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The A-B-C-Ds of Sensible Sun Protection

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ABSTRACT

Ultraviolet (UV) radiation is a carcinogen that also compromises skin appearance and function. Since the UV action spectra for DNA damage, skin cancer, and vitamin D photosynthesis are identical, and vitamin D is readily available from oral supplements, why has sun protection become controversial? First, the media and, apparently, some researchers are hungry for a new message. They have also drawn attention to the emerging evidence of possible vitamin D benefits other than for bone health. Second, the controversy is fueled by a powerful special interest group: the tanning industry. This industry does not target the frail elderly or inner-city ethnic minorities, which are the groups at greatest risk of vitamin D deficiency, but rather fair-skinned teenagers and young adults, who are at highest risk of UV photodamage. Third, evolution does not keep pace with civilization. When nature gave humans the appealing capacity for cutaneous vitamin D photosynthesis, life expectancy was less than 40 years of age; long-term photodamage was not a concern, and vitamin D deficiency, with its resulting skeletal abnormalities (rickets), was likely to be fatal in early life. This article briefly reviews the "pseudo-controversy", as well as the data supporting a revision of the recommendations for vitamin D supplementation. It concludes with a suggested message for patients, many of whom are understandably confused by recent media coverage of the topic.

Keywords: vitamin D, photosynthesis, sun protection

The media and certain elements within the biomedical research community have created a "controversy" regarding the allegedly conflicting goals of skin cancer prevention through sun protection on the one hand, and achieving optimal vitamin D homeostasis on the other. I will attempt to distinguish this pseudo-controversy from the true controversy surrounding the rather poorly documented health benefits of very high vitamin D levels, however achieved.

The somewhat elusive basis of the pseudo-controversy lies in the often unstated assumption that vitamin D levels, specifically, levels of the inactive prehormone 25-hydroxyvitamin D [25(OH)D], which is measured in serum, are best achieved from increased ultraviolet (UV) exposure to enhance photosynthesis of vitamin D within the irradiated epidermis. This assumption has framed discussions in the popular press and on the internet, even though all intervention studies that suggest a benefit for increasing the conventional "normal" or "sufficient" 25(OH)D level in specific population groups have examined the effect of oral vitamin D supplements, not increased exposure to sun or other UV sources.[1] This formulation of the debate also fails to acknowledge that the major motivation for sun exposure in the population

at large is not for improved general health, but rather, it is to attain the cosmetic and lifestyle goal of tanning, at least for people genetically capable of tanning. Thus, reports continue on the "debate" between professional groups with primary interests in skin health versus those who specialize in endocrinologic health, even though often no such debate exists. These deliberations can create confusion among the general public regarding recommended health behaviors.

The Pseudo-Controversy

In recent years, numerous newspaper reporters, freelance journalists, and television news anchors have reported on a "medical controversy" that pits the unwanted effects of acute sunburn, photoaging, and skin cancer against both well-established and postulated benefits of vitamin D photosynthesis. Simplistically stated, these articles and reports ask if the public should maximize vitamin D levels (measured as the biologically inactive storage form of 25(OH)D in serum)[2] through intentional UV exposure to reduce their risk of internal cancers, hypertension, diabetes, multiple sclerosis, and a litany of other disorders that some attribute to "insufficient" vitamin D levels.[3] By framing the issue in this way, the media reports ignore the fact that people can obtain ample vitamin D levels from a combination of diet, supplements, and incidental protected sun exposure,[1,4-7] and that, to date, most intervention studies suggesting a benefit of increased 25(OH)D levels have used oral supplements, not UV exposure.[1,2,8]

Reports often cite low or low normal levels of vitamin D in darkly pigmented individuals, such as inner-city minority groups, or among the frail elderly in order to justify promoting unprotected sun exposure. However, these at-risk groups have inefficient cutaneous vitamin D photosynthesis. In darkly pigmented people melanin absorbs UV photons that generate vitamin D,[9] and the thinned epidermis of the elderly appears to contain less 7-dehydrocholesterol, which is the cell membrane constituent that UVB converts to pre-vitamin D.[10,11] As well, population groups most attracted to sunbathing, i.e., healthy Caucasian teenagers and young adults, including many fair-skinned individuals who tan poorly,[12] are at lowest risk of vitamin D insufficiency, yet at greatest risk of long-term photodamage.

