Acne: Past, Present, and Future

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2/24/1015
Disclosures

- Cofounder, President, and CEO of Skinomics.INC
Acne: A Historical Perspective

- Ancient Egyptian Aku-t - boils, blains, sores, pustules, inflamed swelling
- Fuchs 1840 coined-Acne Vulgaris, Acne Mentagra and Acne Rosacea
- Bloch 1931 proved relationship acne to puberty
Acne and the First Therapies

- Ancient Egypt, Greece, and Rome used sulfur treatments
- 1920s: Benzoyl Peroxide introduced
- 1970s: Tretinoin (original Retin A), antibiotics (minocycline)
- 1980s: Accutane introduced
  - >2000 women became pregnant between 1982 and 2003, majority ending in miscarriage
  - 160 babies with defects born
  - Ipledge system established
Acne affects >80% of the population

- Over 50 million people in the US, and over 150 million in the seven major markets.
- It is among the top 5 most economically burdensome skin diseases in the US
- Total costs predicted to exceed $3 billion 2016
- However, market revenues are stagnant due to patent expirations, generic competition, lack of long term efficacy
Acne Pathogenesis

- Inflammation
- Overgrowth *Propionibacterium acnes*
- Increased androgens, sebum production
- Abnormal differentiation of keratinocytes
Acne Pathogenesis

Obstruction of pilosebaceous duct by cohesive keratinocytes, sebum, and hyperkeratosis

Drugs that normalize pattern of follicular keratinization
- Adapalene
- Isotretinoin
- Tazarotene
- Tretinoin

Drugs with anti-inflammatory effects
- Antibiotics (by preventing neutrophil chemotaxis)
- Corticosteroids (intralesional and oral)
- NSAIDs

Rupture of follicular wall

Inflammation

Increased sebum production

Drugs that inhibit sebaceous gland function
- Antiandrogens (e.g., spironolactone)
- Corticosteroids (oral, in very low doses)
- Estrogens (oral contraceptives)
- Isotretinoin

Compacted cells, keratin, and sebum

Proliferation of Propionibacterium acnes

Drugs with antibacterial effects
- Antibiotics (topical and oral)
- Benzoyl peroxide
- Isotretinoin (indirect effect)
Genetic and Environmental Factors

- Strong familial predisposition related to severity
- Diet inconclusive-possible relation to high glycemic index
- Smoking exacerbates
- Hormonal influences-worsens in puberty
- Medications-lithium, corticosteroids, vitamin B12
- Stress
Types of Acne

- Comedonal
- Inflammatory
- Nodulocystic
- Scarring
Current Acne Therapies

- **Topicals**
  - Benzoyl Peroxide
  - Retinoids
  - Antibiotics
  - Misc ( Azaleic Acid, sulacetamide sulfur, Dapsone gel, glycolic acid, salicyclic acid, natural products)

- **Orals**
  - Antibiotics (doxycycline, minocycline)
  - Isotretinoin
  - Antihormonals (Spironolactone, OCPs)

- **Procedures**
  - Light therapy (PDT)
  - Dermabrasion/Extraction/Injections
US OTC Acne market ~$2.5B by 2016

Top compounds

OTC
- Benzoyl peroxide
- Salicylic acid
- Alpha hydroxy acids
- Sulphur

Rx
- Benzoyl peroxide
- Retinoids
- Antibiotics
- Dominated by generics

US OTC Acne sales
$ millions

2013 2014 2015 2016 2017 2018
2322 2410 2484 2561 2620 2704
3.1%
Acne Market

The Global Market for Prescription Acne and Rosacea Drugs Share by Type 2011

- Retinoids: 59.5%
- Antibiotics: 28.5%
- Other Benzoyl: 9.5%
- 2.5%
Leading Companies with Acne Therapy

- **Stiefel** - a GSK company leading prescription anti-acne with 30.1% of the market, $501 million.
  - Bactroban, Dermovate, Duac, Clindamycin line, Evoclin, Rosac, and many other

- **Galderma** - second with revenues of $450 million and 27.0% market
  - Differin, ClindaGel, Epiduo Gel, Eryacne, Oreacea, and others

