Pharmacist Edition

Skin Therapy Letter ©

Volume 3 • Number 1 • September-October 2008

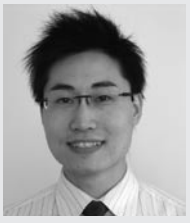
Clinical Evidence. Practical Advice

Editor-in-Chief: Dr Stuart Maddin

Dr. Stuart Maddin, MD, FRCPC
EDITOR-IN-CHIEF

Dr. Stuart Maddin, Chairman of SkinCareGuide, is one of North America's leading dermatologists, and is the author of numerous dermatologic journal articles, monographs and textbooks. In addition to providing consultative input to a number of pharmaceutical and biotech companies, he is the director of the clinical trials unit at the Department of Dermatology and Skin Science, University of British Columbia. Dr. Maddin has also acted in an advisory capacity to a number of drug regulatory agencies, such as the Health Protection Branch (Ottawa), the AAD-FDA Liaison Committee, and WHO (Geneva). He is the founder of the Dermatology Update symposia, now in its 24th year. As well, he is Past President of the Canadian Dermatology Association and served as Secretary-General of the International Committee of Dermatology — International League of Dermatological Societies.

Alex H.Y. Cho, RPh, BScPharm
PHARMACIST ADVISOR



Alex is a graduate of the University of British Columbia's Faculty of Pharmaceutical Sciences. Alex's keen interest in dermatology has been fostered by his primary role as the managing pharmacist at the VGH Skin Care Centre Pharmacy located in Vancouver, BC. The pharmacy is situated in one of Canada's premier clinical and academic dermatology centres. This ideal location, in combination with his collaborative efforts with onsite dermatologists, researchers and nursing staff, have afforded Alex with consistent opportunities to compound topical medications. Additionally, he oversees the pharmaceutical inventory for the Psoriasis and Phototherapy Clinic at Vancouver General Hospital.

Cosmeceuticals: A Practical Approach

J. S. Dover, MD, FRCPC, FRCP
SkinCare Physicians, Chestnut Hill, MA, USA
Yale University School of Medicine, New Haven, CT, USA
Dartmouth Medical School, Hanover, NH, USA

Introduction

The cosmeceutical industry has undergone phenomenal growth over the past decade, and much of this expansion can be attributed to an aging population wanting to sustain a youthful appearance. The availability on drug store shelves of biologically active compounds that exhibit both cosmetic and drug-like effects has created a new group of agents, whose degree of efficacy, in many cases, has been unsubstantiated by science, and they remain unregulated. As such, acquiring a basic knowledge of the major classes of active ingredients that are found in cosmeceuticals will enable healthcare professionals to provide accurate and educational information to consumers.

Categorization and Regulation of Agents

According to US FDA Food, Drug, and Cosmetic Act of 1938:

1. A drug is "intended for use in diagnosis, cure, mitigation, treatment, or prevention of disease," i.e., it affects the structure or function of the body.
2. A cosmetic is intended to be "rubbed, poured, sprinkled, or sprayed on, introduced into, or otherwise applied to the human body or party thereof for cleaning, beautifying, promoting attractiveness, or altering the appearance of skin," i.e., the product cannot alter the structure or function of skin.

Albert Kligman coined the term "cosmeceutical" and defined it in 1984[1] as a formulation that is used to improve the appearance of skin, but is not for therapeutic purposes.

- Many do contain biologically active ingredients.
- Some alter the structure and/or function of skin, thus, according to the regulatory definition, these could be categorized as drugs.
- Most undergo safety testing, but efficacy is not often assessed.
- Categorization and regulation will depend upon how product claims are presented to the public.
- The term "cosmeceutical" is not recognized by the North American regulatory agencies.
- Products considered to be cosmeceuticals circumvent regulation. Under this category, a lower barrier exists for market entry.