What is Vitamin D Insufficiency?

It is virtually impossible to find a definition of this recently coined term in the literature. It loosely refers to levels of 25(OH)D above those classically associated with bone disease and below those found in various observational or epidemiologic studies to be statistically associated with a higher risk of the studied disorder, for example, cancer. These upper cut-off values vary enormously from study to study and author to author, from perhaps 50nmol/L to 150nmol/L, often 75-80nmol/L.[1]

A recent study[13] of 93 healthy young adults who were recruited from the University of Hawaii and a Honolulu skateboard shop, questioned the frequently suggested serum 25(OH)D "sufficiency" cut-off value of 75nmol/L. The investigators based recruitment of this convenience sample of prototypic "surfer dudes" (mean age 24 years, mean body-mass index 23.6 kg/m^2) on a self-reported minimum outdoor sun exposure of 15 hours (mean 29 hours) per week during the preceding 3 months; 40% reported never using sunscreen and the group overall reported an average of 22.4 hours per week of unprotected sun exposure. All were clinically tanned. Nevertheless, the group's mean 25(OH)D level, measured by 2 standard techniques (high-performance liquid chromatography and radioimmunoassay), was 79nmol/L, and 51% had a level below the suggested 75nmol/L cut-off for "sufficiency".[13] These data suggest that a public health goal of >75nmol/L for the entire population might be unachievable through sun exposure.

Regardless of the cut-off used, the great majority of people with insufficient 25(OH)D levels have no detectable disease or health problem and, statistically, they probably never will. On an individual basis, there is no detectable benefit from a high 25(OH)D level and, conversely, no harm from a lower level. Even more curious, in many instances the statistical associations on which the "insufficient" status is based are not measured 25(OH)D levels, but instead presumptive correlates such as insolation (i.e., the amount and intensity of incident UV irradiation) in the general geographic region of residence. In fact, latitude, altitude, season, cloud cover, smog, and other variables affect insolation, which is generally high near the equator and low near the poles; and lifestyle choices introduce enormous variation in sun exposure, even among individuals in identical climates.

The True Controversy

The real controversy is whether increasing a person's conventionally normal serum 25(OH)D level has health benefits, as some epidemiologic studies have suggested, but prospective randomized studies, with the one exception noted below, have not confirmed. A thorough discussion of the quality and consistency of the epidemiologic and observational data available through 2005, which some interpreted to support a health benefit of serum 25(OH) D levels far above those associated with normal skeletal maintenance, is available elsewhere[1] and is beyond the scope of this editorial. However, because prevention of colorectal cancer is often cited as the best established benefit of unconventionally high 25(OH)D levels, a brief discussion of this example is instructive. Several much-referenced reports link colorectal cancer incidence[14-16] to "low" vitamin D levels within the conventional normal range or to a presumptive proxy, i.e., little sun exposure, usually based on residence in a poorly insolated area, as noted above. Although other epidemiologic or observational studies of similar size and design (grade B, level 2 or 3 in the hierarchy of evidence-based medicine)[17] found no statistical relationship or even an inverse relationship between sun exposure and colorectal cancer or closely related diseases,[18-22] the popular media