- **Medicis** - third with revenues $330 million and 25.2% market
  - A/T/S, Solodyne, and Theramycin Z

- Remaining 17.7% is divided
  - Allergan, Mylan Pharmaceuticals, Valeant, Westwood Squibb, and various generic manufacturers

<table>
<thead>
<tr>
<th>Supplier</th>
<th>Market Share</th>
<th>Revenues (in millions)</th>
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</thead>
<tbody>
<tr>
<td>Stiefel</td>
<td>30.1</td>
<td>501.0</td>
</tr>
<tr>
<td>Galderma</td>
<td>27.0</td>
<td>450.0</td>
</tr>
<tr>
<td>Medicis</td>
<td>25.2</td>
<td>420.0</td>
</tr>
<tr>
<td>Others</td>
<td>17.7</td>
<td>293.6</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>100.0</strong></td>
<td><strong>1,664.6</strong></td>
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</table>
Companies with Acne Therapy

- Roche
- Galderma
- Schering AG
- S-A
- Mylan
- Stiefel
- J&J
- Barr
- Ranbaxy
- Dermik
- OLT
- Pfizer
- Target Research Associates
- PharmaDerm
- Access Pharmaceuticals/Strakan
- Doak/Bradley Pharmaceuticals
- Target Research Associates
- PharmaDerm
- Access Pharmaceuticals/Strakan
- Doak/Bradley Pharmaceuticals
- DUSA
- GlaxoSmithKline
- Leo Pharma
- Medicis
- Obagi
- Westwood-Squibb
- SkinMedica
- Summers Labs
- Bradley
- Pharmaceuticals
- Bayer Healthcare
- Ortho Dermatological
- Allergan
- Basilea Pharma
- Upsher-Smith
Topical Rx Acne Therapy

- Benzoyl Peroxide
- Retinoids
- Topical Antibiotics
- Miscellaneous
  - Azaleic Acid
  - Sodium Sulfacetamide
  - Topical dapsone
Benzoyl Peroxide

- Antimicrobial
- Mild peeling agent
- Comedolytic
- Decreases fatty acid and lipid levels
- Benzoyl peroxide has no P. acnes resistance
- In the US, available 2.5% to 10% conc
- 2.5% BP was equivalent to the 5% and 10% concentrations with fewer side effects
<table>
<thead>
<tr>
<th>Product Name</th>
<th>Manufacturer</th>
<th>Formulations</th>
<th>Sizes</th>
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<tbody>
<tr>
<td>Benzac</td>
<td>Galderma</td>
<td>5%, 10% gel</td>
<td>60 g</td>
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<tr>
<td>Benzac AC</td>
<td>Galderma</td>
<td>2.5%, 5%, 10% gel</td>
<td>60 g</td>
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<tr>
<td>Benzac W</td>
<td>Galderma</td>
<td>2.5%, 5%, 10%</td>
<td>60, 90 g</td>
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<tr>
<td>Benzaclin</td>
<td>Valeant</td>
<td>1% gel</td>
<td></td>
</tr>
<tr>
<td>Benzagel</td>
<td>Valeant</td>
<td>5%, 10% gel</td>
<td>45, 90 g</td>
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<tr>
<td>Benzashave</td>
<td>Medicis</td>
<td>5%, 10% shaving cream</td>
<td>120g</td>
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<tr>
<td>Clenziderm MD</td>
<td>Obagi</td>
<td>5% lotion, gel</td>
<td></td>
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<tr>
<td>Desquam-E</td>
<td>Westwood-Squibb</td>
<td>2.5%, 5%, 10% gel</td>
<td>45 g</td>
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<tr>
<td>Desquam-X</td>
<td>Westwood-Squibb</td>
<td>2.5%, 5%, 10% gel</td>
<td>45, 90 g</td>
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<tr>
<td>NeoBenz Micro</td>
<td>Bayer Dermatolgy</td>
<td>3.5%, 5.5%, 8.5%</td>
<td>45g</td>
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<tr>
<td>PanOxyl</td>
<td>Stiefel</td>
<td>5%, 8%, 10% cream</td>
<td>60, 120 g</td>
</tr>
<tr>
<td>Vanoxide-HC</td>
<td>Summers Labs</td>
<td>benzoyl peroxide 5% and hydrocortisone 1/2%</td>
<td></td>
</tr>
<tr>
<td>Zoderm</td>
<td>PharmaDerm</td>
<td>10% urea vehicle</td>
<td>varies</td>
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</tbody>
</table>
Retinoids

