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Promising Therapies for Treating and/or Preventing Androgenic Alopecia

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ABSTRACT

Androgenetic alopecia (AGA) may affect up to 70% of men and 40% of women at some point in their lifetime. While men typically present with a distinctive alopecia pattern involving hairline recession and vertex balding, women normally exhibit a diffuse hair thinning over the top of their scalps. The treatment standard in dermatology clinics continues to be minoxidil and finasteride with hair transplantation as a surgical option. Here we briefly review current therapeutic options and treatments under active investigation. Dutasteride and ketoconazole are also employed for AGA, while prostaglandin analogues latanoprost and bimatoprost are being investigated for their hair growth promoting potential. Laser treatment products available for home use and from cosmetic clinics are becoming popular. In the future, new cell mediated treatment approaches may be available for AGA. While there are a number of potential treatment options, good clinical trial data proving hair growth efficacy is limited.

Key words: AGA, androgenetic alopecia, male pattern baldness, female pattern hair loss

Hair Loss

Hair loss comes in many forms and it is an increasingly common complaint of dermatology clinic patients. While there are many potential diagnoses, the most frequently encountered are androgenetic alopecia (male pattern baldness [MPB]; female pattern hair loss [FPHL]), telogen effluvium, or alopecia areata. Several forms of scarring alopecia also seem to be becoming more common in dermatology clinics. However by far, the near universal hair loss complaint is androgenetic alopecia (AGA) in men and women. The population frequency of AGA varies with ethnicity, but as a rough generalization up to 70% of men and 40% of women will experience some degree of AGA in their lifetime. While the condition is a widespread experience, negative image perceptions[1] mean affected individuals can be highly motivated to seek diagnosis and treatment.

Androgenetic Alopecia

Clinical Presentation

In most men, AGA develops with a distinctive "patterned" hair line recession. In women, the presentation may be less clear; typically women will develop a diffuse thinning over the top of the scalp yielding a "Christmas tree" pattern with more thinning towards the front, though the frontal hairline is maintained.[2] Occasionally men may develop a female presentation of hair loss and women, primarily those experiencing excess androgen activity, may develop a more male-like hair loss pattern. Also of note, frontal fibrosing alopecia in women, a scarring alopecia with hairline recession, has been frequently misdiagnosed as AGA.[3] Diffuse AGA may be difficult to distinguish from telogen effluvium. Indeed, telogen effluvium may spur AGA onset and the increased shedding of telogen effluvium can be an early phase characteristic of AGA. Where diagnosis is in doubt, a biopsy may clarify.[4]

Biochemistry

Research on subjects with androgen insensitivity syndromes, or 5α reductase deficiency, implies that AGA is induced via activation of androgen receptors in hair follicles by dihydrotestosterone (DHT). DHT binds to androgen receptors with five times the tenacity of testosterone and consequently has greater downstream activation potency.[5] Two distinct forms of 5α reductase (types 1 and 2) differ in their tissue distribution; type 2 is most active in hair follicles, but both likely contribute to AGA. The primary precursor of DHT in men is testosterone, but dehydroepiandrosterone (DHEA) and other weaker androgens, are the precursors for DHT in women. The intracellular signaling cascade after androgen receptor binding is poorly understood,

ALSO IN THIS ISSUE: **Age-related Percutaneous Penetration Part 2: Effect of Age on Dermatopharmacokinetics and Overview of Transdermal Products** *(page 5)* & **Update on Drugs** *(page 8)*

but receptor binding leads to increased production of cytokines, such as TGFbeta1 and 2, which promote telogen and dermal papilla cell senescence.[6,7] The density of androgen receptors in hair follicles varies with location. Occipital hair follicles, with a low number of androgen receptors, have little or no response to DHT. Consequently, hair loss is mostly restricted to the scalp vertex and fronto-temporal areas.