Major Classes of Cosmeceuticals

- Sunscreens
  - Considered as OTC drugs; sun protection factor must be proven by *in vitro* and *in vivo* studies.
  - Regarded by dermatologists as the single most important formulation that should be applied daily.
  - Products formulated to meet individual preferences, such as scent and feel, can improve compliance.
- Retinoids
  - Natural and synthetic derivatives of vitamin A
  - Drugs: retinoic acid (tretinoin), adapalene, and tazarotene
    - Substantial scientific data confirm their anti-aging and anti-acne benefits.[2]
    - Retinoic acid is considered by dermatologists to be the anti-aging gold standard.
    - Available only through a doctor's prescription
  - Cosmeceuticals: retinol, retinaldehyde, retinyl propionate, retinyl palmitate
    - In many cases, bioavailability and activity are unproven when formulated.
- Moisturizers
  - Include emollients, occlusives, and humectants.
  - Considered to be the most useful product for the management of various skin conditions (e.g., atopic dermatitis, psoriasis, pruritus, aging skin).
- Other vitamins and minerals
- Antioxidants
  - Include vitamins A, C, and E; alpha lipoic acid; ubiquinone (coenzyme Q-10); idebenone; polyphenols (e.g., catechins, flavenoids); kinetin; botanicals (e.g., teas, grapeseed, grape skins and stems, coffeeberry).
  - Enhance the skin's natural antioxidant protection system with topical application.
  - Reduce free-radical damage by blocking the oxidative processes in cells.
  - Inhibit inflammation that causes collagen depletion.
  - Protect against photodamage and skin cancer.
  - Do not reverse signs of photoaging.
- Hydroxy acids (alpha, beta, poly)
  - Include glycolic acid, lactic acid, citric acid, tartaric acid, pyruvic acid, and malic acid.
  - Can improve skin texture and dyspigmentation.
  - Can induce actual structural changes in skin, so the potential exists for regulatory scrutiny.
- Lightening agents
  - At best, depigmenting agents can achieve modest levels of efficacy.
  - Hydroquinone is considered to be the most effective.
    - Presently under re-evaluation by the US FDA.
    - Sunscreen use is required due to drug-induced photosensitivity.
  - Other examples include kojic acid, glabridin (licorice extract), arbutin, azelaic acid, n-acetyl glucosamine, and vitamin C.
- Botanicals/ plant extracts
  - Have experienced a rapid rise due to the popularity of "natural" compounds.
  - Represent the largest group of additives found in marketed products.
  - Limited scientific data to support efficacy and safety.
- Epidermal growth factors
  - Naturally occurring chemicals in the body that influence cellular proliferation and differentiation.
  - Potential applications include regeneration of damaged or aged skin.
- Proteins/ peptides
  - Can trigger skin repair as needed. There are some indications that they can reduce the signs of aging and accelerate the skin's healing processes.[3,4]

Specific Agents of Recent Interest

OTC Retinoids

- They reduce wrinkles and lentigines.
- Common side-effects include redness, irritation, and an increase in photosensitivity.
- Certain retinoid analogues within the same class of molecules have been shown to provide less irritation, but maintain comparable levels of efficacy.[5]
- 3 classes of retinoids exhibit distinct properties:
  - vitamin A metabolites - trans-retinoic acid, retinaldehyde, adapalene, and tazarotene
  - vitamin A - retinol
  - vitamin A esters - retinyl acetate, retinyl propionate, and retinyl palmitate.
  - In randomized, double-blind, placebo-controlled, human studies comparing retinol, retinyl acetate, retinyl propionate and trans-retinoic acid[5]:
    - statistically significant findings showed retinyl propionate exhibited the highest rating when evaluated for efficacy and non-irritation.
    - 0.30% retinyl propionate demonstrated superior reductions in wrinkles, redness and hyper-pigmentation vs. 0.15% retinol.

Niacinamide (vitamin B_3)

Niacinamide is a precursor of NADH and NADPH, which are co-enzymes essential for various metabolic functions. This B-complex vitamin can improve the barrier function of the epidermis and act as an inhibitor of melanosome transfer resulting in reduced hyperpigmentation.

- In a left-right randomized, double-blind, placebo-controlled study in women aged 25-60 years.
  - Patients applied a formulation containing niacinamide twice daily for 8-12 weeks.

