

# Promoting Collagen with Glycerophospholipids and Other Topics: Literature Findings



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This month's survey of recent patent and research literature describes money-making ideas for personal care product development, including decreasing  $TiO_2$  damage, enhancing hydration with fatty acids, promoting collagen with glycerophospholipids, permanent hair straightening, and copolymers for adhesion in mascara, among others.

## Skin and Skin Care

### Enhancing penetration with PTDs:

Lopes et al. have published on the enhanced skin penetration of P20 phosphopeptide by covalent attachment to protein transduction domains (PTDs).<sup>1</sup> Researchers first evaluated whether non-covalently linked PTDs were capable of increasing the skin penetration of P20. Two different PTDs were studied: YARA and WLR. Porcine ear skin mounted in a Franz diffusion cell was used to assess the penetration of P20 into the stratum corneum (SC) and viable skin (VS). VS consists of the dermis and epidermis without SC. The transdermal delivery of P20 also was assessed. At 1 mM, YARA promoted a 2.33-fold increase in the retention of P20 in the SC but did not significantly increase the amount of P20 that reached the VS.

WLR, on the other hand, did significantly increase the penetration of P20 in VS by 2.88-fold. However, compared with the non-attached form, the covalently linked WLR fragment was two times more effective in promoting the penetration of P20 into the VS. None

of the PTDs promoted transdermal delivery of P20 at 4 hr post-application. It was thus concluded that selected non-covalently linked PTDs can be used as a penetration enhancer but greater skin penetration efficiency can be achieved by covalently binding the PTD to the therapeutic agent.

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**2,2'-Cyclolignans for hair/skin pigmentation:** Greentech disclosed the use of 2,2'-cyclolignans in the cosmetic or pharmaceutical field for inducing, restoring or stimulating the pigmentation of skin or hair.<sup>2</sup> The efficacy of gomisin A on stimulating melanin synthesis in melanocyte B16 was shown.

**Enhancing hydration with fatty acids:** Unilever PLC has created in-shower, rinse-off lotion compositions to enhance skin hydration that comprise from 2–10% free fatty acids.<sup>3</sup> The ratio of unsaturated to saturated fatty acids is 1:1 or greater, and the compositions contain relatively low amounts of oil/emollient and aqueous phase stabilizer/structurant. The use of unsaturated fatty acid, or at least a minimal amount of unsaturated fatty acid as a percentage of the total fatty acid, resulted in unexpectedly high hydration levels. Use of branched fatty acids, with a minimal amount branched as a percentage of total fatty acid, also resulted in superior hydration. Mixtures of unsaturated and branched fatty acids could be used as well. Thus, use of 3% unsaturated oleic acid in the lotion resulted in far greater hydration when compared with

a similar composition containing 3% saturated lauric acid.

**Delivery system for phytosterol sugar esters:** Bioderm Research has disclosed a topical delivery system for phytosterol sugar esters for the treatment of skin conditions.<sup>4</sup> This invention relates to certain sugar esters of phytosterols with the formula:



where  $n = 0, 1, 2$  or  $3$ ;  $R = H, CH_2OH, CH(OH)-CH_2OH, CH(OH)-CH(OH)-CH_2OH$ ; and  $R1 =$  sapogenin, steroid, or terpenoid.

These esters are useful for the topical treatment of a variety of skin conditions including: pigmented spots, acne, loss of cellular antioxidants, collagen loss, loss of skin pliability, loss of skin suppleness, skin wrinkles including fine lines, oxidation, damage from radiation, malfunction of matrix metalloproteases, malfunction of tyrosinases, damage from free radicals, damage from UV, dry skin, xerosis, ichthyosis, dandruff, keratoses, melasma, lentigines, liver spots, dark circles under the eyes, oily skin, warts, eczema, pruritic skin, psoriasis, inflammatory dermatoses, topical inflammation, disturbed keratinization, skin changes associated with aging, nail or skin requiring cleansers, conditioning, conditioning/shampooing of the scalp, and combinations of the above.