Genetics and Diagnostic Tests

AGA susceptibility is largely determined by genetics, though the environment may also play a minor role. Androgen receptor polymorphisms probably make the key determination for androgen responsiveness, but 5α reductase, aromatase, and sex hormone binding globulin (SHBG) genes may also contribute along with other hormone metabolism associated genes.[8] While the complete genetic picture is not clear, at least one company claims to have a gene polymorphism based diagnostic test (HairDX™) that will predict the chances of future AGA development.[9,10] For young patients concerned about hair loss this test may help to define the value of early treatment initiation. Perhaps of more immediate practical significance, a test that predicts responsiveness to treatment with finasteride is also available.[11] In women, serum ferritin levels may also be assessed to determine iron deficiency, thyrotropin levels may be evaluated to rule out thyroid dysfunction, and free testosterone is assessed when androgen excess is suspected. If serum ferritin is low, iron supplementation has been recommended as an enabler of response to other treatments.[2]

Current and Future Treatments

Drug therapies specifically approved for treating AGA are limited to minoxidil and finasteride. Both can be used in combination.[12] Several other drugs are also used off label (see below) and a plethora of treatments with unsubstantiated hair growth claims can be obtained over the counter. Recently, a review and development of evidence-based guidelines for the treatment of AGA in men and women was published, which may assist with treatment decisions.[13]

Minoxidil

Minoxidil (Rogaine®) was originally an antihypertensive therapy but was subsequently developed as a topical treatment (available in 2% and 5% solutions) for hair loss. Minoxidil use is associated with vasodilation, angiogenesis, and enhanced cell proliferation, probably mediated via potassium channel opening.[14] Side effects include contact dermatitis and a transient shedding during the first ~4 months of use. Use of 5% minoxidil in a commercially available foam vehicle that does not contain propylene glycol (potential irritant), reduces the incidence of pruritus.[15] Several products that include minoxidil, sometimes combined with other active ingredients such as tretinoin, are available from different manufacturers in the US.

Finasteride

Finasteride (Propecia®) is the most common treatment approach for MPB. It is a synthetic type II 5α reductase inhibitor that reduces the conversion of testosterone to DHT.[16] Improvement in hair count and thickness is possible, with responsiveness improving over 6 months to 1 year with 1 mg daily intake.[17] Adverse sexual events have been reported more frequently with finasteride. Finasteride has significant, adverse consequences for the development of male embryos and, as such, it is not officially approved for use in women. However, in combination with an effective oral contraceptive, finasteride is being prescribed off label. Small scale studies suggest it may be effective in women where androgen activity is involved in FPHL.[18]

Dutasteride

Dutasteride (Avodart®), a type I and II 5α reductase inhibitor, is on hold in Phase III trials for AGA.[19] It is currently approved for treatment of benign prostatic hyperplasia. Phase II studies for AGA demonstrated a dose-dependent increase in hair growth. The efficacy of dutasteride 2.5 mg/day was superior to that of finasteride 5 mg/day.[20] Side effects are similar to finasteride.

Prostaglandin Analogues

The prostaglandin F2α analogues latanoprost and bimatoprost are used in treating ocular hypertension and glaucoma. A noted side effect was increased eyelash hair growth, a feature that has been investigated in several small scale studies. Bimatoprost (Latisse®) is now available as a treatment for eyelash growth.[21] More recently, latanoprost (Xalatan®) has been investigated for its potential to promote scalp hair growth. Latanoprost significantly increased hair density compared with baseline and placebo and may also encourage pigmentation.[22]

Ketoconazole

A topical shampoo containing 2% ketoconazole (Nizoral®) is available over the counter while higher concentrations are available by prescription only. As an imidazole anti-fungal agent, ketoconazole is effective for the treatment of dermatitis and dandruff, and its action on scalp microflora may benefit those with AGA associated follicular inflammation.[23,24] However, ketoconazole is also an anti-androgen and has been suggested to improve hair growth in AGA through androgen dependent pathways.[25] Ketoconazole shampoo is typically utilized in conjunction with other AGA treatments.