coverage of the topic has selectively and prominently cited the positive reports at the suggestion of interviewed "experts." In 2006, a prospective, randomized, placebo-controlled trial (grade A, level 1 for medical decision making)[17] of vitamin D supplementation (400 IU/day) for 7 years or longer involving more than 36,000 post-menopausal women found no relationship between colorectal cancer risk (incidence or mortality; tumor grade, stage, or size) and supplement use, total vitamin D intake, or amount of sun exposure (crudely and indirectly calculated, as in the positive epidemiologic studies).[8] Although the investigators found an inverse correlation with baseline serum 25(OH)D levels, they found no indication that increasing initially low vitamin D levels by supplementation reduced cancer risk over the subsequent 7 years.[8] An accompanying editorial[23] and the investigators themselves noted that 7 years of supplementation might be too short, the subjects might have received a dose of vitamin D that was too low, they might have had a lifestyle that was too healthy, or they might have been too young (62 years on average) to develop this cancer in large numbers. In brief, the authors concluded that no result is ever definitively negative. Yet, less than 2 months later, the media prominently covered a far less definitive, multivariable model study that statistically inversely linked the risk of cancer, including colorectal cancer, to 6 indirect historical measures of sun exposure and presumptively correlated vitamin D levels,[24] with no reference to the "gold-standard" negative colorectal cancer study.[8]

Most recently, the *American Journal of Clinical Nutrition* published a 4-year randomized, prospective blinded study of 1,179 presumptively healthy postmenopausal Caucasian women in rural Nebraska who were followed for 4 years while taking a calcium (Ca) supplement (n=445), a Ca plus vitamin D (Ca-D) supplement (n=446), or a placebo only (n=288).[2] This study was designed to assess bone fracture risk, but data were also analyzed to assess cancer incidence.[2] The women were interviewed by a study nurse every 6 months and, if they reported a new diagnosis of nonskin cancer, their medical records were reviewed. Fifty women with a newly diagnosed cancer (19 with breast cancer, 3 with colon cancer, and 28 with other cancers) were identified, 13 in year 1 and 37 in years 2-4, representing 6.9% of the placebo group and 3.8% and 2.9% of the Ca and Ca-D groups, respectively, which indicated a significantly reduced relative risk of 0.4 for the Ca-D group. The vitamin D dose (1,000 IU/day) was higher than the current RDA of 400-600 IU/day, depending on age, and increased the average 25(OH)D level in all groups from approximately 71 to 96nmol/L in the Ca-D group by the end of year 1. For the initial and control groups, 25(OH)D levels are of interest in that they are very close to the commonly recommended "sufficient" level of 25(OH)D of ≥75nmol/L and the average 25(OH)D level of 79nmol/L observed in a population of healthy, tanned young men in Hawaii with a self-reported unprotected sun exposure of 22.4 hours/week.[13] The article does not report the 25(OH)D levels of the 50 women who developed cancer vs. the 1,129 who did not, either at baseline or during supplementation; nor does it report data for the original primary endpoint, bone fracture incidence.[2] The apparent protective effect of high dose Ca-D supplementation on cancer risk is certainly of interest, however, and confirmatory studies are eagerly awaited.

Irrelevance of Both Controversies to Sun Protection

A neglected but critical point is that the "true" optimal level of 25(OH)D for musculoskeletal health, cancer prevention, or any of the other claimed benefits is irrelevant to the proven value of sun protection. Whatever this optimal level, ample vitamin D can be obtained from diet, supplements, and incidental sun exposure.[1,4-7] Intentional unprotected sun exposure to increase vitamin D photosynthesis is not only unnecessary, but also inefficient for those at highest risk of vitamin D deficiency.[9-11] The groups most responsive to the media's unprotected sun exposure message are those who have the statistically lowest risk of vitamin D deficiency: healthy fair-skinned adolescents and young adults. Indeed, surveys in the US show that more than 70% of tanning bed users are Caucasian women aged 16-49 years[12] and 95% of all users exceed the exposure levels recommended by the US FDA[25] for maximizing vitamin D photosynthesis. The demographics and exposure habits of the sunbathing public are similar to those of tanning bed users, although the average age is probably even younger and exposures even greater. The safe-sun message promulgated by dermatologists and the American Academy of Dermatology does not target dark-skinned individuals, who already have excellent endogenous sun protection in the form of epidermal melanin. Moreover, the groups at demonstrated risk of vitamin D deficiency have not embraced the "UV advantage" message,[3] perhaps because this message does not target them.