Specific Agents of Recent Interest (continued)

- Results showed a decrease in transepidermal water loss through increased barrier layer lipids.[6,7]
- Another placebo-controlled, double-blind, left-right randomized study looked at 60 women of Japanese descent aged 25-60 years.
  - Split-face treatment twice daily for 8 weeks showed substantial improvement on lentiginous lesions.[8]
- A meta-analysis showed significant reduction in fine lines, wrinkles, hyperpigmented spots, blotchiness, sallowness, sebum production, irritation, and improvement to the skin's barrier function.[9]

Topical Peptides (retinoid alternative)

- Regarded as cellular messengers that are formed from amino acids designed to mimic peptide fragments with endogenous biologic activity; one is a 5 amino acid fragment (pentapeptides lysine-threonine-threonine-lysine-serine [KTTKS]).
- KTTKS plays a role in signaling fibroblasts to produce collagen in the skin,[10] which can improve the appearance of wrinkles.
  - One variation, known as palmitoyl-lysine-threonine-threonine-lysine-serine (Pal-KTTKS) was tested in a controlled, double-blind, left-right randomized, split-face study of 92 photoaged women with Fitzpatrick I-III type skin between 35-55 years of age.
  - Pal-KTTKS concentration was 3ppm; both groups were treated twice daily for 12 weeks
  - Improvements in wrinkle appearance and length were observed.
  - When 3ppm pal-KTTKS was combined with 3.5% niacinamide vs. placebo, an even greater reduction in wrinkle length was noted.

N-Acetyl Glucosamine (NAG)

NAG is a more stable form of glucosamine, and **r**esearch indicates that it may prevent new signs of photodamage from occurring, and fade existing imperfections by interrupting the chemical signals that promote melanin production**.**

- A placebo-controlled study[11] comparing 3.5% NAG with the combination of 3.5% NAG + 3.5% niacinamide on hyperpigmented spots showed a superior reduction in pigmentation in the combination treatment group vs. both the placebo and NAG only groups.
  - When combined, the agents produced synergistic effects.

Use of Scientific Testing to Forecast Future Discoveries

- High throughput screening is presently in use to identify the next generation of active agents for cosmeceutical applications. This method has the capacity to screen thousands of compounds in a matter of days, or even hours.
- Genomic assays can be used to define all genes expressed in the skin. One application includes identifying targets for the management or prevention of skin and other disorders.
- Proteonics is a method of identifying proteins that are encoded by a genome. By promoting an understanding of the molecular mechanisms that cause human diseases, the development of novel therapeutic agents is possible.
- Metabonomics analyzes alterations in the metabolic end-products and the active pathways that result as a response to drugs, environmental influences, and diseases.

Conclusion

Keeping abreast of the latest findings and newest product offerings has become important for providing accurate advice to patients. Products supported by scientific research can be effective as an adjunct to therapy and/or part of a skincare regime. Actively assessing product clinical results, safety testing, and reviews from independent sources will enable clinicians to assist their patients in making informed product selections.

References

1. Kligman AM, et al. *J Am Acad Dermatol* 15(4 Pt 2):836-59 (1986 Oct).
2. Sorg O, et al. *Dermatol Ther* 19(5):289-96 (2006 Sep-Oct).
3. Gold MH, et al. *J Drugs Dermatol* 6(10):1018-23 (2007 Oct).
4. Lupo MP. *Dermatol Surg* 31(7 Pt 2):832-6 (2005 Jul).
5. Bissett DL. Topical retinyl priopionate – clinical comparison: a low irritation retinoid for diminishing wrinkles and hyperpigmentation in photoaged human skin. Presented at: The 60th Annual Meeting of the American Academy of Dermatology; New Orleans, LA; February 22-27, 2002. Poster #P78.
6. Tanno O, et al. *Br J Dermatol* 143(3):524-31 (2000 Sep).
7. Bissett D. *Cutis* 70(6 Suppl):8-12 (2002 Dec).
8. Hakozaki T, et al. *Br J Dermatol* 147(1):20-31 (2002 Jul).
9. Bissett DL, et al. *Dermatol Surg* 31(7 Pt 2):860-5 (2005 Jul).
10. Katayama K, et al. *J Biol Chem* 268(14):9941-4 (1993 May 15).
11. Kimball AB, et al. Topical formulation containing N-acetyl glucosamine and niacinamide reduces the appearance of hyperpigmented spots on human facial skin. Presented at: The 64th Annual Meeting of the American Academy of Dermatology; San Francisco, CA; March 3-7, 2006. Poster #P235.

