



The growth of laser- and light-based procedures has not slowed the demand for effective topical treatments in the medical aesthetics industry. In fact, new ingredients and a growing recognition of the need for skin conditioning prior to and following cosmetic procedures are fueling an influx of new, physician-dispensed skincare lines into cosmetic practices. “Just as we see organic formulations gaining popularity in consumer cosmetics, we are also seeing major interest in science-based products,” says Sam Dhatt, MS, MBA, president and CEO of DermaQuest, Hayward, California. “I see specific growth in post-procedure skincare products that assist in wound healing after laser resurfacing or chemical peels.”

# Skincare Trends

By Linda W. Lewis

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**glimpse**

XanGo Glimpse features green chemistry—cold processing of botanicals like mangosteen, a minimal carbon footprint in the manufacturing process, and a formulation free of chemicals known or strongly suspected of causing cancer or birth defects.

Peptides continue to make news in skincare topicals. Jan Marini Age Intervention Peptide Extreme, for example, features four targeted peptide blends that work to rebuild and rejuvenate any skin type.



X-Cellerate by Results Rx uses L-arbutin and AGP Complex to stimulate fibroblasts and even out skin tone to prepare skin for medical procedures.



A complete pre- and post-procedure regimen available only through physicians' offices, Clinique Medical uses patent-pending Probiotic Technology to improve the skin's own defenses before treatments and to reduce inflammation immediately afterward. Innovative ingredients include hydrocortisone plus glyceritic acid, which slows the breakdown of hydrocortisone and other anti-irritants.



Clinique Medical, a joint venture of pharmaceutical giant Allergan and international cosmetic leader Clinique, is one of the most recent introductions aimed at physicians. The product line was designed for patients undergoing resurfacing procedures or other cosmetic treatments. Its patent-pending Probiotic Technology increases the skin's own defenses with its proprietary Lactobacillus Ferment, which helps maintain the skin's barrier with natural lipids and limits the risk of unintended effects of procedures. The Clinique Medical line includes Probiotic Cleanser, Skin Conditioning Treatment, Recovery Week Complex and Optimizing Treatment Cream. Another new key

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Physicians, including Vic Narurkar, MD, FAAD, board-certified dermatologist, director of the San Francisco Bay Area Laser Institute, and lead investigator in a study evaluating Clinique Medical in use with IPL and fractionated laser treatments, note that the focus on combining topical regimens with laser- and light-based services is likely a growing trend. “Until recently, there were no comprehensive skincare regimens designed specifically to complement in-office skin resurfacing treatments (i.e., using IPL or a fractional laser),” he says.

Beverly Hills, California-based plastic surgeon Michael B. Stevens, MD, PhD, FACS, now offers his patients pre- and post-procedure topical care through the retinoic acid-based Obagi line. “Topical skincare should come first,” he says. “It’s cost effective, low risk and helps to

improve skin condition for better outcomes, including quicker healing and reduced complications.”

“As more physicians embrace the concept of offering patients one-stop shopping, more companies are offering lines exclusively for this market channel,” says cosmetic chemist John Kulesza, PhD, president of Young Pharmaceuticals. “And I believe patients love being able to find higher potency products in their doctors’ offices with better product information than they can find in traditional retail environments.”

“We are seeing continued emphasis on physician-developed skincare lines at the retail level and in doctors’ offices—lines using technologies with sound

scientific support and measurable benefits,” agrees Barbara Green, RPh, MS, vice president, technology and clinical evaluations at The NeoStrata Company, Princeton, New Jersey. “NeoStrata, for example, is targeting regimen groupings in which a few products with complementary technologies are used together to deliver visible clinical results.”

### New Ingredients

While science and results are emphasized in lines directed at medical practices, physician-dispensed lines are also continuing to trend toward **pure and natural ingredients**. “It actually started seven or eight years ago,” notes Howard Murad, MD, a dermatologist and founder of Murad Inc., El Segundo, California, “with a surge in ethnobotany—herbs/foods grown in specific habitats that were found to be high in specific chemicals, such as pomegranates from North Africa, which proved

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Murad aims to give new meaning to “beauty sleep” with its Sleep Reform Serum and Supplements designed to help the skin “sleep” with gamma-aminobutyric acid to encourage muscle relaxation, methyl-sylfonimethan to reduce inflammation, and body and skin relaxing melatonin in the supplement and the topical.