Diosgenin gluconate was prepared with 10% w/w water, 5% w/w diosgenin, 81% w/w polyethylene glycol and 4% w/w gluconolactone. The ingredients were mixed and heated at 80–95°C for 2 hr and a clear solution was obtained. The resulting diosgenin gluconate can be used directly in subsequent cosmetic preparations.

**Promoting collagen with glycerophospholipids:** Unitika Ltd. has published on collagen production promoters containing glycerophos-

pholipids.<sup>5</sup> The company aimed to develop inexpensive, safe and effective collagen promoters for the food, drug and cosmetics industries to improve skin aging and roughness. The collagen production promoter disclosed contains the active ingredient glycerophospholipid—specifically a glycerophospholipid such as phosphatidylcholine, lysophosphatidylcholine,

phosphatidylserine, lysophosphatidylserine, phosphatidylethanolamine, lysophosphatidylethanolamine, phosphatidylinositol, lysophosphatidylinositol, phosphatidic acid, lysophosphatidic acid, phosphatidylglycerol or lysophosphatidylglycerol. In addition, the active has an unsaturated fatty acid as part of its structure. The effect of 1,2-dioleoyl-sn-glycero-

3-phosphate sodium salt (DOPA Na) on collagen production in cultured human fibroblast NHDF cells was thus examined.

**Particle coating to decrease TiO<sub>2</sub> damage to cells:** Pan et al. have published on the adverse effects of rutile and anatase titanium dioxide nanoparticles on human dermal fibroblasts as well as an approach to protect cells from this damage via a particle coating.<sup>6</sup> Both types of particles can impair cells—decreasing cell size, proliferation, mobility and their ability to contract collagen; however, anatase particles are the most damaging. Individual particles were shown to penetrate easily through the cell membrane in the absence of endocytosis while some endocytosis was observed for larger particle clusters. Once inside, the particles are sequestered in vesicles, which continue to fill up with increasing incubation time until they rupture.

These particles were therefore coated with a dense grafted polymer brush and tested. Using flow cytometry, the coated particles were shown to prevent adherence to the cell membrane and thus penetration into the cell, which effectively decreases the formation of reactive oxygen species (ROS) and protects the cells, even in the absence of light. Considering the broad applications of titanium dioxide nanoparticles in personal health care products, the functionalized polymer coating could play a potentially important role in protecting cells and tissue from damage.

## Hair and Hair Care

**Permanent hair straightening:** Ogawa et al. have published on the chemical reactions that occur during permanent hair straightening using thioglycolic acid (TGA) and dithiodiglycolic acid (DTDGA).<sup>7</sup> For decades, a curing method for hair straightening has been practically applied that consists of the reduction of the hair molecule followed by washing, heat treatment and oxidation. Two different reduction systems were examined by the authors: one containing TGA only and the other a bicomponent system containing TGA and DTDGA. The reaction mechanism

was proposed on the basis of amino acid analysis of hair samples obtained at various treatment steps. New equilibrium reactions were assumed to be established in the reduced fiber after washing, which could successfully explain the experimental results.

When TGA is used for the reduction, hair is severely damaged due to the formation of mixed disulfide groups. Thus, when the TGA-only system was examined, mixed disulfide groups were formed in the hair fiber and the number of groups incorporated was dependent upon the concentration of TGA. In the heat-treatment step at 180°C for 3 sec, the mixed disulfide groups were wholly converted into the thiol groups of cysteine residues.

However, when the bicomponent system was applied, only the thiol groups were linked to the protein chains, even under hot permanent conditions at 45°C for 15 min. DTDGA thus serves as not only a reduction-regulating agent, but also as a thio-reforming agent. There-

fore, it was concluded that DTDGA acts as an anti-damage agent in hair straightening formulations.

