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Rising Drug Costs: The Impact on Dermatology

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ABSTRACT

In the US prescription drug costs are rising faster than any other component of health care expenditures, and show no signs of slowing[1]. Spending on prescription drugs has been estimated by the Health Care Finance Administration (HCFA) to be rising by approximately 12% per year, more than twice the rate for national health care expenditures (5.1%)[2]. Factors driving the rise in prescription drug costs include the introduction of new drugs, and consumer demand.

KEY WORDS: *co-pay, prescription costs, brandname drugs, generic drugs*

More New Drugs and Faster Approvals

The majority of new drugs are highly effective, offer better therapy than agents currently in use, and are targeted to specific niche markets. In 1997 and 98, 88 new drugs were approved by the US Food and Drug Administration (US FDA), including the "block buster" hit *Viagra,* and the nonsedating antihistamines: *Claritin, Allegra* and *Zyrtec*. In 1999, we saw the approval of the male pattern baldness agent, *Propecia* and the Cox-2 inhibitor, *Celebrex*. These products represent "life-style drugs". They improve the quality of the patient's life, but may not be medically necessary. Antihistamines currently rank as the second most commonly prescribed class of prescription drug for managed care organizations.

New drugs are arriving on the market faster. The US FDA has slashed the time for new drug approval from 31 months in 1988, to 11.7 months in 1998. The number of drugs in development and seeking approval has also increased. These include very expensive "designer drugs" and biologic response modifiers, such as interferons and colony stimulating factors.

Consumer Marketing

The increase in cost has been partially driven by consumer demand. In 1997, the US FDA approved direct consumer marketing. Since then, direct marketing to consumers has expanded to a $1.3 million/year enterprise, an increase of more than 23% over the last year alone. Patients are much more savvy about their medical conditions and their treatment options. They often arrive at the doctor's office, literature search in hand, requesting the latest, and often the most expensive, new therapy.

Approximately 85% of patients in the US are now covered by a third party payer for prescription costs and as a result, they pay a lower, flat rate (co-pay) for their medications. This is a driving factor for both cost and consumer demand. Co-pays for prescriptions are relatively low when compared to the prescription cost, and there is no incentive for either the patient or the provider to write for an equally effective, but lower cost alternative drug. While 60% of third party payers offer a tiered patient payment structure, with a higher co-pay on brand name drugs than the co-pay for generic drugs, the difference in cost is not sufficient to change prescribing behavior. Most patients do not pay proportionately for the total cost of the prescription, although such price restructuring has been advocated.

Cost Control Efforts

Pharmacy benefit managers negotiate with pharmacies for discounted rates on prescriptions. Often these discounted rates reimburse pharmacies for medication acquisition costs only and include deeply discounted or no dispensing fees. Pharmacies pass

Medication	AWP*
Antibiotics	*(cost per capsule)*
• Cephalexin 500mg	$ .21**
• Dicloxacillin 250mg	$ .38**
• Trovafloxacin 100mg (#30)	$1.78
Antifungal creams	*(cost per gram)*
• Ketoconazole	$ .93
• Miconazole (OTC)	$ .10
• Terbinafine	$1.93
Antifungal oral agents	*(cost per tablet)*
• Itraconazole 100mg	$6.80
• Ketoconazole 200mg	$3.73
• Terbinafine 250mg	$7.30
Antihistamine tablets	*(cost per tablet)*
• Cetirizine 10mg	$1.86
• Fexofenadine 60mg	$ .99
• Loratidine 10mg	$2.37
• Loratidine reditabs 10mg	$2.53
Anti-inflammatory agents	*(cost per tablet/capsule)*
• Azathioprine 50mg	$1.46
• Cyclophosphamide 50mg	$3.56**
• Cyclosporin 100mg	$5.93
• Dapsone 100mg	$ .20
• Mycophenolate mofetil 500mg	$4.50
Retinoids	*(cost per tablet/capsule)*
• Acitretin 25mg	$8.00
• Isotretinoin 40mg	$6.64

Table 1: Some agents frequently prescribed by dermatologists[4].

*AWP: average wholesale price in US dollars; **HCFA established price for Medicaid recipients.

a higher percentage of operating expenses along to those patients not covered by third party payers. The net result:

1) Prescription costs are rising rapidly, particularly for those patients not covered by insurance.
2) Premiums and deductibles for prescription drug plans are rising fast, but not fast enough to keep up with soaring drug costs.