- Reduce follicular hyperkeratinization
- Reduce Sebum production
- Increase cell turnover
## Retinoids Rx

### Common Retinoid Formulations

<table>
<thead>
<tr>
<th>Product Name</th>
<th>Manufacturer</th>
<th>Formulations</th>
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<tbody>
<tr>
<td>Atralin Gel</td>
<td>Valeant Pharmaceuticals</td>
<td>0.05% gel</td>
</tr>
<tr>
<td>Avita (all-trans retinoic acid)</td>
<td>Mylan/Mylan Pharmaceuticals</td>
<td>0.025% polypropolysol 2 cream</td>
</tr>
<tr>
<td>Differin (adapalene)</td>
<td>Galderma</td>
<td>0.1% gel, 0.1% lotion</td>
</tr>
<tr>
<td>Oratane</td>
<td>Douglas Pharmaceuticals</td>
<td>Cream</td>
</tr>
<tr>
<td>Retin-A (all-trans retinoic acid)</td>
<td>Ortho Dermatological</td>
<td>0.01% to 0.1% cream and gel</td>
</tr>
<tr>
<td>Tazorac (tazarotene)</td>
<td>Allergan</td>
<td>0.05% and 0.1% gel, cream</td>
</tr>
<tr>
<td>Tretin X</td>
<td>Triax Pharmaceuticals</td>
<td>Cream 0.025%, 0.05%, 0.01%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Gel 0.01%, 0.025%</td>
</tr>
</tbody>
</table>
Topical Antibiotics

- Clindamycin
- Erythromycin

Inhibit protein synthesis by irreversibly binding to the ribosomal 50S subunit of *P. acnes*

- Erythromycin is bactericidal, clindamycin is both bactericidal and bacteriostatic
## Common Topical Antibiotic Formulations