**Preventing oxidative color loss:** Brown et al. have disclosed a method for preventing color loss in oxidatively dyed hair.<sup>8</sup> This method includes washing the hair with a shampoo composition and rinsing the composition from the hair. The shampoo composition contains 5–50% w/w anionic surfactant, 0.025–5% w/w synthetic cationic polymer, and enough water to equal 100% w/w. The cationic polymer has a cationic charge of 3 meq/g and forms lyotropic liquid crystals upon combination with the anionic surfactant.

**Frizz management:** L'Oréal disclosed a process for managing a keratinous substrate such as hair with a composition including: a phospholipid; a polyamine; a fatty monoamine or a fatty quaternary amine; at least one nonionic surfactant; an alkyl(ether) carboxylate with approx. 6–40 carbon atoms or an alkyl(ether)phosphate with

approx. 6–40 carbon atoms; at least one water-insoluble material; and at least one film former.<sup>9</sup> Thus, 1.5 g/swatch of 5% polyetherimide, 20% PPG-5 ceteth 20<sup>a</sup>, 2% laureth-5 carboxylic acid, 3% mineral oil and 3% polyvinylpyrrolidone<sup>b</sup> was massaged into hair swatches for 15 sec and allowed to stand at RT for 1 min. Good anti-frizz properties were documented.

**Pastel hair coloring:** Henkel AG & Co. has disclosed the pastel coloring of hair involving consecutive bleaching and dyeing steps, including:<sup>10</sup> application of a hair bleaching preparation for up to 45 min, rinsing off the bleaching agent, application of the hair dye containing at least one natural dye, and rinsing off the hair dye. The hair dye contained ammonia rather than amines, hydrogen peroxide and other peroxides. This hair dye formulation also can include

<sup>a</sup>Procetyl AWS (INCI: PPG-5 Ceteth 20) is a product of Croda Inc., Edison, N.J., USA.

<sup>b</sup>PVP K90 (INCI: Polyvinylpyrrolidone) is a product of International Specialty Products, Wayne, N.J., USA.

**Formula 1. Self-tanning preparation<sup>12</sup>**

Stearic acid	2.00% w/w
Dicaprylyl ester	3.00
Octyldodecanol	2.00
C <sub>12-15</sub> alkyl benzoate	4.00
Cetyl alcohol	2.00
Cetearyl ethylhexanoate (and) isopropyl myristate	2.00
Glycerin	6.00
Ethylhexyl methoxycinnamate	2.00
Titanium dioxide	1.00
Cetyl palmitate	1.00
Glyceryl stearate	1.00
Phenoxyethanol	0.40
Butyl-methoxydibenzoyl methane	2.00
Fragrance ( <i>parfum</i> )	qs
EDTA	0.20
Carbomer	0.20
Folic acid	0.05
Magnesium aluminum silicate	0.20
Methylparaben	0.10
Vitamin A acetate	0.10
Glycyrrhetic acid	0.10
Dihydroxyacetone	1.50
Propylparaben	0.05
Butylated hydroxytoluene	0.05
Water ( <i>aqua</i> )	qs to 100.00

cationic polymers, amino acids, vitamins, ubiquinones, purine derivatives, saccharides, 2-furanone derivatives, taurine and bisabolol.

**Preventing hair dye fade:** Takara Belmont Co. has developed oxidative hair dyes formulated with post-dye treatment agents of cinchona bark extracts and antioxidants.<sup>11</sup> The post-hair dye treatments have a pH 4.0–7.0 at the time of use, and the complete hair dye has a pH of 7.0–12.0 at the time of use. A hair dye preparation containing ammonia water, p-phenylenediamine, resorcin, m-aminophenol, cinchona bark extract and ascorbic acid was mixed with a second preparation (pH 3.0) containing hydrogen peroxide at 1:1 by wt. to give a mixture with a pH 7.0–12.0. Hair dyed with the mixture was resistant to discoloration by UV irradiation.