Retinols continue to set the standard for well-researched product ingredients. Procyte's new NEOVA Matrix AR contains patented retinol technology.



GliSODin Skin Nutrients' new line confirms the trend toward inside-out skin health.

to be especially effective at preventing and treating sun damage.”

As the century turned, antioxidants became all the rage: Green tea, gogiberry, Revalskin's CoffeeBerry and other botanical extracts showed significant effects when tested in vitro and in some limited in vivo studies.

“Our latest find is durian extract from Southeast Asia,” says Dr. Murad. “It contains numerous fatty acids, as well as other valuable fruit acids. We use it in Durian Cell Reform to increase cell turnover and provide intensive hydro protection.”

Another new antioxidant is BioActive X<sup>3</sup> Complex, which is found in Glimpse Intuitive Skin Care from XanGo, a global nutrition company. The complex, which

diets meant to stimulate them constitute another major skincare trend. In a review of cosmeceutical agents published in the July 2008 issue of *Clinical Medicine: Dermatology* (Libertas Academica), Thomas C. Tsai and Basil M. Hantash, MD, PhD from the Program for Regenerative Medicine at Stanford University School of Medicine, Stanford, California, define growth factors as “large proteins that are synthesized by a variety of cells in the body and play an important role in the regulation of immunity, cell division, wound healing and tissue regeneration.” They report that TNS Recovery Complex (SkinMedica) has shown some interesting results but needs to be tested in controlled studies, as have

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uses mangosteen extract, combines three exclusive xanthone-rich ingredients that, according to Japanese in vitro studies, contain 30 times more antioxidant potency than green tea. The study also indicated anti-inflammatory action and collagen stimulation.

“**Peptides** are still a growing segment in the industry, as well,” says Dhatt, “and I don't see this trend slowing down anytime soon. If peptides can be delivered into the skin, with their smaller molecular size and assisted delivery systems, they can mimic many skin functions without irritation, which is extremely compelling in cosmetic science. There are also peptides that stimulate the body's own growth factors, which can potentially replace using growth factors from human sources.”

Skin **growth factors** and ingre-

Citrix CRS Cream (Topix Pharmaceuticals) and Pal-KTTKS (P&G Beauty).

Since the size of growth hormone proteins makes them largely unsuitable for topical treatments, many formulators are working with short-sequence peptides (oligopeptides) containing the receptor binding motif of specific growth-factor proteins instead.

“Growth-factor stimulators aren't really new; we've had them in our products for at least five years,” says Dr. Murad. But they are just now becoming a marketing trend with lots of companies using the term. The Murad Professional line features proprietary Immuno-Skin Complex, a sequence of biopeptides formulated to strengthen skin immunity and stimulate the growth factors that regulate dermal matrix remodeling.

The TNS Recovery Complex, which

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was introduced in August 2007, has found an enthusiastic following in medical aesthetic practices. It contains vascular endothelial growth factor, transforming growth factor (TGF)-beta-1 and soluble collagen and matrix proteins. Manufacturer studies show it promotes collagen synthesis, blood vessel formation, and fibroblast and keratinocyte proliferation.

Topix Citrix CRS Cream with human growth factor TGF-beta-1 stimulates collagen growth and strong tissue structure. The CRS delivery system ensures vitamin C and TGF-beta-1 stability while enhancing penetration. A study done by Mitchell Goldman, MD, showed that after 60 days, patients experienced a 30% increase in collagen and a 50% decrease in lines and wrinkles.

In September 2008 Senetek introduced Pyratine-6, which it dubbed "revolutionary cytokinin-based skincare." The company says the new technology works faster than kinetin to reduce roughness and redness. Jerry L. McCullough, MD, et al. published an independent study on Pyratine-6 in the February 2008 issue of *Journal of Drugs in Dermatology*. Dr. McCullough concluded, "Treatment with Pyratine-6 (0.1%) over 12 weeks showed improvement in roughness and skin moisturization in two weeks and hyperpigmentation and fine wrinkles in four weeks." Adverse effects were minimal and transient.