Anti-androgens

Several synthetic anti-androgens can be used as inhibitors of 5α reductase activity and can also block androgen receptor binding. The efficacy of topical anti-androgen compounds for AGA has been investigated in some small studies,[18] but this approach is not generally considered.[13] More commonly, anti-androgens are combined with estrogens for the treatment of FPHL. Treatment approaches using oral anti-androgens are significantly more popular in Europe than North America. Cyproterone acetate, available in Canada but not in the US, has been used for FPHL to some effect. However, spironolactone is typically the preferred oral anti-androgen for hair loss in North America.[26]

Estrogens

Estrogens are indirect anti-androgens, and are sometimes used for the treatment of androgenetic alopecia in women in the form of a birth control pill. When used systemically, estrogens increase SHBG production, which binds to androgens, including testosterone, reducing their bioavailability. Topical estrogen compounds are also commercially available in Europe.[13] Hair follicles have estrogen receptors and it is believed that topical compounds may act on the hair follicles as direct hair growth promoters as well as by antagonizing androgen activity. However,

large clinical studies demonstrating efficacy are lacking and topical treatment is not generally available in North America.

Laser Treatment

Laser/light treatment for hair loss has become very popular in the last few years; it has also been promoted as a preventative measure against AGA. Several different manufacturers provide lasers and light sources of varying wavelengths and with different suggested modes of use. While some laser machines are designed for use at home on a daily basis, others are only available through clinics for weekly or monthly use. Whilst there is evidence that laser light can stimulate hair growth at some wavelengths,[27] the biological mechanism by which it occurs has not been defined. With one exception,[28] clinical data from large scale, placebo controlled trials is lacking. While lasers may be options that patients wish to independently explore, so far they have not become a significant treatment approach in most dermatology clinics.[29]

Surgical Treatment

The hair follicles on the scalp occiput are relatively androgen resistant. This enables their transplantation to balding areas to provide a permanent treatment for AGA. Significant advances have been made in surgical hair restoration techniques. Follicular unit transplantation (FUT) is widely available from transplant clinics in North America and beyond. More recently, specialized techniques have been developed involving individual hair follicle and unit extraction (FUE) to avoid scarring from strip graft harvesting. Hand held motorized devices are now available for the extraction of grafts and most recently robots capable of automated hair follicle extraction have been developed and are commercially available.[30] Hair transplant costs vary from $5,000 to $20,000 per session and sometimes more depending on the number of grafts and the surgeon. One or two sessions may be required depending on the extent of hair loss. Surgical treatment is limited by the hair density in the donor region and the reluctance of some patients to undergo what is a fairly invasive procedure.

Cell Mediated Treatment

Several companies and academic research groups are focused on the development of cell mediated treatments for AGA. Two main approaches are under investigation: the direct injection of cultured cells or the use of cell secreted factors as a hair growth promoting product. It has been shown that cells from the hair follicle mesenchymal tissue can be cultured and then used to induce new hair follicle formation from epithelial tissue. The injected cells can also migrate to resident hair follicles to increase their size.[31] Alternatively, cells are cultured and the culture supernatant is processed to produce a compound rich in hair growth promoting factors, such as Wnt proteins, for use in treatment. These cell mediated treatment approaches are still in Phase I or II trials, but may be available in a few years. Also of note, currently gaining popularity in the marketplace is platelet rich plasma (PRP) isolated from whole blood. Platelets have multiple growth factors associated with them as well as other potentially stimulatory mediators. Some hair transplant surgeons use this product to encourage transplanted graft growth.[30] PRP is also available from some clinics as a standalone treatment for AGA, though so far there is only one small published study in support of this approach.[32]