### Self-tan/Sun Care

**Self-tanner composition:** Beiersdorf AG has disclosed cosmetic or dermatological formulations of dihydroxyacetone; glycyrrhetic acid and/or glycyrrhizine; and optionally eryth-

rulose in cosmetic preparations for self-tanning.<sup>12</sup> An example is shown in **Formula 1**.

**Validating sunscreen agents:** Lee et al. have published on the determination and validation of six sunscreen agents in sun care products through ultra performance liquid chromatography (UPLC) and high performance liquid chromatography (HPLC).<sup>13</sup>

Methylene bis-benzotriazolyl tetra-me butylphenol and bis-ethylhexyloxy phenol methoxyphenyl triazine are sunscreen agents that have hydrophobic behaviors in common. They typically are not assayed with the sunscreen agents ethylhexyl methoxycinnamate, isoamyl p-methoxycinnamate, ethylhexyl salicylate or ethylhexyl triazone, since these materials have hydrophilic behaviors in a single chromatographic run. For this reason, products containing methylene bis-benzotriazolyl tetra-me butylphenol and bis-ethylhexyloxy phenol methoxyphenyl triazine require more time to assay. Therefore, the development of a rapid, selective and reproducible determination method for the simultaneous examination of

**Formula 2. Mascara<sup>15</sup>**

Copolymer A	3.20 parts
Polyacrylic acid sodium salt	0.05
Alkyl acrylate copolymer ammonium salt	12.00
Polyvinylpyrrolidone	1.00
Sorbitan stearate	0.50
Stearic acid	1.00
2-amino-2-methyl-1-propanol	0.60
Beeswax	6.00
Carnauba wax	2.50

methylene bis-benzotriazolyl tetra-methylphenol and bis-ethylhexyloxy phenol methoxyphenyl triazine with hydrophilic sunscreen agents would be beneficial to reduce the examination time required and to improve the quality control of sun care products.

In this paper, an HPLC and UPLC system is used to examine the sunscreen agents. Several evaluations of mixtures of eluents and columns were obtained

for the optimal condition of separation. In HPLC, the optimal peak resolution was obtained through ethanol-water gradient elution and a 75-mm C18 column with a 3.5- $\mu$ m-sized particle on a flow rate of 1.0 mL/min. In UPLC, the most distinctive peak resolution was obtained through methanol-water gradient elution and a 50-mm C18 column with a 1.7- $\mu$ m-sized particle on a flow rate 0.4 mL/min. Both of these chromatographic determination methods could be used to examine six types of sunscreen agents without any interference from other product excipients in the agents. The proposed determination methods were validated for specificity, linearity, repeatability, system stability, intermediate precision and accuracy. Consequently, HPLC and UPLC methods could be used as rapid, selective and proper applications to assay sunscreen agents in sun care products.

## Color Cosmetics

**Solid powder cosmetics:** Tokiwa Corp. and Nippon Menard Cosmetic

Co., Ltd. have disclosed compression-molded solid powder cosmetics with excellent impact resistance and spreadability.<sup>14</sup> The cosmetics, useful for makeups, contain  $\geq 30\%$  w/w inorganic powders selected from mica, titanate mica and their surface-treated products; 0.2-4.0% w/w candelilla wax; and 0.5-4.0% w/w glycerin tris(caprylate/caprate). An eye color containing 27.68% w/w mica<sup>c</sup>, 11% titanate mica<sup>d</sup>, 0.2% candelilla wax and 2.0% w/w glycerin tris(caprylate/caprate)<sup>e</sup> showed uniform spreadability, a nonsticky feel, a moist feel on skin, and no cracking or peeling after falling.

**Copolymers for adhesion in mascara:** Pias Corp. has disclosed eyelash cosmetics containing urethane acrylate

<sup>c</sup>Mica Powder SA-310 (INCI: Mica) is a product of Kobo Products Inc., South Plainfield, N.J., USA.