<table>
<thead>
<tr>
<th>Product Name</th>
<th>Manufacturer</th>
<th>Formulations</th>
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<tbody>
<tr>
<td>Acanya</td>
<td>Valeant</td>
<td>2.5% gel</td>
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<tr>
<td>Aczone Gel</td>
<td>Allergan</td>
<td>5% aqueous solution</td>
</tr>
<tr>
<td>Adoxa</td>
<td>PharmaDerm Pharmaceuticals</td>
<td></td>
</tr>
<tr>
<td>Altabax</td>
<td>Stiefel</td>
<td>1% Ointment</td>
</tr>
<tr>
<td>A/T/S (erythromycin)</td>
<td>Medicis</td>
<td>20% cream</td>
</tr>
<tr>
<td>Avar Gel</td>
<td>DUSA</td>
<td>10% gel, cream</td>
</tr>
<tr>
<td>Azelex (azelaic acid)</td>
<td>Allergan</td>
<td></td>
</tr>
<tr>
<td>Bactroban</td>
<td>Stiefel</td>
<td>Cream, ointment</td>
</tr>
<tr>
<td>Benzaclain Topical Gel Pump</td>
<td>Sanofi-Aventis</td>
<td>1% 6.5%, 2.5%</td>
</tr>
<tr>
<td>Benzamycin (erythromycin)</td>
<td>Valeant</td>
<td>3% erythromycin with 5% benzoyl peroxide gel</td>
</tr>
<tr>
<td>Cefuroxime</td>
<td>Basilea Pharma</td>
<td></td>
</tr>
<tr>
<td>Cenlia system</td>
<td>Upsher-Smith</td>
<td>10% cream, foam</td>
</tr>
<tr>
<td>Cleocin T (clindamycin)</td>
<td>Pfizer</td>
<td>1% clindamycin</td>
</tr>
<tr>
<td>ClindaGel</td>
<td>Galderma</td>
<td></td>
</tr>
<tr>
<td>Clindamycin Phosphate</td>
<td>Target Research Associates</td>
<td></td>
</tr>
<tr>
<td>ClindaMax</td>
<td>PharmaDerm</td>
<td>1% lotion</td>
</tr>
<tr>
<td>ClindaReach</td>
<td>DUSA</td>
<td>1% Pledgets</td>
</tr>
<tr>
<td>Clindets</td>
<td>Stiefel Laboratories</td>
<td></td>
</tr>
<tr>
<td>Clindoxyxl</td>
<td>Stiefel</td>
<td>1% gel</td>
</tr>
<tr>
<td>Differin</td>
<td>Galderma Laboratories</td>
<td></td>
</tr>
<tr>
<td>Difluocortic</td>
<td>Stiefel</td>
<td>Gel</td>
</tr>
<tr>
<td>Erythrocin (erythromycin)</td>
<td>GlaxoSmithKline</td>
<td>2% gel</td>
</tr>
<tr>
<td>Epiduo Gel</td>
<td>Galderma</td>
<td>0.1%/2.5% gel</td>
</tr>
<tr>
<td>Erycetra</td>
<td>Galderma</td>
<td></td>
</tr>
<tr>
<td>Erycette (erythromycin)</td>
<td>Ortho Dermatological</td>
<td>2% swabs</td>
</tr>
<tr>
<td>Evocin</td>
<td>Stiefel</td>
<td>Foam</td>
</tr>
<tr>
<td>Finacea</td>
<td>Bayer Healthcare</td>
<td></td>
</tr>
<tr>
<td>Fucidin (outside of U.S.)</td>
<td>Leo Pharma</td>
<td>Cream and ointment</td>
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<tr>
<td>Klaran</td>
<td>Sanofi-Aventis</td>
<td>Lotion 10%</td>
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<tr>
<td>Metrogel</td>
<td>Galderma</td>
<td>Gel</td>
</tr>
<tr>
<td>Nuoxgel</td>
<td>WraSer</td>
<td>Lotion 3%</td>
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<tr>
<td>Oreaexa</td>
<td>Galderma</td>
<td></td>
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<tr>
<td>Rosac</td>
<td>Stiefel</td>
<td>Cream</td>
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<tr>
<td>Rosanil</td>
<td>Galderma</td>
<td>Soap, lotion</td>
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### Topical Antibiotics cont.

<table>
<thead>
<tr>
<th>Product</th>
<th>Manufacturer</th>
<th>Formulation</th>
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</thead>
<tbody>
<tr>
<td>Rosula line</td>
<td>PharmaDerm Pharmaceuticals</td>
<td>Gel cleanser 10%</td>
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<tr>
<td>Rozex</td>
<td>Galderma</td>
<td></td>
</tr>
<tr>
<td>Stevamycin</td>
<td>Stiefel</td>
<td>Available only outside US</td>
</tr>
<tr>
<td>Solodyn</td>
<td>Medicis</td>
<td></td>
</tr>
<tr>
<td>Tetraysal</td>
<td>Galderma</td>
<td></td>
</tr>
<tr>
<td>Theramycin Z (erythromycin)</td>
<td>Medicis</td>
<td>2% solution</td>
</tr>
<tr>
<td>Veltin</td>
<td>Stiefel</td>
<td>1% ointment</td>
</tr>
<tr>
<td>Ziana</td>
<td>Medicis</td>
<td>1.2% clindamycin</td>
</tr>
<tr>
<td>Zindaclin</td>
<td>Crawford Healthcare</td>
<td>0.025 tretinoin gel</td>
</tr>
</tbody>
</table>
Miscellaneous

- Azaleic Acid
- Sodium Sulfacetamide
- Dapsone
Azelaic Acid

- Dicarboxylic acid found in wheat, rye, and barley
- Bacteriostatic and bactericidal
- Normalizes follicular keratination,
- Comedolytic
- Treats hyperpigmentation
- Available in US 20% concentration
- No bacterial resistance
Sodium Sulfacetamide