Several methods to control spiraling prescription costs are in place with more to come. Closed formularies, in which a limited number of medications are covered, are common to Health Maintenance Organizations (HMOs) and some pharmacy benefits programs. Provider profiling tracks prescribing patterns of physicians and is used by HMOs and pharmacy benefit managers for performance improvement activities. Some pharmacy benefit managers are negotiating with pharmaceutical companies to control direct advertising in the community. Expensive medications such as *Accutane* are increasingly subject to preauthorization by benefit programs.

Impact on Dermatology

Clinicians should be aware of the costs of various medications used in the management of acute and chronic skin diseases. A retrospective analysis of nondermatologist and dermatologist prescribing patterns noted that the nondermatologists used a combination antifungal/topical steroid preparation 7 times more often than the dermatologists[3]. Substituting a less expensive, yet just as effective, antifungal agent would result in annual savings of $10-25 million.

Table 1, while not exhaustive, lists some average wholesale prices (AWP) of agents frequently prescribed by dermatologists[4]. Pharmacy acquisition costs are typically discounted from the AWP. The cost to the patient is calculated based on pharmacy acquisition costs, plus a dispensing fee. Third party payers negotiate prescription reimbursement costs with a deeply discounted fee structure. The average co-payment by patients for generic drugs is currently $6.19 (range $5-10), and $12.56 for brand name drugs (range: $5-$20)[2]. Some pharmacy benefit programs require a higher co-payment for brand name drugs off-formulary with the average co-pay for these agents at $26 (range: $10-50). The final cost paid by the patient, and by insurance companies, varies widely.

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Herbal Anti-Inflammatory Agents for Skin Disease

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ABSTRACT

Herbs have been used in clinical medicine for thousands of years. However, it is only in recent times that we have been able to employ scientific methods to prove the efficacy of many of these herbs and to give us a better understanding of their mechanisms of action. This article will focus on the use of herbs in various dermatological conditions characterized by inflammation and pruritus. Topical preparations of many of these herbs are more commonplace in Europe. However, their availability is increasing in the US. As this is occurring we are witnessing a growing marriage between alternative and traditional medicines.

Key Words: herbs, anti-inflammatory, astringent, antipruritic

The process of inflammation involves the release of vasoactive mediators and chemotactic factors such as histamine, leukotrienes, proinflammatory prostaglandins and lymphokines. These substances are responsible for the capillary dilation and increase in permeability, resulting in swollen, inflamed tissues.

Turmeric

Many herbs have demonstrated anti-inflammatory activity. Turmeric *(Curcuma longa),* the major ingredient of curry powder and prepared mustard, has a long history in both Chinese and Ayurvedic (Indian) medicine as an anti-inflammatory agent. The volatile oil fraction of turmeric has demonstrated potent anti-inflammatory activity in a variety of experimental animal models, while curcumin, the yellow pigment of turmeric is even more potent in acute inflammation[1]. When used orally, curcumin inhibits leukotriene formation, inhibits platelet aggregation and stabilizes neutrophilic lysosomal membranes, thus inhibiting inflammation at the cellular level[2]. Curcumin is reported to possess greater anti-inflammatory activity than ibuprofen[3]. At low levels, curcumin is a prostaglandin inhibitor, while at higher levels it stimulates the adrenal glands to secrete cortisone[4]. Formulation difficulties due to the yellow color of curcumin has made topical use slow in coming. However, recent developments in technology may change that. The standard oral dose of curcumin is 250-400 mg, three times a day.

Licorice root

Licorice root *(Glycyrrhiza glabra)* has been used for centuries to treat inflammatory and viral diseases. The active part of the root contains glycyrrhizin, (a triterpene saponin), at concentrations ranging from 7-10%. It is converted to glycyrrehetic acid (GA) in the body. This herb has been used extensively in Europe as an anti-inflammatory agent, and in Japan as an antiviral agent with success in treating chronic hepatitis. It has been shown to inhibit the activity of proinflammatory prostaglandins and leuktrienes, and appears to have a cortisone-like effect making it useful as an anti-inflammatory[5,6]. In one study the effects of topical corticosteroids were significantly enhanced by the addition of 2% GA[7]. Another study reported that the use of topical ointments containing active isomers of GA exerted anti-inflammatory activity in a number of subacute and chronic dermatoses[8]. When compared, topical corticosteroids were superior in the treatment of acute atopic dermatitis. However, GA was superior when treating chronic conditions such as contact dermatitis, seborrheic dermatitis, psoriasis and other conditions characterized by inflammation and pruritus[8]. Although topical preparations are not available in the US, compresses can be prepared by adding 3 gm (1 tsp) of the extract in 150 ml of water. Orally, the dosage depends on the form in which it is taken. In powdered root form, the dose is 1-4 gm daily. In fluid extract form, the dose is 1 tsp before meals and as a solid extract, the dose is 1/2 tsp before meals. Generally speaking, although herbs have far fewer side effects, they do exist and caution must be exercised in patients with hypertension when using oral licorice root. Elevations in blood pressure have been reported. Much smaller doses, or none at all, should be used for patients with cardiac or renal histories.

