Integumentary Perfections



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1. The Skin

2. Product Design

3. Economic Analysis







Skin Layers



- Semi-permeable barrier between body and environment
- Contains three layers: epidermis, dermis and subcutaneous



Source: http://cancer.healthcentersonline.com/skincancer/basalcellcarcinoma.cfm



- The outermost layer of the epid<u>ermis is the</u> stratum corneum
 - Approximately 20 cell layers thick
 - Location in which desquamation occurs
 - Desquamation is the shedding of the top layer of cells in the stratum corneum
 - Approximately 1 layer per day is released





Stratum Corneum

- Contains hydrophilic cells (keratinocytes) surrounded by a hydrophobic lipid bilayer (lipid lamellae)
- Contains natural moisturizing factors (NMF) which are responsible for the absorption and retention of water.



Brick-like pattern of the stratum corneum (skin barrier)





- Reduced or low water content in the Stratum Corneum results in a compromised barrier (chapping)
- This compromised barrier must be restored in order to prevent transepidermal water loss



Compromised Barrier



Intact Barrier

Source: http://www.cetaphil.com.au/importance_of_your_skin_more.asp





Skin Disorders



Xerosis (Dry Skin)

- Natural moisturizers
 Stratum Corneum are removed
- Caused by overexposure to water, sun, or cold weather
- Symptoms include dry, itchy skin



Source: University of California, San Fransico, www.uscf.edu



Ichthyosis Vulgaris

 Incurable, genetic disorder affecting production and/or desquamation of cells

■ Caused by

- Iow water content in Stratum Corneum
- enzymatic reactions controlling desquamation are inhibited
- Symptoms include dry, thickened, scaly skin







Treatment Therapy



Three key steps to effectively treat the disorders

- Promote desquamation
- Deliver moisturizing agents to underlying skin
- Restore the skin's lipid bilayer



Transdermal Diffusion

- Percutaneous absorption mostly occurs via transcellular diffusion (Pathway 2)
- Other pathways are
 - Intercellular diffusion (Pathway 1)
 - Diffusion through skin appendages (Pathway 2)



Source: A Geoscience Approach to Modeling Chemical Transport Through the Skin

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Moisturizer Formulation

The simplest vehicle for skin moisturizers are emulsions
For lotions, oil-in-water emulsions are used
Water is the continuous phase
Oil is the dispersed phase



Contigned Composition

Lotions have active and inactive ingredients
 Ingredients are characterized by a combination of properties (e.g. effectiveness, smoothness, thickness, etc.)

Product Design



Lotion Composition



- Since skin moisturizers are considered cosmetic products, they do not have to adhere to FDA regulations
- Cosmetics are subject to restrictions on the concentration of certain ingredients
 determined by the Cosmetic Ingredient
 Review





Product Design



Customer Satisfaction Assessment

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- A model was developed to assess the consumer needs
- The model measures how satisfied the consumer is with the properties of the lotion
- Consumer rates lotion characteristics correlated to a physical properties

$$\begin{split} S_i &= \sum w_i y_i \\ S_i &= satisfaction \ (0-100) \\ w_i &= weight \ of \ property \ (0-1) \\ y_i &= property \ satisfaction \ (0-100) \end{split}$$

Consumer Surveys



- Consumer surveys were used to determine the satisfaction of the consumer for each property
- The consumers rated the lotion properties based upon extremes (i.e. very thin to very thick)
- Consumer ratings were then correlated to the physical properties of the lotion (surface tension, viscosity, etc.) to find consumer satisfaction



Consumer Satisfaction Assessment

Ordained surveys were completed to determine the best product and the importance of each property.

Please indicate your <u>preference</u> for each property on the indicated scale (Scale of 1-X). With 1 being your <u>desired</u> product, and the highest number (X) being your <u>worst</u> product.

Thickness: Thickness of the Lotion (Scale of 1-4) Extremely Thick:____ Moderately Thick:____ Moderately Thin:____ Very Thin:____

Durability: The ability for the lotion to wash off or rub off. The Lotion lasts for...**(Scale of 1-7)** 30 minutes: _____ 1hr: ____ 2hrs: ____ 3hrs: ____ 4hrs: ____ 5 hrs: ____ 6hrs: ____

Absorption Rate: How long it takes the moisturizing chemicals to officially absorb into the skin (Scale of 1-7) 1min:_____ 2min:_____ 4min:_____ 5min:_____ 6min:_____ 8min:_____ 10min:____



Survey Results

Property	Weight of Property
Effectiveness	24.36%
Thickness	10.16%
Durability	15.19%
Absorption Rate	13.92%
Smoothness	14.61%
Greasiness	11.44%
Spreadability	10.31%

