years) subjects over 24 weeks, resulted in a significant improvement in the fine wrinkles associated with aging. The treatment significantly increased GAG (glycosaminoglycan) and
AHAs, such as glycollic and lactic acids, have been used under the supervision of a dermatologist at high concentrations (50% or more) to remove the top layer of the epidermis, leaving new fresh-looking epidermis. Such treatments are carried out under very close supervision, and healing of the skin takes several days and is followed closely by the practising dermatologist. At lower concentrations, such as 8%, glycollic acid cream can reverse some of the changes in the epidermis and dermis caused by excessive sun exposure, and the regulatory bodies in various countries has set upper limits to the amount of AHA which can safely be applied to the skin as a cosmetic. At these lower levels, the appearance of the epidermis may be improved, and there may be some increase in dermal collagen and mucopolysaccharide synthesis, and this may help to produce an improvement in the appearance of fine wrinkles. A number of products contain these low levels of AHAs.

**Hydroquinone and skin lightening**

There is a market for cosmetic products that lighten skin by reacting with the melanin pigments. There are various reasons for using such products, including the treatment of hyperpigmented photo-damaged skin as well as the so-called ‘age-spots’. Thus a recent study tested the effect of a cream containing 4% hydroquinone (quinol) plus 0.3% retinol against 0.05% tretinoin (ATRA) cream in the treatment of photo-aging. The hydroquinone-containing cream more effectively diminished the skin damage in terms of dyspigmentation, fine wrinkles and tactile roughness over a treatment period of 16 weeks. However, although retinol can be used in cosmetics, the use of hydroquinone requires a prescription in many countries. In fact, the regulations with respect to hydroquinone are different in different countries, and in some countries its use is banned completely.

**Conclusion**

The number of skincare products available is increasing rapidly as many companies attempt to meet the needs of an aging population with an interest in anti-aging technology and maintaining their youthful appearance. Although the term ‘cosmeceutical’ is frequently used to describe today’s products, a clear definition of the term does not exist, and topical applied products are either classified as drugs, which require a prescription, or cosmetics.

**References**


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