The interest among the media and public in the pseudo-controversy is nevertheless real and persistent. Why? The sun protection message is old, dating back at least 23 years,[26] and its intended audience views it as wimpy, like the "buckle up" seatbelt message. Real men, and rebellious, fun-loving, and spontaneous adolescents do not wear sunscreen (or seatbelts). Moreover, many people, especially teenagers, want to sunbathe to acquire a "sexy" tan, not to reduce their risk of age-associated disease decades later.[27] In addition, relaxing in the sun and making one's own vitamin D have a back-to-nature holistic appeal for many individuals. It is therefore not surprising that the print and electronic media continue to cover the pseudo-controversy: it sells. However, press releases crafted by representatives and employees of the USD $5 billion/year indoor tanning industry[28,29] have greatly facilitated the media's natural tendency to pursue a "new" and controversial story, especially if it is one their audience wishes to hear.

The indoor tanning industry's concern for the public health would be more credible if its coverage of the issues were more balanced, and a decade or so of extolling the virtues

of UVA lamps (not the UVB lamps that it now touts as "healthful") had not preceded the current campaign.[30-32] Before publication of the epidemiologic studies questioning the adequacy of conventional vitamin D recommendations, the industry argued strenuously that indoor tanning was superior to natural sun exposure precisely because people could tan with less UVB exposure (and, of course, less vitamin D photosynthesis).[33] Indeed, a review of the industry's public positions over the 30 years of its dramatic growth in annual revenues[34] reveals a series of opportunistic, contradictory positions. There can be no doubt that the goal of the tanning industry is to sell tanning sessions, not to safeguard the public's health.

One Dermatologist's Recommendation to Patients

Common sense and overwhelming medical/scientific literature support the fact that fair-skinned people benefit from regular, lifelong, safe sun practices. Moreover, people who wear high-sun protection factor (SPF) sunscreen in season, probably synthesize vitamin D maximally in exposed areas during incidental sun exposure.[35] Although some have claimed that sunscreens block all UV (and hence, all vitamin D photosynthesis[36]) this is not the case. By definition, sunscreens allow continuous transmission of a fraction of erythemogenically weighted incident UV photons equal to 1/SPF of the total (e.g., 1/15th or 7% for an SPF 15 product). Moreover, studies have shown that sunscreen users customarily apply half or less of the FDA-stipulated amount of product required to generate the stated level of protection (2mg/cm^2) and hence achieve far less protection.[37] If people require 2-8 minutes of unprotected summer sun exposure to maximize their cutaneous vitamin D synthesis,[3] they could accomplish this in approximately 10-20 minutes of exposure after applying an SPF 15-30 sunscreen in the customary manner.[37,38] Most critically, regardless of one's complexion, or the extent of UV exposure, daily oral vitamin D supplementation can completely compensate for the lack of cutaneous vitamin D photosynthesis.[1] Of note, those rare individuals with compromised absorption of orally-administered vitamin D should be advised to use intramuscular injections or very high-dose oral supplements.

Despite the above considerations, many patients ask their dermatologist to recommend a "safe" or "prudent" amount of sun exposure. Such recommendations must be individualized, as the risk-benefit ratio varies enormously within the population. Moderate or even generous sun exposure might have little effect on a darkly pigmented person's risk of subsequent photoaging and skin cancer while promoting higher 25(OH)D levels; but even quite modest exposure could promote development of precancerous and cancerous lesions in already-photodamaged fair skin without increasing the already maximized vitamin D photosynthesis. A rule of thumb might be that any sunburn dose is too much by a factor of at least 3, as maximal vitamin D synthesis is achieved after approximately one-third of a minimal erythema dose.[39] Individuals who never sunburn or who live in climates that never allow them to sunburn are relatively "safe" from the damaging effects of unprotected sun exposure. People with complexions or living circumstances associated with the possibility of frequent sunburns probably have no "safe", minimum unprotected exposures. Such unprotected exposures would only be a few minutes in length, but in the course of their routine activities, this higher-risk group would almost certainly exceed the prudent exposure time on a daily basis.