Study Population: 48 Males, 50 Females, 2 Not Specified, Total = 100

Product Design



Property Correlations





- The effectiveness of a lotion is determined by how well the lotion can treat the skin problems associated with Xerosis and Ichthyosis Vulgaris.
 - Severely dry skin
 - Thickened skin
 - Dismantled lipid bilayer

Depends on percutaneous absorption modeled by

$$\frac{C_{w}}{C_{w}^{o}} = 1 - \frac{x}{L_{sc}} - \frac{2}{\pi} \sum_{n=1}^{\infty} \left(\frac{1}{n} \sin \left(\frac{n \pi x}{L_{sc}} e^{-\frac{D_{sc} n^{2} \pi^{2} t}{R_{sc} L_{sc}^{2}}} \right) \right)$$



Effectiveness

Consumer Rating		
1	No Skin Scales Present	
2	Few Skin Scales Present	
3	Some Skin Scales Present	
4	Skin Moderately Scaly	
5	Skin Very Scaly	

Best Product: Preference (1), Concentration (0.5)





- $\gamma_{se} = \gamma_s \gamma_e \cos \theta$ $\gamma_{se} = surface \ tension \ of \ skin - emulsion$ $\gamma_s = surface \ tension \ of \ skin$ $\gamma_e = surface \ tension \ of \ emulsion$ $\theta = contact \ angle$
- Wetting is an application of adsorption at a liquid-solid interface.
- Wetting is defined as the displacement of one fluid by another on a given surface.
- Durability and Spreadability depend on wetting properties
- For solid surfaces, like the skin, the contact angle of the liquid must determined using Young's Equation

Source: The Handbook of Cosmetic Science and Technology Image Provided From: The Water Break Test



- Durability is how easily the lotion rubs or washes off and depends on adhesional wetting
- The adhesional wetting is the ability of a fluid to adhere to a surface
- The adhesional wetting is quantified by the work of adhesion, W_a
- The work of adhesion is the reversible work required to separate the unit area of liquid from a surface

 $W_{a} = \gamma_{e} (\cos \theta + 1)$ $\theta = contact \ angle$ $\gamma_{e} = surface \ tension \ of \ emulsion$

Durability

Consumer Rating	
1	30 min
2	1 hr
3	2 hrs
4	3 hrs
5	4hrs
6	5hrs
7	6hrs

■ Best Product: Preference (7), Contact Angle (0°)





- Spreadability is characterized by how easily the lotion spreads over the skin and depends on spreading wetting
- Spreading wetting is how well one fluid displaces another fluid on a given surface (The two fluids are air and lotion) and if the spreading is spontaneous
- Spontaneity depends on the free energy, the interfacial area and the surface tension
- The Spreading coefficient identifies the spontaneity of a fluid to spread

$$S_{se} = \gamma_s - (\gamma_{se} + \gamma_e)$$

$$\gamma_{se} = surface \ tension \ of \ skin - emulsion$$

$$\gamma_s = surface \ tension \ of \ skin$$

$$\gamma_e = surface \ tension \ of \ emulsion$$

Source: Comparison of surface free energy between reconstructed epidermis and in situ human skin



Spreadability

Consumer Rating	
1	0% Spreading
2	7% Spreading
3	25% Spreading
4	50% Spreading
5	75% Spreading
6	93% Spreading
7	100% Spreading

Best Product: Preference (4.5), Contact Angle (72°)



Thickness

Thickness is the viscosity and shear rate of the lotion

 $\eta = 1 + I(\lambda)\phi$ $\phi = volume \ fraction \ of \ dispersed \ phase$ $I(\lambda) = \frac{5.5 \left[4\lambda^7 + 10 - \left(\frac{84}{11}\right)\lambda^2 + \left(\frac{4}{\kappa}\right)(1 - \lambda^7) \right]}{10(1 - \lambda^{10}) - 25\lambda^3(1 - \lambda^4) + \left(\frac{10}{\kappa}\right)(1 - \lambda^3)(1 - \lambda^7)}$ $\lambda = (the \ volume \ fraction)^{1/3}$



 $\kappa = vis \cos ity \ of \ dispersed \ phase / vis \cos ity \ of \ continuous \ phase$

Shear rate can be related to film thickness $D = \frac{dv}{dt}$

$$D = \frac{dv}{dy}$$

where D is the shear rate dv is the change in velocity

dy is the film thickness

Source: Evaluation of theoretical viscosity models for concentrated emulsions at low capillary numbers

Thickness

Consumer Rating	
1	Extremely Thick
2	Moderately Thick
3	Moderately Thin
4	Very Thin

Best Product: Preference (2.3), Film Thickness (0.25cm)



Viscosity v. Shear Rate: http://www.rheologyschool.com

Smoothness

- Smoothness is based on how the skin feels after the lotion is applied.
- The skin becomes rough and chapped when the moisture level of the skin is below 10%.
- Smoothness is based on the amount of fatty oils present in the lotion.
- Smoothness is a function of the greasiness of the lotion. This correlation was found experimentally.