Cosmeceuticals: A Panel Discussion About Educating the Public

Introduction

A panel presentation about cosmeceuticals was presented at the 2008 Dermatology Update meeting held April 10-12 in Whistler, BC. The panelists included 4 dermatologists: Jeffrey Dover, MD, Charles Lynde, MD, Catherine Zip, MD, and Jason Rivers, MD, who discussed cosmeceuticals and the role they play in adjunct therapy/effective skincare regimes in current dermatology practice.

They began by noting that on a daily basis they are asked by their patients to recommend skin care products. In order to be better prepared to address consumer queries and to convey practical information, medical professionals should gain fundamental knowledge of the active agents and available product variations. The panelists suggested that the healthcare provider's role can be two-fold: to arm consumers with basic, evidence-based information regarding the science behind various active agents, and to make general recommendations based on a patient's skin-type and individual medical background. They felt that dermatologists' combined understanding of the skin, drug compounding, pharmacodynamics, and pharmacokinetics, placed them in a unique position to influence patient behaviours, and that because of this they must adopt a well-rounded, informed, unbiased approach. While the panel members agreed that professional codes of conduct discourage them from endorsing specific products, they said that, in general, patients actively seek their recommendation and they often make suggestions from each class of skin care products. They concurred that the focus of their recommendations should be placed on providing education about how cosmeceuticals can be incorporated into existing skin care regimes.

Physician Endorsement

The term "dermatologist recommended" is often seen on product labels, and likely, the intended message being conveyed is that a panel of experts has assessed the product's efficacy and validated its claims.* The panelists all agreed that there must be evidence for efficacy, not just the extravagant claims that are frequently made.

Consumer Needs

Individual consumer needs and preferences can greatly assist in dispensing the proper information and narrowing down the types of products for which they can search. Consumer purchasing behaviours are complex and driven by information that is gleaned from multiple sources, as well as being steered by factors such as product efficacy, packaging, and cosmetic acceptability, i.e., patient adherence can be influenced by the product's feel, scent, etc. Because some active agents (e.g., retinoids, acne medications, botanicals, etc.) can produce sensitizing reactions, it is essential for patients to be counselled on expected side-effects, as well as mitigating factors.

The widely accepted skin care regime that these dermatologists recommend for photoaging is a morning application of a sunscreen, followed by use of a prescription retinoid in the evening, provided that tolerability to retinoids is not a concern. It is important to note that this basic regimen cannot be generalized across all populations; recommendations must be individualized.

Moisturizers

Reproducible, scientific evidence has shown that moisturizers yield both therapeutic and cosmetic benefits. Most act by improving barrier function with lipids and oils (decreasing transepidermal water loss) rather than by introducing moisture into the skin. Humectants, such as urea and lactic acid, have some ability to attract water from the dermis and the external environment. The efficacy of moisturizers is mainly derived from their ability to temporarily seal the epidermis and break the dry skin cycle.

Sunscreens and Vitamin D Deficiency

Recently, there has been a great deal of media coverage and published medical literature regarding vitamin D deficiency. As a result, patients are concerned that the use of sunscreens may put them at risk for vitamin D deficiency, and many are asking their physicians for clarification of this pseudo-controversy. There is very little evidence to support the hypothesis that sunscreens modify vitamin D levels. The general consensus in the scientific community is that sufficient levels of vitamin D

Sunscreens and Vitamin D Deficiency (continued)

can be attained from natural sources, i.e., through diet and moderate sun exposure. As this debate is unlikely to resolve in the near future, the panelists recommend continued regular use of a broad spectrum sunscreen with a minimum sun protection factor (SPF) rating of 30, in combination with daily oral vitamin D supplementation at a dose of 800-1,000 IU/day. Daily calcium supplements that include vitamin D are encouraged for women due to their susceptibility to osteoporosis later in life.