Although the much discussed epidemic of vitamin D insufficiency has been linked by some to the overuse of sunscreens, there is little or no evidence that this is the case, even if such an epidemic exists. Those population groups most likely to be vitamin D deficient (and presumably insufficient, if that term is accepted) are indeed unlikely to use sunscreens at all; these groups include inner city dark-skinned minorities, frail elderly who are often home-bound or institutionalized, and Middle Eastern women who wear the bourka, and therefore expose very little skin to the sun.

Strong evidence suggests that many individuals in these groups derive at least a musculoskeletal benefit from vitamin D supplementation, although they infrequently consult a dermatologist in this regard. Strong evidence also suggests that long-term oral vitamin D supplementation at doses up to 10 times the current RDAs are safe,[4,40] and many endocrinologists and nutritionists now suspect that the RDAs are too low. Therefore, it seems quite reasonable to recommend to all older patients who practice sun safety and to anyone even remotely concerned about vitamin D "sufficiency" that he/she take 1,000 IU of vitamin D daily, especially in the winter months. Routine measurement of the serum 25(OH)D level does not seem warranted, as the test is expensive and the "normal" or "optimal" range is debatable; in any case, the treatment for "low" levels is supplementation at this dose.

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Novel Topical Drug Delivery Systems and Their Potential Use in Acne Vulgaris

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ABSTRACT

A vast spectrum of topical anti-acne agents has emerged in response to new insights that have been gained through the understanding of disease pathophysiology and the need for clinicians to adopt an individualized therapeutic approach. Because topical agents are most commonly used for acne management, this article reviews some novel vehicle delivery advances that are poised to further enhance the efficacy of topical acne formulations, and/or offer the possibility of simplified dosing regimens that may improve treatment outcomes.

Key Words: acne vulgaris, drug administration, topical therapies

When it comes to the delivery of a drug to a specific site, topical formulations are probably among the most challenging products to develop. An effective topical formulation needs to provide a stable chemical environment in a suitable dispensing container in order to accommodate multiple compounds that may have different, if not incompatible, physicochemical characteristics. Once applied, a topical formulation must interact with the skin environment, which can influence the rate of the release of the compound(s) in order to achieve adequate skin absorption. The excipients themselves will exert additional physical effects on the skin, such as drying, occluding, or moisturizing. Research and technology have brought a better understanding of the physics, chemistry, pharmacodynamics, and pharmacokinetics for drugs used to treat acne. These insights have resulted in new delivery systems that are capable of enhancing the efficacy, tolerability, and cosmetic acceptability of topical formulations.[1-3]

Formulary Considerations

The challenge of developing a successful topical product stems from the several requirements that a formulation must meet:

1. Container Selection and Product Stability

Depending on the properties of the combined ingredients, a dispensing container will be chosen (i.e., tube, jar, can, etc.) to provide a stable physicochemical environment that protects the active compound(s) from chemical degradation. The formulation can be a liquid or semi-solid, monophasic or multiphasic (e.g., oil-in-water or water-in-oil); it is largely dependent on the characteristics of the active compound(s) and on the condition of the skin to be treated.

2. Skin Penetration

Once the product is applied on the skin, a complex interaction occurs between the formulation, the active compounds, and the skin itself. The penetration of the active compound(s) into the skin follows Fick's first law of diffusion, which describes the transfer rate of solutes as a function of the concentration of the various ingredients, the size of the treatment surface area, and the permeability of the skin. However, the skin's permeability can be influenced by many factors, such as the drying, moisturizing, or occluding effects of the excipients in the formulation, which, in combination, can modulate the release of the product at the treatment site. In acne, the site of action is inside the pilosebaceous unit and, therefore, an efficacious anti-acne formulation should facilitate the penetration of the active compound(s) into this extremely lipophilic environment.