 $S = \mu(-0.0174G + 2.098)$ where S is the smoothness μ is the skin friction coefficient = 0.236 G is the concentration of fatty oils

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Smoothness

Consumer Rating	
1	Very Smooth
2	Moderately Smooth
3	Moderately Rough
4	Very Rough

Best Product: Preference (1), Smoothness (0.37)





The Absorption Rate is how long it takes the ingredients to absorb into the skin and is characterized by the steady state intercellular diffusion time

$$t_{ss} = \frac{0.45L_{SC}^2R_{sc}}{D_{sc}}$$

 $t_{ss} = Diffusion S.S time$

 D_{sc} = effective diffusion coefficient of 3 – phase stratum corneum continuum

 R_{sc} = retardation factor of the 3 – phase stratum corneum continuum

 L_{sc} = distance into stratum corneum from the surface

Source: A Geoscience Approach to Modeling Chemical Transport through Skin



Absorption Rate

Consumer Rating	
1	1min
2	2min
3	4min
4	5min
5	6min
6	8min
7	10min

Best Product: Absorption Rate (1min-2min)



Greasiness

- The greasiness is characterized by the look/feel of the skin after the lotion is applied
- The greasiness can be determined by the amount of fatty oils present in the lotion
- Fatty oils leave the skin looking greasy/oily because of its high concentration of triglycerides or fatty acids
- If a lotion is too greasy the stratum corneum can become swollen and inflamed
- If the lotion does not have enough oils, the skin can remain rough and chapped.

Greasiness

Consumer Rating	
1	Very Greasy
2	Moderately Greasy
3	Moderately Dry
4	Very Dry

Best Product: Preference (2.8), Greasiness (13% Fatty Oils) **Consumer Preferences: Adjusted Greasiness** 100.00% 80.00% **Consumer Satisfaction** 60.00% $y = -0.3122x^2 + 1.6109x - 1.0568$ 40.00% $R^2 = 0.9936$ 20.00% 0.00% 2 3 4 **Consumer Ratings**

Maximum Satisfaction Product

Lotion Property	Satisfaction Score
Durability	87%
Greasiness	95%
Smoothness	74%
Thickness	95%
Effectiveness	100%
Spreadability	99%
Absorption Rate	82%

Product Satisfaction: 81% Competitor Satisfaction: 77%

 β = NPW=

Product Design



Manufacturing

Manufacturing Procedure

- Two separate phases make up lotion: aqueous and oil phases
- Must completely combine two phases
- Steps in lotion formation:
 - 1) Heat and mix aqueous and oil phases separately
 - 2) Combine both phases into one batch
 - 3) Perform post treatment modifications (i.e. decrease particle size)

Process Flow Diagram



Equipment Costs

Equipment	Cost
Storage Tanks	\$10,000
Water Phase Mixing Tank	\$8,000
Oil Phase Mixing Tank	\$4,000
Bath Sonicator	\$60,000
Homogenizer	\$11,000
2 Pumps	\$11,500
Colloid Mill	\$25,000
Total Cost	\$129,500



Buckeye, AZ

37 miles from Phoenix, AZ
Population: 25,406
Located within the southwest market
Inexpensive property value
High Productivity
Low Labor costs





Source: http://www.rlmartin.com/photos/scenic/arizona/default.htm



$$S = (\alpha d_1)^{\rho} + (\beta d_2)^{\rho}$$



 $profit_1 = (p_1 - a_1)d_1$



Summary of Parameters

D = 500,000 $Y \approx 3,000,000$ $\alpha = 1$ $\rho = .75$ $p_2 = \$12.13$ $p_1 = \$8 \rightarrow \15

Beta	TPC (a ₁)
.82	\$4.30/bottle
.85	\$4.80/bottle
.9	\$5.00/bottle
.95	\$5.50/bottle
1	\$5.50/bottle