- Competitive antagonist to para-aminobenzoic acid (PABA), an essential component for bacterial growth.
- Keratolytic
- *P. acnes* resistance has not been recognized
Topical Dapsone

- Antiinflammatory
- Antimicrobial
- Treats neutrophilic disorders
  - Dermatitis herpetiformis
  - Leprosy
  - Malaria
Natural Products

- Tea tree oil
- Alpha hydroxy acid (from citrus fruits)
- Zinc
- Green Tea Extract
- Brewers yeast (CBS 5926-oral)
- Honey
- Yogurt

“There's also other stuff out there to treat your pimples that might work. You might hear about herbal and natural treatments, but so far there's no proof that they work” AAD.org
Natural Products

**Vital ET® [ Ashland Inc. ]**
Vital ET® is a new and unique bio-functional form of Vitamin E. It delivers proven anti-erythemal and anti-inflammatory benefits. The properties of Vital ET® can be used in the formulation of products...

[View Documents]

**Brillian-KS25: Tocopheryl Phosphate/Tween-80 [ Beijing Brilliance Bio ]**
Brillian-KS25 is derived from Tocopheryl Phosphate/Tween-80. It is used to reduce inflammation, dispel acne, and prevent sunburns. This product mainly used in sunscreen and anti-acne cosmetics...

[View Documents]

**Epicutin-TT [ CLR North America ]**
Epicutin-TT is a cyclodextrin-tea tree oil (approx. 10%) complex designed for application to problem skin. It is recommended for use in emulsified and gel-type cosmetics as well as facial care sticks for...

[View Documents]

**Marine-c Thiopeptide Solution (PF-WP) [ Infinitec ]**
Marine-c Thiopeptide Solution (PF-WP) is an effective, natural, safe, marine therapy for the treatment of skin imperfections. It is ideal for use in applications for anti-acne and sensitive skin.

[View Documents]

**Poria Cocos Extract [ Spec-Chem Industry Inc. ]**
Poria Cocos Extract exhibits a novel anti-acne activity and an oily skin controlling activity. This product is now used in many famous cosmetic brands to regulate the production and flow of sebum...

[View Documents]
Oral Therapy

- PO antibiotics
- Isotretinoin
- Antihormonals
  - Spironolactone
  - OCPs
Oral Antibiotics

- Minocycline/Doxycycline
- Antibiotic properties against P.acnes
- Anti-inflammatory properties
- Treatment lasts weeks to years
Isotretinoin

- Only acne treatment that addresses all factors in acne pathogenesis
- Reverses follicular hyperkeratination,
- Antimicrobial against *P. acnes*
- Involutes sebaceous glands
- Anti-inflammatory. Reduces the resistance of *P. acnes* on the skin
Antihormonals

- Spironolactone
  - Diuretic
  - Decreases virilization
    - Androgenic acne
    - Increased hair growth
    - Increased sebum production
- OCPs
Sample patient: Treatments often do not resolve disease

Acne patient → Trial OTC BP or salicylic acid → Trial Rx PO antibiotics → Development of Resistance (~73% in 1995)

Multiple visits to Derm. → Development of irritation/noncompliance

Trial Rx Combo BP/retinoids/topical Abx
**Acne Pathways**

**FGFR2**

- BP induces downregulation by lysosomal receptor degradation
- Azelaic acid inhibits mitochondrial ATP
- Tetracyclines inhibit expression FGR2b downstream matrix metalloproteinases
- Retinoids attenuate FGFR2 pathway
- Erythromycin inhibits retinoid catabolism

Bodo C Melnik¹, Gerd Schmitz² and Christos C Zouboulis³ Anti-Acne Agents Attenuate FGFR2 Signal Transduction in Acne. *Journal of Investigative Dermatology* (2009) **129**, 1868–1877; doi:10.1038/jid.2009.8; published online 19 February 2009
Challenges to current Therapy

- Stagnant Market
- Side effects leading to poor compliance
- Increasing antibiotic resistance
- Treatment to the disease not the individual
Stagnant Market