3. Cosmetic Acceptability

In today's self-image conscious world, patients are looking for topical products that are not only safe and effective, but also cosmetically acceptable and easy to apply. This is especially true in acne, where the esthetic aspect is one of the primary reasons why patients seek dermatologic consultation. Moreover, acne patients are mainly comprised of teenagers or young adults, and therefore, products that offer convenience and are minimally disruptive to daily routines increase the level of compliance, and ultimately, the efficacy of the topical therapy. For example, vehicle considerations for prescribing should take into account the application of the drug on large, hairy surfaces like the chest and the back. This may require formulations that spread easily, or in the case of facial acne, the ideal formulation should leave minimal residue or oiliness.

Common Topical Acne Treatments	Cutaneous Side-effects	Potential Novel Systems for Agent Delivery
Retinoids (e.g., adapalene, tazarotene, tretinoin)	Burning, peeling, erythema, dryness, photosensitivity	Microsponges, liposomes, nanoemulsions, aerosol foams
Benzoyl peroxide	Dryness, erythema, peeling, hair and clothing discoloration	Polymers, fullerenes
Clindamycin phosphate	Erythema, dryness, allergic contact dermatitis	Aerosol foams, polymers, nanomemulsions
Erythromycin	Dryness, erythema, peeling, allergic contact dermatitis	Aerosol foams, polymers, nanomemulsions
Salicylic acid	Dryness, erythema, peeling	Polymers, microsponges

Table 1: Cutaneous side-effects from topical acne treatments and potential novel systems for agent delivery

Current Topical Therapy for Acne Vulgaris

Topical treatment is the most common and popular way to manage acne and there are a variety of therapies available (Table 1) that are frequently administered in combination in order to target concurrent multiple pathogenic factors. In general, topical monotherapy is indicated for mild-to-moderate acne, such as comedonal and/or papular variants; combination therapy is reserved for more severe or refractory disease.

Novel Topical Delivery Systems

Aerosol Foams

Aerosol foams have become an increasingly popular type of topical formulation for a variety of skin conditions including acne vulgaris. The vehicle base of the foam can have a liquid or semi-solid consistency that shares the same physicochemical characteristics of conventional vehicles like creams, lotions and gels, but it maintains desirable properties such as moisturizing/ fast-drying effects, or higher drug bioavailability. The aerosol base is dispensed through a gas-pressurized can that discharges the foam. The product characteristics (i.e., texture, bubble size and thickness, viscosity, density, persistence, stability, and spreadability) are determined by the type of formulation and the dispensing container that are selected to suit the specific treatment needs. In acne, foams may be preferred for application on large hairy surfaces (e.g., chest and back) or on the face as cleansers, because they are easier to apply.

Liposomes

Liposomes are frequently used as vehicles in pharmaceuticals and cosmetics for a controlled and optimized delivery to particular skin layers. Liposomes are spherical vesicles whose membrane consists of amphiphilic lipids (i.e., lipids that are hydrophilic on one side and lipophilic on the other side) that enclose an aqueous core, similar to the bilayer membranes of living cells. Because liposomes offer an amphiphilic environment, they may encapsulate hydrophilic substances in their aqueous core and lipophilic substances in their lipid bilayer. This unique dual release capability enables the delivery of 2 types of substances once they are applied on the skin; each differs in its effects on skin permeability, which may enhance the desired therapeutic benefit.[4,5]

Nanoemulsions

Nanoemulsions are a class of emulsions (i.e., water-in-oil or oil-in-water formulations) that are characterized by the dispersion of very small-sized droplets when mixed. Nanoemulsions are not formed spontaneously, as they require unique thermodynamic conditions, specialized manufacturing processes, and specific surfactants that can stabilize the nano droplets. Nanoemulsions are suitable for the transport of lipophilic compounds into the skin and, therefore, they may be an ideal vehicle for use in acne to increase the penetration of the active compounds inside the lipophilic environment of the pilosebaceous unit. In addition, nanoemulsion particulates will not clog the pores and they can produce additional therapeutic effects, such as increased skin hydration and viscoelasticity.[6]