The US FDA is currently modifying its monograph on sunscreens, and new guidelines will be released within the next 2-3 years. The current SPF rating system only measures UVB coverage. The changes include an additional methodology that will determine a sunscreen's UVA protection factor using a 4-star rating system.

Contact Sensitivity

The panelists all agreed that contact sensitivities from cosmetics and cosmeceutical products occur, but incidences remain largely unreported to physicians, especially if reactions are mild. Botanical agents are some of the most potent contact allergens. The misperception is that because these cosmetic additives are naturally or plant derived, they pose little or no risk in causing skin sensitivities. Fragrances are also common sources of contact allergens. The present system of ingredient labelling represents an additional layer of confusion when consumers attempt to identify and avoid certain ingredients. For example, a product can claim to be preservative-free; however, the label may disguise an ingredient as a fragrance, when in actuality, it is a preservative with a scent added.

Initiatives by Industry

All the panelists agreed that the cost of any cosmeceutical product is not necessarily a reflection of its efficacy or quality. Increasingly, there is a noticeable effort on the part of larger cosmeceutical manufacturers to engage in clinical studies. The data generated can frequently be found at medical forums as poster presentations and presented at industry-sponsored educational forums/symposia. These attempts to evoke consumer confidence are a first step in the right direction and may form the basis of more accurate product representations.

Education and Information

Most reputable cosmeceutical companies make the scientific data behind specific formulations readily available. However, the panelists stressed that clinicians should be aware that for many cosmeceuticals, much of the scientific data used to support their claims are based on *in vitro* studies, and that while human studies are performed, the final formulation of the product has frequently not been tested in humans. There is a wealth of information on the internet, but panellists warned that clinicians should be aware that much of the content is based on conjecture and inference and they need to pay close attention to the source of the information/data that supports the content. The panel mentioned that it is common to find many of the reputable cosmeceutical manufacturers presenting their research at scientific meetings; these occasions are ideal for assessing the quality of the data used to support product claims, and health professionals are encouraged to participate in/attend such opportunities. Feedback from participants suggests that there is a need for more of these sessions on adjunct therapy.

The panelists concluded by agreeing that based on the myriad of informational sources, an inquisitive and discerning approach is required to assess the available data on cosmeceuticals. Health professionals need to actively seek and evaluate the information being shared, i.e., through well designed *in vitro* and *in vivo* clinical studies. These educational efforts will hopefully contribute to the accurate dissemination of information by medical professionals and to informed decision-making on the part of consumers.

* Editor's note: In response to consumer confusion about cosmeceutical products, SkinCareGuide has established a new professional review process for OTC skincare products to provide professional reviews of skin care product claims. The overall purpose is two-fold. First, the Dermatology Review Panel (DRP) assists consumers and medical professionals to easily identify nonprescription skincare products that meet independent approval standards with regard to product claims. Secondly, the DRP encourages manufacturers to engage in more clinical research. Readers can get more information by going to: http://www.dermatologyreviewpanel.ca.

New Evidence for the Treatment and Management of Actinic Keratoses

M. Sapijaszko, MD, FRCPC

Division of Dermatology, Department of Medicine, University of Alberta, Edmonton, AB
Western Canada Dermatology Institute, Surgical Unit, Edmonton, AB

Background

Increasingly, patients are seeking medical consultation for the management of photodamage, actinic keratoses (AKs), and nonmelanoma skin cancer (NMSC), which is now a global epidemic. The 2 most prevalent forms of NMSC are basal cell carcinoma (BCC) and squamous cell carcinoma (SCC).

- The earliest clinically recognizable manifestation of SCC is AKs.
- The impact of skin malignancies is substantial. They commonly result in considerable deformities, either from the disease itself or from the results of selected therapies.
- The incidence of both AKs and SCC continues to rise.