In October 2008, San Diego-based Histogen, which calls itself a regenerative medicine company, announced a new cosmeceutical venture, Histogen Aesthetics. Headed by Lawrence A. Rheins, PhD, the company is developing a line of products based on its ReGenica Complex launched in early 2009 and distributed exclusively via physicians' offices. ReGenica is formulated with neonatal foreskin cells treated with enzymes and nutrients, which are maintained in an "embryonic-like state." As the cells in the culture grow, they release growth factors and extracellular matrix into the vitamin mixture. The

final product is an aqueous solution containing a complex mixture of actives such as keratinocyte growth factor, soluble human collagen and natural cellular antioxidants. The mimicking of in utero conditions provides the correct microenvironment for these cells

to produce extracellular insoluble and soluble factors.

"What I like is that we are not adding outside growth factors; we're working with the skin's own physiology," says Rheins. "Most dermatology problems have a base of chronic inflammation,

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and this technology will address that.” The company is distributing the line through dermatologists and plastic surgeons “because we want their feedback,” says Rheins.

Also introduced in October 2008, Estée Lauder’s new Time Zone Line features sirtuins, which the company calls “the next big thing” in antiaging skincare products. In “Sirtuins: A Breakthrough in Antiaging Research” (*Cosmetics & Toiletries*, January 2008) by Isabelle Imbert, PhD, et. al., from ISP Global Skin Research Center in Sophia Atipolis, France, the researchers explore the latest literature on this “recently discovered family of proteins” and conclude that cells where SIRT1 was induced with an appropriate SIRT1 expression optimization activating compound (STAC) show a decrease in cell senescence; overall studies suggest that “SIRT1 expression optimization is an important strategy in the fight against aging,” say Imbert, et al. The Estée Lauder Time Zone Line combines its Sirtuin EX-1 compound with Tri-Hyaluronic Acid Technologies, which contain high molecular weight hyaluronic acid, hyaluronic acid fragments and anti-hyaluronidase technology to revive aging skin, and plump and tone it with optimum hydration.

“The bottom line is that while it’s nice when an expensive skincare product—and human growth factors are expensive—appears more effective than a placebo, it must be compared to a retinoid to assess its true efficacy,” says Young Pharmaceutical’s Kulesza of growth factors in skincare formulations. “Retinoids are unquestionably safe and effective for the treatment of photoaging. Any manufacturer of a product claiming to treat photoaging must ultimately compare its product to a retinoid and, so far, I’m not seeing that done. I do think the SIRT-1 research is exciting; however, I am not convinced that any of the present ingredients claiming to mediate SIRT-1 activity have been sufficiently validated.”

### RECENT RESEARCH

“New ingredients are introduced every day from around the globe, and data or information on ingredients is presented in a wide variety of ways, sometimes making it difficult to understand the findings and how they translate into cosmetic skin benefits,” explains Laura J. Goodman, MS, P&G Beauty Science. “Ingredients are tested in the laboratory in what we call a ‘simple vehicle’ (dissolved in water or another solvent) or ‘formulation’ (in a cream or gel). Ingredients can be evaluated in vitro or in vivo. Occasionally, in vitro test results can predict how an ingredient will perform in vivo, but not always. There are many steps between discovering a new ingredient and ensuring that it is in a formulation that allows for safe, effective delivery into the skin. It is important to understand how an ingredient has been evaluated and what safety testing has been done on it.

“As you gather information on new ingredients and products, I recommend asking for claims substantiation. Claims substantiation documents should inform you about what testing has been done and how particular claims on the ingredients or products are supported.”

You can also look for published studies. Below is a compilation of some of the research published in peer-reviewed journals or presented at major professional meetings since our previous skincare trends article that was written in August 2007. They are presented by date, with the most recent first.

**T Biro, MD, PhD, et al.,** Role of endocannabinoids in skin health, *FASEB J*, October 2008

**CD Mnich, et al.,** Green tea extract reduces induction of p53 and apoptosis in UVB-irradiated human skin independent of transcriptional controls, *Exper Dermatol*, October 2008.

**JC Murray, MD, et al.,** A topical antioxidant solution containing vitamins C and E with ferulic acid protects human skin from sunlight damage and DNA mutations associated with skin cancer,

presented at The Academy for Investigative Dermatology, October 2008.