Alternative Treatments

Numerous products marketed direct to the consumer contain blends of herbal, vitamin and mineral components, though independent data supporting their claims as hair growth promoters are absent. Some of the more common herbs that patients may take include saw palmetto (*Serenoa repens*), black cohosh (*Actaea racemosa*), dong quai (*Angelica sinensis*), false unicorn (*Chamaelirium luteum*), chaste berry (*Vitex agnus-castus*), and red clover (*Trifolium pratense*) which are claimed to have anti-androgenic or estrogen promoting activity. Other products may contain biotin, caffeine, melatonin, copper complexes, and various proprietary compounds with diverse purported modes of action.[13,33]

Conclusion

Overall, there are a number of treatment options currently available to people with AGA, though the clinical data supporting their use is often very limited. Finasteride and minoxidil are still the most common therapeutic drugs prescribed for AGA. New treatment approaches are under active investigation.

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Age-related Percutaneous Penetration Part 2: Effect of Age on Dermatopharmacokinetics and Overview of Transdermal Products

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ABSTRACT

Transdermal drug delivery allows for a constant rate of drug administration and prolonged action, which can be beneficial to elderly patients who are often polymedicated. Several studies have compared dermatopharmacokinetics in the young and elderly with conflicting results. Despite the potential limitations of age-related changes in skin factors and cutaneous metabolism, marketed transdermal products generally do not report age-related differences in pharmacokinetics. This overview discusses the current data, summarizes marketed product findings and highlights the importance of further studies to evaluate age-related dermatopharmacokinetics.

Key words: transdermal, elderly, dermatopharmacokinetics, percutaneous penetration, cutaneous metabolism

Introduction

The rate of growth of the older population (65 years old and over) has greatly exceeded the growth rate of the US population as a whole. According to the United States Census Bureau's projections, about 1 in 8 Americans were elderly in 1994 and by the year 2030 it will increase to 1 in 5.[1] Furthermore, there has been a surge of interest in transdermal drug delivery to produce systemic effects. Transdermally delivered drugs include scopolamine, nitroglycerin, nicotine, clonidine, fentanyl, estradiol, testosterone, lidocaine, and oxybutynin. Recently, transdermal formulations have also been introduced for rivastigmine, rotigotine, selegiline, buprenorphine, granisetron, and methylphenidate. The current US transdermal market exceeds $3 billion annually.[2]

The advantages of percutaneous drug penetration over the oral route include circumvention of gastrointestinal absorption and hepatic first-pass metabolism (contrary to assumption, the skin also has a first-pass effect for some compounds), minimization of adverse effects secondary to peak plasma drug concentrations, and improved patient compliance. Additionally, percutaneous drug delivery harbors no risk of infection, which can be a complication with parenteral administration. Disadvantages include skin sensitivity and irritation by patches and the reservoir effect of skin, which allows for continued diffusion after patch removal. This overview provides a basis for understanding the effect of aging on dermatopharmacokinetics and discusses currently marketed transdermal products.

Dermatopharmacokinetics

Percutaneous absorption depends on passive diffusion across the stratum corneum, which has an excellent barrier function that undergoes structural and functional changes with increasing age. Typically, drugs that are candidates for percutaneous absorption must be pharmacologically potent and satisfy the following physicochemical properties when considering a formulation: aqueous solubility >1 mg/ml, lipophilicity $10<K_{o/w}$ (oil-water partition coefficient) <1000, molecular weight <500 Da, melting point <200°C, pH 5-9, and a dose deliverable <10 mg/day.[3] Changes in the barrier properties of aged skin may have an impact on the type and amount of drugs that are able to undergo successful percutaneous absorption.