Actinic Keratoses

AKs are skin neoplasms that reflect cumulative UV damage to the epidermis. All AKs should be treated; they represent clinical evidence that patients have sustained sufficient UV damage to the epidermis to cause visually abnormal skin changes and alteration in the DNA structure.

- The risk of progression of AKs to invasive SCC was estimated to range from 0.025%-16% per year.[1]
- Risk factors for AK development include blonde hair, blue eyes, fair complexion, an inability to tan, a history of long-term sun exposure, and immunosuppression, such as that seen in organ-transplant recipients.

Treatment

Successful treatment of AKs rests on the:

- choice of appropriate modality
- medical status of the patient
- the patient's lesion account
- characteristics (e.g., size, duration, and growth pattern)
- anatomic location.

Several treatment options are available for AKs, including topical drug therapy and local destruction.

Locally Destructive Measures

Locally destructive therapies are specialized, office-based, and physician-administered, and are well suited to treat:

- individual lesions (e.g., cryosurgery, curettage, excision, or electrosurgery)
- extensive diffuse disease (e.g., dermabrasion, chemical peels, or laser ablation).

Cryosurgery

- Is the "gold standard" of locally destructive measures.
- Liquid nitrogen separates the epidermis from the dermis; it destroys both dysplastic and intact cells.
- Can be associated with patient discomfort.
- Can result in scar formation or dyschromia.
- Success rate is highly technique-dependent.

Topical Drug Therapy

Imiquimod

- The only approved topical immune response modifier approved by Health Canada and the FDA for the topical treatment of AKs and superficial BCCs (sBCCs).
- Enhances innate and acquired immune response by increasing regional antiviral, antitumor, and immunoregulatory activities.
  - Success in treating AKs and sBCCs is due to cytokine production stimulation, especially interferon.
- Side-effects include erythema, itching, and burning.
- Potential for improved patient compliance due to simplified dosing regimen.
  - Dosing at 2-3 times/week for imiquimod vs. twice daily for 5-fluorouracil (5-FU)

5-fluorouracil (5-FU)

- 5-FU is a commonly used topical treatment.
- It is a structural analog of the DNA precursor, thymine.
- The majority of people being treated with 5-FU will have moderate-to-severe erythema.
- Inhibits the enzyme thymidylate synthetase, and:
  - interferes with the DNA synthesis.
  - creates unbalanced growth and triggers cell death in both healthy and abnormal cells.
  - has its greatest effect on more rapidly dividing cells.

Photodynamic Therapy (PDT)

- PDT photosensitizers are activated by visible light.
- Creates cytotoxic oxygen species and free radicals,

Topical Drug Therapy (continued)

which selectively destroy rapidly proliferating cells.

- 5-aminolevulinic acid is a topical photosensitizer that:
  - is absorbed more by rapidly dividing cells.
  - is converted to protoporphyrin IX (PpIX), which is a potent photosensitizer within the cell. Activation of PpIX by physician-administered visible light produces singlet oxygen and free radicals, which leads to cell destruction.

Combination Therapy

In clinical practice, physicians frequently combine a physical/destructive modality, e.g., liquid nitrogen cryotherapy to treat visible AKs, with imiquimod to target the underlying field cancerization. This combination of cryotherapy and topical immunomodifier brings together a targeted approach through the precise immune system destruction of subclinical AK lesions, likely offering enhanced AK clearance. In a recent study:[2]

- imiquimod or vehicle was applied twice weekly for 8 weeks following 3- to 5-second cryotherapy of target AKs within a 50cm^2 fields on the face or scalp.
- at 12 weeks, more subjects treated with imiquimod achieved clearance of subclinical and total AKs.