**BS Park, et al.,** Adipose-derived stem cells and their secretory factors as a promising therapy for skin aging, *Dermatol Surg*, October 2008.

**JM Crowther, et al.,** Measuring the effects of topical moisturizers on changes in stratum corneum thickness, water gradients and hydration in vivo, *Brit J Dermatol*, September 2008.

**TC Tsai and BM Hantash, MD, PhD,** Cosmeceutical agents: a comprehensive review of the literature, *Clin Med: Dermatol*, July 2008.

**EB Souto and RH Muller,** Cosmetic features and applications of lipid nanoparticles (SLN, NLC), *Int J Cosmetic Sci*, June 2008.

**C Barba et al.,** Cosmetic effectiveness of topically applied hydrolysed keratin peptides and lipids derived from wool, *Skin Res and Tech*, May 2008.

**GJ Fisher et al.,** Fibroblast collapse and therapeutic implications, *Arch Dermatol*, May 2008.

**BA Green, et al.,** Antiaging effects of topical lactobionic acid: results of a controlled usage study, *Cosmet Dermatol*, February 2008.

**C Millikin, et al.,** Additive benefits of the cosmetic ingredients niacinamide and N-acetyl glucosamine towards the in vitro regulation of melanin production, presented at the World Congress of Dermatology, October 2007.

**MK Robinson, et al.,** Immune and inflammatory gene expression profiles of chronological (intrinsic) skin aging and photoaging, presented at the World Congress of Dermatology, October 2007.

**DL Bissett, et al.,** Topical niacinamide formulations reduce the appearance of facial skin redness while formulation or other nicotinates induce skin flushing, presented at the World Congress of Dermatology, October 2007.

**R Osborne, et al.,** In vitro skin structure benefits with a new antiaging peptide, Pal-KT, presented at the World Congress of Dermatology, October 2007.

**KE Burke,** Interaction of vitamins C and E as better cosmeceuticals, *Dermatol Ther*, September 2007.

**RC Mehta and FE Fitzpatrick,** Endogenous growth factors as cosmeceuticals, *Dermatol Ther*, September 2007.

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**“DNA repair ingredients and non-human based stem cell technology** are also of interest in today’s antiaging skincare market, and this segment will continue to grow,” predicts Dhatt, who says that one of the most interesting new ingredients he has come across in a long time is PhytoCellTec Malus Domestica (apple stem-cell extract). Introduced by a Swiss company, Mibelle Biochemistry, in February 2008, and studied in the U.S. by Gary Goldfaden, MD, a clinical dermatologist in Hollywood, Florida, it is a liposomal preparation of stem cells from the Uttwiler Spätlauber apple, a tannin-rich variety that has unique storage longevity. A patent-pending plant cell culture technology was developed to cultivate dedifferentiated callus cells. Company in vitro studies have shown that PhytoCellTec Malus Domestica protects the longevity of skin stem cells, delays senescence of essential cells, combats the signs of chronological aging and regenerates the skin. A small human trial showed a 15% reduction in wrinkle depth after four weeks of use.

### What’s Next?

Most of the ingredients and formulations introduced in the past year are relatively untested and their true value is yet to be determined. “New research on skin actives depends largely on having reliable screening assays to study effects on skin. As more sophisticated assays are available, companies will better understand the effects of their ingredients on skin and understand how to optimize complementary or synergistic effects,” says Green. For example, the presentation by Murray et al. (see “Recent Research” on page 36) on a topical antioxidant solution containing vitamins C and E with ferulic acid employs a more advanced antioxidant screening model that demonstrates the usefulness of a material in helping to prevent damaging DNA mutations following UV exposure. NeoStrata is working on similar research with some of its newer patented antioxidant materials.

Innovations in skin care can come from discovering useful new properties of botanicals or other chemical combinations, but often they come from a study of the human body itself. Murad Inc. continues to create new products based on Dr. Murad’s research into the role water loss plays in cell health and how to strengthen

cell walls and prevent cellular dehydration and impaired function. “The human body is the source of all kinds of useful chemicals that we can unlock under appropriate circumstances,” says Dr. Murad. 

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