- While top 5 performing anti-acne topicals had sales exceeding 950 million in 2013, all had expired patents, no innovative targets, and limited market growth.
- ~90% in the preclinical pipeline consist of reformulated versions of retinols and/or antibiotics.
- Of the 74 clinical trials actively recruiting acne patients > 45% are using antibiotics, BP or retinoids as the intervention.
# Rx in Development

## Prescription Acne, Actinic Keratosis and Rosacea Formulations in Development

<table>
<thead>
<tr>
<th>Product</th>
<th>Developer</th>
<th>Phase</th>
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<tbody>
<tr>
<td>BF-200 ALA</td>
<td>Biofrontera</td>
<td>AA</td>
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<tr>
<td>CIP-Isotretinoin</td>
<td>Cipher Pharmaceuticals</td>
<td>AA</td>
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<tr>
<td>Duac Low Dose</td>
<td>Stiefel</td>
<td>AA</td>
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<tr>
<td>AZA Foam</td>
<td>Bayer Dermatology</td>
<td>III</td>
</tr>
<tr>
<td>CLS001</td>
<td>Cutanea Life Sciences</td>
<td>III</td>
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<td>Eralesse</td>
<td>Leo Pharma</td>
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<td>PEP005 Topical</td>
<td>Peplin</td>
<td>III</td>
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<td>Tazarotene</td>
<td>Stiefel</td>
<td>III</td>
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<td>ASC-19</td>
<td>AndroScience Corp</td>
<td>II</td>
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<td>CD07805/47</td>
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<td>DER45-EV Gel</td>
<td>Sol-Gel Technologies</td>
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<td>IDP 107</td>
<td>Valeant Pharma</td>
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<td>PCL-016</td>
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<td>Topical Minocycline Foam</td>
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<td>PRK 124</td>
<td>Senetek</td>
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<td>Rambazole</td>
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<td>Topical Retinoic acid</td>
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<td>Pyratine-XR</td>
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</tr>
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<td>Syn 0117</td>
<td>Evocutis</td>
<td>PC</td>
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Side Effects Topicals

- Irritation
- Redness
- Dryness
- Peeling
- Photosensitivity
Side effects Oral Rx

- Antibiotics
  - Nausea/vomiting
  - Photosensitivity
  - Hyperpigmentation
  - Esophagitis
  - Teratogenic
  - Long term risk IBD

- Isotretinoin
  - Teratogenic
  - DISH (diffuse interstitial skeletal hyperostosis)
  - Psuedotumor cerebri
  - Photosensitivity
  - Xerosis
  - Elevated cholesterol/TGs/LFTs
  - IBD
Antibiotic Resistance

- PO and topical antibiotics mainstay of acne therapy for 50 years
- 5 million prescriptions for oral antibiotics are written each year
- Resistance in acne has continued to rise from 20% in 1978 to 72.5% in 1995,
- Investigations linking resistant strains to higher counts of *P. acnes* and therapeutic failure
- Resistance to *P. acnes* develops in 50% of individuals following treatment with both topical and oral antibiotics.
Antibiotic Resistance

- Antibiotic-resistance occurs when genetic elements, such as transposons and plasmids, are transferred to other strains or species within the resident skin flora.
- However, with erythromycin, clindamycin, and tetracyclines, resistance is associated with point mutations in rRNA.
- Most resistance of *P. acnes* to erythromycin is cross-resistant to clindamycin.
Acne Future: Addressing the Challenges

- Innovative Targets
- Combination Therapy
- Tailored/personalized therapy
Innovative Targets
Looking to Nature

- Salix tree-salicylic acid-(Aspirin)
- Pacific Yew-Taxols-(Paclitaxel)
- Opium poppy-(Morphine)
Antioxidants

- Resveratrol (3,5,4′-trihydroxystilbene) polyphenol
- Red wine, colored berries, peanut plant.
- Fresh grape skins contain 50-100µg/g
- Red wine contains 1.5-3 mg/liter
Resveratrol’s role in plants

- Antioxidant
- Expression correlated to environmental stress and pathogenic attacks
- Stressors: sunlight, arthropod assault, fungus
- High stress environments increase resveratrol production.
Resveratrol and Health