NPW vs Starting Price with Beta as a Parameter

Price Response $S = (\alpha d_1)^{\rho} + (\beta d_2)^{\rho}$ Unsaturated Market Saturated Market **Price Changes** $p_{2} = p_{2,o} - \varphi \left(p_{2,o} - a_{2} \right) \left(\beta \frac{d_{2,o} - d_{2}}{d_{2,o}} \right)^{\alpha_{1}/\alpha_{2}}$ $D = d_1 + d_2$ $D > d_1 + d_2$ $d_1 = \left(\frac{\alpha}{\beta}\right)^{\rho} \frac{p_2}{p_1} \left[\frac{Y - p_1 d_1}{p_2}\right]^{1-\rho} \left(d_1\right)^{\rho} \qquad d_1 = \frac{D}{1+\gamma}$ $Max(profit_1 = (p_1 - a_1)d_1)$ $\gamma = \left(\frac{\alpha}{\beta}\right)^{\frac{\beta}{\rho-1}}$ $d_2 = \frac{Y - p_1 d_1}{p_2}$ 2 3 5 6 8 9 12 1 4 107 Our price \mathbf{p}_1 \mathbf{p}_1 \mathbf{p}_2 \mathbf{p}_3 \mathbf{p}_3 \mathbf{p}_4 \mathbf{p}_4 \mathbf{p}_5 \mathbf{p}_2 $\mathbf{p}_5 \mathbf{p}_6$ \mathbf{p}_6 Their price \mathbf{p}_1 \mathbf{p}_2 \mathbf{p}_3 \mathbf{p}_3 \mathbf{p}_4 \mathbf{p}_4 \mathbf{p}_5 \mathbf{p}_5 \mathbf{p}_6 \mathbf{p}_2 \mathbf{p}_6 \mathbf{p}_7

<i>D</i> = 500,000
<i>Y</i> ≈ 3,000,000
$\alpha = 1$
$\rho = .75$
$p_2 = \$12.13$
$a_2 = \$7$
$p_{1i} = \$8 \longrightarrow \15
$p_{1\max p} = \$7 \rightarrow \20

Beta	TPC (a ₁)
.82	\$4.30/bottle
.85	\$4.80/bottle
.9	\$5.00/bottle
.95	\$5.50/bottle
1	\$5.50/bottle

NPW vs Starting Price w Beta as a Parameter

$$S = (\alpha d_1)^{\rho} + (\beta d_2)^{\rho}$$
Unsaturated Market Saturated Market Price Changes
$$D > d_1 + d_2 \qquad D = d_1 + d_2 \qquad D' > d'_1 + d'_2$$

$$d_1 = \left(\frac{\alpha}{\beta}\right)^{\rho} \frac{p_2}{p_1} \left[\frac{Y - p_1 d_1}{p_2}\right]^{1-\rho} (d_1)^{\rho} \qquad d_1 = \frac{D}{1+\gamma} \qquad d'_1 = \left(\frac{\alpha'}{\beta'}\right)^{\rho'} \frac{p_2}{p_1} \left[\frac{Y' - p_1 d'_1}{p_2}\right]^{1-\rho'} (d'_1)^{\rho'}$$

$$d_2 = \frac{Y - p_1 d_1}{p_2} \qquad \gamma = \left(\frac{\alpha}{\beta}\right)^{\frac{\rho}{\rho-1}} \qquad d'_2 = \frac{Y' - p_1 d'_1}{p_2}$$

 $Max(profit_1 = (p_1 - a_1)d_1)$ $Max(profit_2 = (p_2 - a_2)d_2')$

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Summary of Parameters Perfect Information

D = 500,000
<i>Y</i> ≈ 3,000,000
$\alpha = 1$
$\rho = .75$
$p_{2i} = \$12.13$
$p_{2\max p} = \$7 \rightarrow \20
$a_2 = \$7$
$p_{1i} = \$8 \longrightarrow \15
$p_{1\max p} = \$7 \rightarrow \20

Beta	TPC (a ₁)
.82	\$4.30/bottle
.85	\$4.80/bottle
.9	\$5.00/bottle
.95	\$5.50/bottle
1	\$5.50/bottle

NPW vs Starting Price with Beta as a Parameter

Co

Summary of Parameters Imperfect Information

D = 500,000	D' = 600,000	Beta	TPC (a ₁)
$Y \approx $3,000,000$	<i>Y′</i> ≈ \$3,600,000	.82	\$4.30/bottle
		.85	\$4.80/bottle
$\alpha = 1$ $p_{\alpha} = \$12.13$	$\rho = .75$ $p_{11} = \$8 \rightarrow \15	.9	\$5.00/bottle
$p_{2\max p} = \$7 \rightarrow \20	$p_{1max p} = \$7 \rightarrow \20	.95	\$5.50/bottle
$a_2 = \$7$		1	\$5.50/bottle

NPW with Imperfect Information

NPW with Imperfect Information

Any Question?