Substantial literature reviews *in vivo* percutaneous absorption in neonates and normal healthy adults.[4-8] However, the quantitative evaluation of skin barrier function has been minimally addressed in the elderly. Christophers and Kligman conducted studies in the 1960s that suggested the skin permeability in the elderly (>66 years old) was different from that of younger adults (<29 years old).[9] *In vitro* studies using human cadaver skin demonstrated the permeability of fluorescein was seven times greater in skin from older than younger subjects. However, another *in vitro* study using skin from living subjects found no difference in the permeability of water between the two groups. They also conducted an *in vivo* study with ^{14}C-testosterone applied to the backs of young and old subjects and found penetration to be greater in the younger (19-30 years) than the older (71-82 years) group over 24 hours.[9] Furthermore, the absorption capability of the skin microcirculation was assessed by the clearance of intradermally injected radiolabeled sodium and was shown to be decreased in the elderly, suggesting that changes in the microcirculation occurred in the dermis of the elderly.[9]

DeSalva and Thompson reported contrasting results; they observed similar clearance rates of intradermally injected radiolabeled sodium administered in the face and hands of subjects 50 years of age or older, but the rates were slower in subjects 30 years of age or younger.[10] However, when administered into the hand, the clearance of radiolabeled sodium was slower in subjects aged 71 years or older than subjects 60 years of age or younger.

Tagami measured the permeability of tetrachlorosalicylanilide (TCSA) across the stratum corneum *in vivo* and discovered that the permeation times of TCSA through the skin of both flexor and extensor forearm sites were significantly shorter in young (22-39 years) than in old (62-82 years) subjects. The TCSA penetration time took 2-2.5 hours in the former and about 1.5 hours in the latter. This was accomplished by stripping the stratum corneum at various time points after application and assaying for the TCSA via fluorescence.[11] The efficiency of cutaneous microcirculation was also assessed by the clearance of intradermally injected radiolabeled sodium. Clearance was unchanged between age groups for the extensor forearm, but significantly longer in aged (61-80 years) than in young (20-32 years) subjects for the midback area.[11]

Roskos and colleagues made *in vivo* measurements of percutaneous absorption in young (18-40 years) and old (>65 years) subjects using standard radiotracer methodology with ^{14}C-radiolabeled compounds.[12] Percutaneous absorption was quantified from urinary excretion profiles and corrected for incomplete renal elimination. Permeation of hydrocortisone, benzoic acid, acetylsalicylic acid, and caffeine was significantly lower in aged subjects, while the absorption of testosterone and estradiol was similar in the two groups (Table 1). This suggests that aging can affect percutaneous absorption *in vivo* and that relatively hydrophilic compounds are more sensitive, while highly lipophilic compounds may still be able to dissolve readily across the stratum corneum.

While the aforementioned studies indicate there are age-related differences in the percutaneous penetration and clearance of drugs, discrepancies abound. Some suggested greater absorption in the older subjects, others suggested greater absorption in younger subjects, and still others found no difference. Consequently, based on these studies, it is difficult to elucidate if the elderly are at increased risk secondary to altered percutaneous penetration. Furthermore, in practice, no significant differences in absorption of drugs from transdermal delivery systems have been demonstrated between young and old individuals.

Marketed Transdermal Products

Given the potential differences in skin from individuals of varying age, pharmacokinetics with transdermal delivery may be altered. Table 2 summarizes the available pharmacokinetic data reported in the US FDA's New Drug Application (NDA) submissions and drug labels for transdermal products relative to the subjects' age. As shown, in studies where the subject age was stratified relative to pharmacokinetic parameters, the majority of transdermal products do not report age-related differences in their pharmacokinetic profiles. The lack of age-related reports indicates that the skin, although the rate-limiting step for absorption, is not the major factor for observations of age-related effects. In other words, the skin in addition to other factors, including the active ingredient's physiochemical characteristics and patch formulation components, determine whether a specific drug will have pharmacokinetic differences across age groups.

Discussion

Comorbid medical conditions in the elderly are often treated with polypharmacy, which may result in unwanted drug-drug interactions and adverse effects.[14] Swallowing difficulty either as a symptom of the disease or secondary to aging is an additional consideration. Transdermal delivery of drugs may alleviate complications due to polypharmacy and swallowing difficulties while facilitating steady-state concentrations. Marketed transdermal products generally do not report age-related differences in pharmacokinetics, suggesting that skin factors play a minor role in comparison to the drug's chemistry and transdermal formulation.