- Cancer prevention (colon, liver, myeloma, lymphoma)
- Protects the heart
- Protects the brain (i.e. Alzheimers)
- Reverses diabetes
- Improves obesity
- Aging
French Paradox

- Decreased mortality in French men
- High saturated fat diet
- Increased red wine consumption
Resveratrol Applications
Dermatology

- Wound healing
- Anti-inflammatory
- Photoprotection
- Estrogenic
- Chemotherapy
- Antimicrobial
- Anti-aging
Acne Pathogenesis

- Inflammation *
- Overgrowth * _P. acnes_ *
- Increased androgens, sebum *
- Abnormal differentiation of keratinocytes
- Impaction of follicles

* Resveratrol targets
Antibacterial against P. acnes

Antibacterial against P. acnes

Fig. 3 Electron microscopy demonstrating antimicrobial effect of resveratrol. Electron microscopy images of P. acnes left untreated (a, b) or incubated for 24 h (c, d) with resveratrol. Images were taken at ×10,000 magnification (a, c) or ×29,000 magnification (b, d). Scale bar is 1 μm (a, c) or 1/2 μm (b, d).
Wound healing

- Inflammatory phase
  - Antioxidant-balances ROS
- Migratory and Proliferative phase
  - Increases VEGF, angiogenesis
- Remodeling Phase
  - Accelerates wound contraction
Resveratrol Acne Study

- Clinical assessment-Resveratrol gel 53.75% mean reduction in the GAGS score compared with vehicle 6.10%
- Histologic analysis- Resveratrol gel 66.7% mean reduction in microcomedones compared with vehicle 9.7%
- All patients satisfied with treatment
- No side effects
Combination Therapy

- Combine BP (no resistance) with other topical therapies (retinoids, antibiotics)
- 5% benzoyl peroxide/1% clindamycin combination topical gel is superior to clindamycin monotherapy
- Reformulations of generic compounds creating novel combinations has become standard
Comparative Bactericidal Activity

Combination Resveratrol/BP

- Combination is more effective than either compound alone *in vitro*
- Evaluating whether this translates to enhanced efficacy, better tolerability at lower therapeutic doses of benzoyl peroxide
- Resveratrol has anti-androgenic, anti-inflammatory, and antibacterial properties that may target three of the four major pathogenic factors in acne formation.
Personalized Medicine

- Treat the individual, not just the disease
- Data informatics
  - 23&me-Disease risk assessment
  - Foundation Medicine
- Tailored therapy
  - Pharmacogenomics
    - Cancer Immunotherapy
    - Herceptin for Her2 positive breast CA
    - BRAF inhibitors for BRAF mutated melanoma
Personalized Acne Therapy

- Profile a patient's cutaneous flora
- Address hormonal contributions
- Target specific type of acne
  - Inflammatory (BP, antibiotics, isotretinoin)
  - Comedogenic (retinoids)
  - Cystic/Scarring (isotretinoin)
- Developed tailored therapy to above factors
Personalized Acne Therapy
Skinomics Model

- Acne patients had different “pathogenic” *P. acnes* strains than compared to healthy skin
- Diagnostic kit can profile skin at baseline (prior to treatment) and monitor response to treatment
Personalized Therapy

- Pathogenic *P. acnes* strains have different metabolism than healthy strains
- Develop drug targets specific to killing pathogenic stains or enhancing strains associated with a healthy skin biome
- Deliver Probiotics of healthy skin flora for maintenance
Personalized Acne Therapy

Acne patient → Trial OTC BP or salicylic acid → Tailored Therapy → Long term resolution

Profile Flora

Maintain with healthy flora
Formulation questions

- Benzoyl peroxide highly volatile with oxygen
  - Encapsulate
  - Vacuum/pump dispensers
- Stabilize resveratrol (antioxidant) with benzoyl peroxide (oxidant)
  - Encapsulate
- Probiotic stability and bioavailability
  - Culture viability
  - Storage methods (room temp, refrigeration)
References


11. Packaged facts, the US Cosmeceuticals Market 2008


References