Polymers

Polymers are large molecules consisting of repeating structural units, or monomers that are connected by covalent chemical bonds. These compounds serve as the building blocks of natural (e.g., paper and amber), biological (e.g., proteins and nucleic acid), or synthetic (e.g., plastics and polyethylene) materials. Today, applications for synthetic polymers can be found in nearly every industry, and their versatility has given rise to technological advancements within the pharmaceutical sector that address a variety of medical needs. For example, in dermatology, there are new acrylic-acid polymers that turn into a gel in the presence of water by trapping water into microcells. Inside these aqueous microcells, hydrophilic compounds can remain in a solution, whereas non-hydrophilic compounds may be dispersed in suspension. The result is a stable gel-like formulation that is easy to use and releases the active compound(s) once they are applied on the skin. Moreover, these polymer-based gels can be mixed with other excipients, such as moisturizers and emollients, to provide additional clinical benefits. Recently

introduced anti-acne formulations that combine clindamycin 1% with benzoyl peroxide 5% (Duac®, Stiefel Laboratories; BenzaClin®, Dermik) utilize this novel polymer-based gel technology that exhibits efficacy and excellent tolerability.[7]

Microsponges

Microsponges are biologically inert particles that are made of synthetic polymers with the capacity to store a volume of an active agent up to their own weight. Furthermore, the particles serve to protect the entrapped active compound from physical and environmental degradation. The microsponge technology can be utilized in a variety of formulations, but is more frequently manufactured as gels. Once applied on the skin, microsponges slowly release the active agent(s).

Emulsifier-free Formulations

Emulsifier-free formulations are also a growing area of development for dermatologic and cosmetic products. Most skin care products are emulsions, i.e., a mixture of 2 or more materials that are not miscible with each other; as such, according to the second law of thermodynamics, they are inherently unstable. As a result, they require the addition of surfactants ("emulsifiers") that stabilize the formulation to guarantee an adequate shelf life. Furthermore, once these surfactant agents are applied on the skin, they tend to emulsify and remove the natural lipids of the epidermis. Consequently, the pharmaceutical industry has been developing surfactant-free emulsions as alternatives to conventional formulations by using stabilizers, such as polymeric emulsifiers or solid particles, in order to yield sufficiently stable products with a cosmetically pleasant appearance.

Fullerenes

Fullerenes are molecules composed entirely of carbon that resemble a hollow sphere. Rouse, et al., showed that once fullerenes come into contact with the skin, they migrate through the skin intercellularly, as opposed to moving through cells.[8] Therefore, a fullerene could be used to "trap" active compounds and then release them into the epidermis once they are applied on the skin. Moreover, fullerenes, themselves, are thought to be potentially potent antioxidants. Data are reported in the literature showing that fullerenes are well tolerated and they hold substantial promise in dermatologic and cosmetic applications.[9,10]

Conclusion

Much progress has been made to improve the performance of topical anti-acne care products in recent years. New excipients, refined processing techniques, and a better knowledge of the physicochemical properties of vehicles and drugs have led to the development of new delivery systems that may result in more advanced anti-acne therapies. Well controlled clinical trials will be required to confirm the clinical benefits of these new formulations in terms of efficacy, tolerability, compliance, and cosmetic acceptability.

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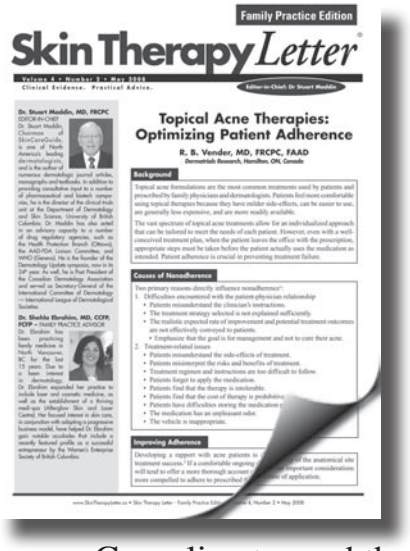