Additional investigations may be beneficial in helping determine if the elderly should have different topical dosing regimens to ensure efficaciousness with minimal adverse effects. This is especially important for drugs that have a narrow therapeutic window, such as fentanyl and clonidine.[15] Also, future studies would benefit from the inclusion of older subjects, as prior studies have largely focused on individuals younger than 70 years. Continued efforts should be directed at enhancing transdermal delivery design and predicting which topical drugs are likely to have altered pharmacodynamics in the elderly.

Compound	Molecular Weight	Aqueous Solubility	log $K_{o/w}$[a]	Cumulative % Dose Absorbed[b]	
				Young (22-40 years)	Old (>65 years)
Testosterone	288.4	Insoluble	3.32	19.0 ± 4.4 (n=6)	16.6 ± 2.5[c] (n=8)
Estradiol	272.4	Almost insoluble	2.49	7.1 ± 1.1 (n=5)	5.4 ± 0.4[c] (n=5)
Hydrocortisone	362.5	0.28 g/L	1.61	1.5 ± 0.6[d] (n=3)	0.54 ± 0.15[d,e] (n=7)
Benzoic acid	121.1	3.4 g/L	1.83	36.2 ± 4.6 (n=7)	19.5 ± 1.6[f] (n=8)
Acetylsalicylic acid	180.2	3.3 g/L	1.26	31.2 ± 7.3 (n=5)	13.6 ± 1.9[g] (n=7)
Caffeine	194.2	21.7 g/L	0.01	48.2 ± 4.1 (n=5)	25.2 ± 4.8[f] (n=7)

Table 1: Percutaneous penetration data and physicochemical parameters for six drugs

[a] Data from Bucks et al. (1988)[13]; solubilities obtained from the Merck Index.
[b] Mean ± SE (standard error).
[c] Not significantly different from the young control group ($p > 0.05$).
[d] If averaged together with the data from Bucks et al. (1988)[13] (mean ± SE = 3.27 ± 0.73; n=8), then $p < 0.01$.
[e] Significantly different from the young control group ($p = 0.06$).
[f] Significantly different from the young control group ($p < 0.01$).
[g] Significantly different from the young control group ($p < 0.05$).

Table from Roskos KV, Maibach HI, Guy RH. The effect of aging on percutaneous absorption in man. *J Pharmacokinet Biopharm* 1989;17(6):page 623, Table 1.[12] Reprinted with kind permission from Springer Science and Business Media.

Product	Active Drug	Wear Duration	Age Groups Tested	Pharmacokinetics (According to Label)
Catapres-TTS® (NDA 018891)	Clonidine	Weekly	Adult	No age-relationship reported
Estraderm® (NDA 019081)	Estradiol	Twice weekly	Post-menopausal and aged	No age-relationship reported
Durogesic® (NDA 019813)	Fentanyl	72 hours	Child and adult	In children, 1.5 to 5 years old that are non-opioid-tolerant, the fentanyl plasma concentrations were approximately twice as high as that of adult patients. In older pediatric patients, the pharmacokinetic parameters were similar to that of adults.
Nicoderm CQ® (NDA 020165)	Nicotine	Daily	Adult	No age-relationship reported
Testoderm® (NDA 020489)	Testosterone	Daily	Adult and aged	No age-relationship reported
Lidoderm® (NDA 020612)	Lidocaine	12 hours	Adult	No age-relationship reported
Flector® (NDA 021234)	Diclofenac epolamine	Twice daily	Adult	No age-relationship reported
Butrans® (NDA 021306)	Buprenorphine	7 days	Adult	No age-relationship reported
Emsam® (NDA 021336)	Selegiline	Daily	Adult and aged	The effect of age on the pharmacokinetics or metabolism of selegiline has not been systematically evaluated.
Oxytrol® (NDA 021351)	Oxybutynin	3 to 4 days	Adult	No age-relationship reported
Daytrana® (NDA 021514)	Methylphenidate	9 hours	Children and adolescents	No age-relationship reported
Neupro® (NDA 021829)	Rotigotine	Daily	Middle-aged and elderly	Plasma concentrations in patients 65 to 80 years of age were similar to those in younger patients, approximately 40 to 64 years of age. Although not studied, exposures in older subjects (>80 years) may be higher due to skin changes with aging.
Exelon® (NDA 022083)	Rivastigmine tartrate	Daily	Younger adults and elderly	No age-relationship reported
Sancuso® (NDA 022198)	Granisetron	Up to 5 days	Adult	No studies have been performed to investigate the pharmacokinetics of granisetron in elderly subjects.
Qutenza® (NDA 022395)	Capsaicin	1 hour	Adult and elderly	No dose adjustments are required in geriatric patients.