Head-to-Head European Study

A recent comparative study by Krawtchenko, Stockfleth, and colleagues[3] evaluated 5% imiquimod with cryotherapy and 5-FU for the treatment of AKs. This pivotal study addresses several critical components in the therapeutic management of AKs that include clinical observation, histologic assessment, cosmetic outcome, and sustained clearance.
Histologically confirmed AKs were treated as follows:

Patients	Therapy Used	Therapy Details
26 patients	5% imiquimod	3 times/week for 4 weeks, 4 week rest period followed by the second cycle of 3 times/week for 4 weeks
24 patients	5% 5-FU	b.i.d. for 4 weeks
25 patients	Cryotherapy with liquid nitrogen	20 - 40 seconds for each lesion for up to 2 treatments

The assessment was performed after the treatments (Test of Cure [TOC] 6 weeks after cryotherapy, 4 weeks after 5-FU, and 8 weeks after imiquimod therapies), and at 12 months following the end of treatment. Treatment dosages were based on levels approved by the European Medicines Agency.

Therapy Group	Clinical Clearance at TOC	Histological Clearance at TOC	Sustained Clearance at 12 months	Excellent Cosmetic Outcome (% of pts)
Cryotherapy	68% (17 of 25)	32% (8 of 25)	4% (1 of 25)	4%
5% 5-FU	96% (23 of 24)	67% (16 of 24)	33% (8 of 24)	4%
5% imiquimod	85% (22 of 26)	73% (19 of 26)	73% (19 of 26)	81%

- The TOC clearance rate was similar between 5-FU and imiquimod.
- In terms of extended efficacy, imiquimod demonstrated significantly greater sustained clearance rates at 12 months.
- The cosmetic outcome at 12 months also favoured the use of imiquimod.

The differences in the results may be explained by their mode of action.

- Cryotherapy indiscriminately destroys good and bad cells.
- 5-FU interferes with DNA synthesis (again good and bad cells).
- Imiquimod selectively stimulates the immune system to act against subclinical and clinically visible abnormal cells.
- Targeted treatment with cryotherapy combined with field therapy using imiquimod may yield optimal clearance rates.

Previous research initiatives lacked the thorough comparative approach taken by this evidence-based study in exploring these common AK treatments. Data presented confirms that treatment with a topical immunomodifier provided superior sustained clearance and cosmetic outcomes in comparison with other commonly used therapies. Furthermore, these new study findings suggest that imiquimod should be considered by physicians as one of the first therapeutic options in the treatment of AKs.

References

1. Glogau RG. *J Am Acad Dermatol* 42(1 Pt 2):23-4 (2000 Jan).
2. Tan JK, et al. *J Cutan Med Surg* 11(6):195-201 (2007 Nov-Dec).
3. Krawtchenko N, et al. *Br J Dermatol* 157(Suppl 2):34-40 (2007 Dec).

SIGN UP FOR YOUR FREE SUBSCRIPTION

Skin Therapy Letter©

Pharmacist Edition

Editor-in-Chief: Dr Stuart Maddin

Go online to www.SkinPharmacies.ca and sign up today!

Go online to read this new dermatology publication for Pharmacists

- Peer reviewed articles
- Patient counseling advice
- Current treatment information

To get more information, Canadian medical professionals and consumers can access all of our sites from www.SkinCareGuide.ca or go directly to:

Patient sites:

AcneGuide.ca	BotoxFacts.ca	ColdSores.ca	DermatologyCare.ca
EczemaGuide.ca	FungalGuide.ca	HerpesGuide.ca	Lice.ca
MildCleanser.ca	MohsSurgery.ca	PsoriasisGuide.ca	PsoriaticArthritisGuide.ca
RosaceaGuide.ca	SkinCancerGuide.ca	Sweating.ca	UnwantedFacialHair.ca

Medical Professional sites:

SkinPharmacies.ca SkinTherapyLetter.ca Dermatologists.ca

We would love to hear from you!
Please email us with your comments and topic suggestions to
skintherapyletter@skincareguide.com

The following companies have provided an unrestricted educational grant for the distribution of our 2008 publications:

Dermik - The Dermatology Division of sanofi-aventis Canada Inc.

Graceway Pharmaceuticals LLC

Johnson & Johnson Inc.

LEO Pharma Inc.

Procter & Gamble

Stiefel Laboratories