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Scalp Psoriasis	**Calcipotriene 0.005% + Betamethasone Dipropionate 0.064% Topical Suspension** *Taclonex Scalp®* Leo Pharma/ Warner Chilcott	The US FDA approved this topical suspension in May 2008 for the once daily treatment of moderate-to-severe psoriasis vulgaris of the scalp in adults ≥18 years of age. This new vehicle facilitates ease of use.
Scalp Psoriasis	**Calcipotriene 0.005% Topical Solution** Nycomed US, Inc./ Fougera	The US FDA approved the first generic formulation of calcipotriene scalp solution (comparable brand, Dovonex®, Leo Pharma/ Warner-Chilcott) in May 2008 for the topical treatment of chronic, moderately severe psoriasis of the scalp.
Neurotoxin	**Botulinum Toxin Type A** *Reloxin®* Medicis Pharmaceutical Corp./ Ipsen Ltd.	The US FDA accepted a Biologics License Application in May 2008 to market this neuromuscular blocking agent for aesthetic indications. Marketing is anticipated to commence in the US during the second quarter of 2009.

Drug News

Acne	A recent study by Fenner, et al.* explored the therapeutic efficacy of cephalexin in acne patients who were non-responsive to or unsuitable candidates for conventional therapies. Cephalexin is a broad-range, first-generation antibiotic of the cephalosporin class that is commonly used in the treatment of infections of the respiratory and urinary tracts. The study was a retrospective chart review of 93 patients, and the assessed aggregate data included patient demographics, history of therapies received, clinical response, and adverse effects. Clearance was noted in 4% of acne patients, 45% were considered to be much improved, 29% somewhat improved, 16% had no change, and 6% experienced worsening of symptoms at the first follow-up visit. The average length of treatment was 6 months. Analyses also revealed the prior use of systemic antibiotic(s) for acne by 84% of subjects; 7% experienced adverse effects. Study findings indicate that inclusion of cephalexin may be beneficial for treatment-refractory acne or in patients who are not suitable candidates, due to medical contraindications, for traditional therapies. Further investigations are warranted to confirm the safety and efficacy of cephalexin for the treatment of acne. *Fenner, et al. *Pediatr Dermatol* 25(2):179-83 (2008 Mar-Apr).
Psoriasis	Tumor necrosis factor-alpha blocking agents (anti-TNF-α) have been shown to be effective in the management of rheumatoid arthritis (RA), psoriatic arthritis, and psoriasis. Recent case reports describe the emergence of psoriasis as an adverse effect in RA patients undergoing anti-TNF-α treatment. The primary objective of the study was to ascertain if the incidence rate of psoriasis was higher in RA patients treated with TNF-α antagonists when compared with patients who received traditional disease modifying anti-rheumatic drugs (DMARDs). The rates of occurrence of psoriasis were also examined for 3 anti-TNF-α agents indicated for RA. The data analyzed was accessed from The British Society for Rheumatology Biologics Register. The study population consisted of 9,826 subjects treated with anti-TNF-α therapy and 2,880 subjects treated with DMARDs. For inclusion, each patient must have reported an adverse event that is defined as new onset psoriasis. Incidence rates of psoriasis were calculated as events per 1,000 person years and compared using incidence rate ratios (IRR). Findings revealed 25 cases of psoriasis were reported by anti-TNF-α treated patients vs. none by those receiving DMARDs; the rate of new onset psoriasis in TNF-α treated patients was higher at 1.04 (95% CI 0.67, 1.54) per 1,000 person years as compared with 0 (upper 97.5% CI 0.71) in those treated with DMARDs. Furthermore, a significantly higher incident rate was observed in patients treated with adalimumab as compared with those treated with etanercept (IRR 4.6 [95% CI 1.7, 12.1]) or infliximab (IRR 3.5 [95% CI 1.3-9.3]). Additional research is necessary to confirm these findings. The full article is viewable at: http://ard.bmj.com/cgi/rapidpdf/ard.2007.087288v1. Harrison MJ, et al., *Ann Rheum Dis*, ARD Online First, published on April 2, 2008 (accessed June 1, 2008).