Table 2: Pharmacokinetics and age relationship in marketed transdermal products

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Update on Drugs

Name/Company	Approval Dates/Comments
Taliglucerase alfa for injection *Elelyso*™ Pfizer Inc. Protalix BioTherapeutics	The US FDA approved this enzyme replacement therapy in May 2012 for the long-term treatment of adults with a confirmed diagnosis of Type 1 (non-neuropathic) Gaucher disease. It is the first approved plant cell-expressed drug that is derived from a proprietary manufacturing system (ProCellEx®, Protalix BioTherapeutics), using genetically engineered carrot cells. Treatment is administered every other week by a health care professional.

Device News

Nd:YAG surgical laser *Fotona® XP Laser System Family* Fotana D.D.	US FDA 510(k) clearance was granted to this Nd:YAG laser device in March 2012. Intended uses include: matrixectomy, radical nail excision, periungual and subungual warts, plantar warts, neuromas, and temporary increase of clear nail in patients with onychomycosis.
Q-switched laser for melasma *Spectra*™ Lutronic Inc.	This Q-switched laser device received FDA clearance in March 2012 for the treatment of melasma. A controlled split face study of this 1064 nm Q-switched laser, at low fluence and short pulse widths, demonstrated statistically significant reductions in the appearance of melasma.
Diode hair removal laser *Advantage*™ Lutronic Inc.	The FDA granted regulatory clearance in April 2012 to market this hair removal laser. The manufacturer's press release describes the unit as providing optimal efficacy by utilizing a larger spot size, which reduces treatment time and penetrates deeply to maximize hair removal outcomes.
Low-level laser diode device for circumferential reduction *i-Lipo*™ Chromogenex Technologies	FDA clearance was granted to this novel direct skin contact laser device in April 2012 for fat reduction and body contouring. According to the manufacturer, the unit emits low levels of laser energy, generating chemical signaling in fat cells and breaking down stored triglycerides into free fatty acids and glycerol, which are released though channels in cell membranes. The fatty acids and glycerol are transported to body tissues for use during metabolism to yield energy. In conjunction, a period of post-treatment exercise facilitates metabolism and elimination of the released fatty acids from the body.
Multiwavelength diode laser *Evolve® HPD* Biolitec, Inc.	FDA device clearance was granted to this diode laser in April 2012. The laser system is generally indicated for use in incision, excision, vaporization, abalation, hemostasis, or coagulation of soft tissue.

Drug News

In March 2012, the FDA issued a safety notice to healthcare professionals and cautioned consumers to avoid the use of skin creams, beauty and antiseptic soaps, or lotions that may contain mercury, a potent toxin that can cause neurological symptoms, kidney damage, and birth defects. Over the last few years, more than 35 products containing unacceptable levels of mercury have been uncovered by the agency. The products are illegally imported and sold in the US, or brought into the country for personal use. They are marketed as skin lighteners and anti-aging treatments to remove age spots, freckles, blemishes, and wrinkles, or as acne treatments. Consumers are urged to check product labels or listed ingredients for any mention of mercurous chloride, calomel, mercuric, mercurio, or mercury, and discontinue use immediately if found. For more information:
http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm296261.htm