

stearic acid, cholesterol acetate, and ceramide C, collectively referred to as physiological lipids.<sup>78</sup>

The surface hydrophilic film and the intercellular lipids in the stratum corneum (together the skin lipids) are susceptible to deterioration from surfactants in soaps and other skin cleansers with resultant loss of normal barrier function. These skin lipids may also be impaired by inflammatory skin conditions such as eczema and psoriasis.<sup>9</sup> Several non-physiological strategies have been developed to treat dry skin. Occlusive products containing beeswax, lanolin, mineral oil, paraffin, petrolatum, propylene glycol, silicones, and squalene are designed to prevent evaporative water loss.<sup>10,11</sup> Humectants are hygroscopic substances that can absorb water from the air. When applied to the skin they can draw water from the environment or underlying layers of the skin to moisturize the stratum corneum. Humectants include alpha hydroxy acids, glycerin, hyaluronic acid and derivatives, pyrrolidone carboxylic acid, tyrosine, sorbitol, and urea.<sup>10,12,13</sup>

### Taurine

Taurine (2-aminoethane sulfonic acid) is a sulfur-containing amino acid that is present in high concentrations in mammalian tissues and plays an important role in several essential biological processes. It is widely distributed throughout the human body and found in high concentrations in the epidermis<sup>14</sup> where it contributes to homeostasis, mainly through its antioxidant<sup>15,16</sup> osmoregulatory and membrane stabilization properties.<sup>17-19</sup> Taurine is an important scavenger of reactive intracellular carbonyl and glycation intermediates.<sup>20</sup>

Other beneficial properties attributed to taurine include antimicrobial, cytoprotection, photoprotection, antioxidant, antiinflammatory, osmoregulatory, and inhibition of glycation.<sup>21</sup> In addition to powerful humectant properties, taurine contributes significantly to the prevention of skin aging. The formation of advanced glycation end products (AGE)<sup>22</sup> impairs the function of collagen and structural proteins associated with aging skin.<sup>23-25</sup> By decreasing AGE formation, taurine can prevent photo-aging and normal chronologic skin aging.<sup>25,26</sup> Topical taurine also promotes wound healing<sup>27,28</sup> and plays a key role in osmoregulation and maintaining keratinocyte hydration.<sup>29</sup>

### The Taurine Transporter and Osmoregulation

Taurine contributes most significantly to the cellular pool of organic osmolytes in the epidermis and plays an important role in restoring cell volume following osmotic disturbances.<sup>30</sup> Aside from the stratum corneum, the most important physiological process involved in retaining water in the cells of the epidermis is the taurine transporter (TauT). Taurine is actively and selectively transported into the cells of epidermis, where it is the single most abundant osmolyte, acting as a cytoprotectant

to maintain cellular integrity. The TauT is present in high levels in the granular layer (stratum granulosum) and to a lesser degree in the spinous layer (stratum spinosum).<sup>29,31</sup>

Taurine has significant effects on the physiology of the damaged epidermis. The TauT is activated within minutes after the skin is exposed to irritation, dehydration, ultraviolet radiation, and other stressors. It appears to be the most important immediate cytoprotective response to these stressors<sup>19,32</sup> and it accelerates skin barrier repair;<sup>29</sup> however, TauT expression and activity become diminished in aging and photodamaged skin.<sup>33</sup> TauT is also activated by vitamin-A analogs.<sup>34</sup>

### A Novel Skin Moisturizer

A novel product comprising two patented technologies<sup>35,36</sup> has been developed for delivering cytoprotective osmoregulation in conjunction with other ingredients for optimum moisture management (Tetros<sup>®</sup> ULTRA, Intense Hydration for Stressed Skin; TetraDerm<sup>™</sup> Group LLC, Grosse Pointe, MI). The product has been formulated with natural physiological lipid ceramides, free fatty acids, and cholesterol esters, which restore and protect the stratum corneum moisture barrier. Some of the specific ingredients included are lecithin, glycerin, taurine, palmitic acid, cholesterol, tyrosine, hydroxypinacolone retinoate (HPR), sodium hyaluronate, ceramide, and sodium PCA. The product supports the hydrophilic layer by avoiding the use of surfactants. The natural moisturizing factors pyrrolidone carboxylic acid and tyrosine bind water in the extracellular spaces of the epidermis. Ceramides are sphingolipids that play an essential role in structuring and maintaining the water permeability barrier function of the skin.<sup>37</sup> The structural hydrating polymer hyaluronic acid is a potent natural humectant. HPR is a retinoid activator of the TauT, which stimulates osmoregulation and cytoprotection.

The selected lipids and potential lipid precursors in the product are present in ratios that resemble the natural complexity of biological membranes. The product is formulated with different nano and micro compartments (RepairOderm Technology<sup>™</sup>), which delivers hydrophilic and hydrophobic actives together, with different rates and depth of delivery, without changing composition or concentrations of excipients. The formulation enables penetration through stratum corneum and epidermis without disturbing normal skin barrier function. Controlled ingredient release and penetration depth enhance the capability of lipid precursors to promote skin lipid biosynthesis.

A mouse model was used to demonstrate how physiological lipids penetrate the viable epidermis.<sup>38</sup> Palmitic and stearic acid were labeled with trace amounts of a fluorescent fatty acid (Bodipy<sup>®</sup> 493/503; Thermo Fisher Scientific Inc., Carlsbad, CA). Petrolatum, which fluoresces spontaneously but is not absorbed into the epidermis, was also applied as a control.