Dandruff in the 21st Century

A new understanding of the cause of dandruff has spurred innovation in treatment options.

“Gorgeous hair is the best revenge.”
—Ivana Trump

Dandruff affects more than 40% of the total adult population, and while hardly life-threatening, it is certainly a condition no one wants. Dandruff treatments have been around for many years, but the specific yeast responsible for dandruff was only accurately identified in 2007. And now, by clarifying the source of the problem, a spate of recent research is making a new generation of more effective antifungal products possible.

In the U.S., antifungal products are classified as drugs—they must perform in a clinically substantiated way. Many compounds used to treat dandruff are listed in Table 1, with those officially recognized by the U.S. Food and Drug Administration (FDA) noted. There are also a number of botanicals that claim antifungal effects, as well as traditional cures such as egg oil in Chinese medicine.

The Mechanics

The most obvious consequence of dandruff is the abundance of white flakes in hair and on clothes. But another problem associated with dandruff is red, scaly, itchy, irritated skin that is closely related to seborrheic dermatitis, an inflammatory skin disorder that affects the scalp, face and torso. It targets the sebaceous gland-rich areas of the skin in particular, and that clearly includes the scalp.

There are three key factors influencing the development of dandruff: a specific yeast, abundant sebum and individual susceptibility. The activity of the yeast must be addressed to treat the condition at a fundamental level, and so we must examine it in some detail.

Yeasts are fungi, with more than 1,500 known species. They use organic compounds as a source of energy and do not require sunlight to grow. Yeast has been used for thousands of years, notably giving mankind leavened bread and alcoholic beverages.

The ones of particular interest for understanding and treating dandruff are Malassezia globosa and restricta, especially the globosa. This identification was the result of research by Dawson1 and his team at Procter & Gamble. Yeast is prevalent all over our bodies as a component of normal skin flora. Malassezia are lipid-dependent, and are particularly delighted to be in the scalp where there is a copious supply of sebum to provide necessary nutrition.2 It has been suggested that Malassezia lipid dependency is due to a defect in its synthesis of myristic acid, a precursor of long-chain fatty acids. Sebum is broken down by the lipases excreted by yeast into fatty acids that are used as nutrition, and one particularly troublesome product of the breakdown of triglycerides is oleic acid. As the oleic acid builds up on the scalp, it becomes a primary source of inflammation.

For people with dandruff, skin cells may mature and be shed in two to seven days, compared to a normal scalp where 28 days typically would be required. This increased turnover creates clusters of corneocytes that adhere to each other and make the particles we see. One biological molecule that helps make large dandruff particles is ICAM-1 (Intercellular Adhesion Molecule-1). The structural characteristics of ICAM-1 create protein-binding sites for numerous ligands, and, as a result of these binding characteristics, ICAM-1 has classically been assigned the function of intercellular adhesion.

Zinc here is beneficial in that it can lower the expression of adhesion molecule ICAM-1, reducing the formation of visible dandruff clusters. Thus, the most common active for antifungal shampoo in the U.S. is zinc pyrithione (ZPT), which is used in P&G’s Head & Shoulders hair care shampoo products, the market leader. Understandably, then, the focus of much research has centered on exactly how ZPT works, where the main questions concern how ZPT reduces irritation and the exact mechanism for its action against Malassezia globosa.

The dandruffed scalp always involves inflammation, where interleukin 1α (IL-1α) plays a main role. Elevated levels of IL-1α in the scalp have a positive correlation with the degree of inflammation, and an excess of IL-1α also affects hair growth and hair loss. Zinc has good anti-inflammatory activity, which can inhibit the expression of scalp IL-1α, as well as the capacity of surfactants that induce the expression of IL-1α.

However, ZPT must be carefully formulated in a shampoo and effectively deposited on the hair during use in order to be effective. And because ZPT is not soluble in shampoo base, it must be suspended, meaning a clear shampoo is not a possibility. ZPT particles come in different shapes and sizes, and only a proper particle can be uniformly deposited on the scalp. So the correct particle specification and an effective delivery system is a necessity for product performance. Once there, the ZPT controls the Malassezia yeast by interfering with transport through the cell wall.

### Table 1. Antidandruff Actives

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<thead>
<tr>
<th>Active Ingredient</th>
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<tbody>
<tr>
<td>Citroenelic acid</td>
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<tr>
<td>Coal tar*</td>
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<tr>
<td>Climbazole</td>
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<tr>
<td>Hexamidine disethionate (HD)</td>
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<tr>
<td>Ketoconazole</td>
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<tr>
<td>Piroctone olamine</td>
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<tr>
<td>Salicylic acid*</td>
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<tr>
<td>Selenium sulfide*</td>
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<tr>
<td>Sulfur*</td>
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<tr>
<td>Undecylenic acid</td>
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<tr>
<td>Zinc pyrithione*</td>
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<tr>
<td>Zinc thiosalicylate</td>
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* FDA approved
New Possibilities

Research pointing to new treatments for dandruff includes a paper by Holm et al. studying the effects of antimicrobial peptides and cell-penetrating peptides on Malassezia sympodialis, the most common yeast in individuals with atopic eczema. Several cell-penetrating peptides were shown to be nontoxic to mammalian cells while possessing growth inhibitory activity on the yeast.

Perhaps the most fascinating recent paper, very illuminating from a mechanistic prospective, is by Reeder et al. and a large group of mostly P&G co-authors. They started by examining the activity of ZPT against a model yeast, Saccharomyces cerevisiae, because the model yeast is easier to work with than Malassezia globosa. However, they did extend the work to globosa, where they found ZPT to mediate growth inhibition through an increase in copper in the scalp fungus. The summary of the paper puts it succinctly in rigorously scientific prose: "A model is presented in which pyrithione acts as a copper ionophore, enabling copper to enter cells and distribute across intracellular membranes. This is the first report of a metal ligand complex that inhibits fungal growth by increasing the cellular level of a different metal."

Chasing Better Results

To put this all more simply: Yeast living in the scalp use sebum as food. Part of the breakdown products of sebum is oleic acid, which irritates the skin. Cell turnover increases, flakes build up into clumps and they form visible dandruff. ZPT-containing shampoos interfere with the yeast cell by penetrating its walls and upsetting its internal ionic balance, leading to the death of the yeast and curing (at least temporarily) the dandruff condition.

This is pretty demanding science, but it is not often that a commonly used consumer product like an antidandruff shampoo can lead so deeply into the frontiers of research. And when a company like P&G publishes so much of its findings, it is an even more special opportunity to see the depth of the beauty industry's commitment to understanding its products—and through that understanding making them better. ■ GCI

References

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