<sup>d</sup>Timiron Starluster MP-115 (INCI: Titanate Mica) is a product of EMD Chemicals Inc./Rona, Gibbstown, N.J., USA.

<sup>e</sup>Myritol 318 (INCI: Caprylic/Capric Triglyceride) is a product of Cognis, Monheim am Rhein, Germany.

copolymers with excellent adhesion properties.<sup>15</sup> The cosmetics contain the copolymers from methyl methacrylate, methacrylic acid and/or acrylic acid, urethane acrylates and optionally polyacrylic acid salts, alkali agents, water-dispersible film-forming agents, water-soluble polymers, fatty acids, nonionic surfactants, oil phase-forming agents, fibers and colorants. An example of a mascara is shown in **Formula 2**.

It can be concluded  
that DTDGA acts as  
an anti-damage agent  
in hair straightening  
formulations.

## Dentifrice

**Stabilizing color in oral peroxide formulations:** Colgate-Palmolive Co. has disclosed color-stable, peroxide-containing dentifrice formulations with dye encapsulated silica shell nanoparticles.<sup>16</sup> The composition for minimizing the color fade of an oral care composition is comprised of an organic dye such as FD&C Blue No. 1 encapsulated in a silica shell nanoparticle matrix; approx. 0.1–1% w/w of a physiological stable fluoride ion compound; and 1–2% w/w of a peroxide species compound such as hydrogen dioxide. The encapsulated silica shell dye nanoparticle stabilizes the color against degradation in the presence of peroxide and fluoride ions.

## Interesting Compositions

**Vesicle-silica complex:** Shiseido Company Ltd. has developed compositions containing a vesicle-silica complex and provided a process for the production of this composition.<sup>17</sup> The vesicle-containing composition exhibits improved stability and can release a medicinal or perfume component contained therein at a sufficiently reduced rate upon administration to a living

body or application to the surface of the skin. A water-soluble silane derivative having a specific structure was added to and mixed with an aqueous composition containing a vesicle composed of a surfactant, thereby producing a vesicle-silica complex in which the polymerization of silica has proceeded on the outer surface of the vesicle to coat the outer surface with silica.

Glycerin-substituted tetraethoxysilane was prepared at 0.5% w/w and mixed with a 5% w/w polyoxyethylene dimethylpolysiloxane solution to form a vesicle-silica complex. Also, a transparently-dispersed cosmetic lotion containing 0.3% w/w polyethylene glycol dimethylpolysiloxane, 5% w/w dipropylene glycol, 0.5% w/w glycerin-substituted silane derivative, 0.05% limonene and a balance to 100% w/w of water was formulated.

**Multifunctional polygala extracts:** Maruzen Pharmaceuticals Co., Ltd. has disclosed title agents, cosmetics, foods and beverages containing extracts of *Polygala chinensis*, *Polygala japonica*, and/or *Polygala arvensis* as active ingredients. These actives can be used: as antioxidants, as platelet aggregation inhibitors, as TNF-alpha-formation promoters, in skin-lightening cosmetics, in foods, in beverages, as anti-inflammatory agents, in antiaging products, as anti-obesity agents, and as immunostimulating agents.<sup>18</sup>

The extracts promote the biosynthesis of IV collagen and glutathione, promote the proliferation of epidermis keratinocyte and fibroblast cells, promote the expression of HAS3 mRNA and aquaporin mRNA, show estrogenic activity and are useful for the treatment of UV-damaged skin. Therefore, 80% ethanol extract of *Polygala chinensis*, *Polygala japonica*, and *Polygala arvensis* scavenged superoxide with IC50 values of 55.7, 50.0 and 71.8 µg/mL respectively, and inhibited cAMP phosphodiesterase with IC50 values of 75.2, 76.4, and 81.3 µg/mL, respectively.

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