Bromelain

Bromelain, a mixture of proteolytic enzymes from the stem of the pineapple plant, has demonstrated anti-inflammatory activity in a wide variety of conditions. It appears to inhibit the production of pro-inflammatory prostaglandins, induce production of anti-inflammatory Series 1 prostaglandins, and reduce capillary permeability[9]. Bromelain is quite useful postoperatively as an agent to speed healing and reduce postsurgical pain and swelling.

Willow bark

Willow bark *(Salix alba)* contains salicin, known for its antipyretic and pain relieving activity since ancient times. Available in many forms, willow bark extract can be found in many topical and oral products primarily in health food stores.

Witch hazel

Witch hazel *(Hamamelis virginiana)* has been used for centuries by Native North American tribes to soothe inflamed skin. Much of the anti-inflammatory properties of witch hazel extracts can be

Herb	Dosage	Side effects
Turmeric, Indian saffron *(Curcuma longa)*	250-400 mg, 3 times/day	None known[18]
Licorice root *(Glycyrrhiza glabra)*	1-4 gm daily	• Elevated blood pressure • 30-40gm/day for extended periods can lead to electrolyte imbalances[18]
Bromelain, Pineapple *(Ananas comosus)*	80-320 mg, 2-3 times/day for 8-10 days[19]	• Ethyl acrylate, an aromatic component of the juice can produce dermal sensitization • Occasional gastric disturbances or diarrhea[19]
White willow bark *(Salix alba)*	To make a tea: 1-2 tsp of powdered bark steeped in 1 cup boiling water for 8 hours[19]	• Can cause Reye's syndrome in children ≤ 16 years with a viral illness[19] • Can cause GI irritation when taken internally[19]
Witch hazel *(Hamamelis virginiana)*	External decoction: 2-3 gm fine cut powdered bark in 150 ml water[19]	For external use only. If taken internally, GI and hepatic damage can occur[18]
Chamomile *(Matricaria recutita* and *Chamaemelum nobile)*	3 gm whole flower head, 3-4 times/day, between meals[19]	None known[19]
Yarrow *(Achillea millefolium)*	External: 100 gm/20 l hot water for sitz bath[19]	Contact dermatitis[18]
Oak bark *(Quercus alba)*	3 gm/day of cut herb. For rinses, compresses and gargles: 20gm/l water[19]	None known[19]
Walnut leaf *(Juglans regia)*	2-3 gm dried leaf/100ml water[19]	None known[19]
Fenugreek *(Trigonella foenum-graecum)*	Internal: 6 gm/day External: 50 gm powdered seed/l hot water for poultice[19]	• Excess dosage may cause hypoglycemia[18] • Repeated external applications can cause undesirable skin reactions[19]

Table 1: a review of some herbs with anti-inflammatory properties.

explained by the presence of astringent tannins, which enhance the soothing effects[10]. However, it is important to note that commercially available witch hazel extract does not contain tannins because they are lost in the distillation process. Nonetheless, it is still believed to be soothing when applied to inflamed skin.

Chamomile

Chamomile refers to two distinct plants. *Matricaria recutita* is known as German or Hungarian chamomile, and *Chamaemelum nobile* is known as Roman or English chamomile. Although the plants are not identical, they are used for the same types of conditions. The active constituents of chamomile include the terpenoids (bisabolol, matricin, chamazulene) and flavenoids (apigenin, luteolin)[11]. Studies have documented the anti-inflammatory and soothing effects of creams containing chamomile in patients with various inflammatory dermatoses[12]. It is often used in a variety of cosmetic products and as soothing compresses.

Yarrow

Yarrow *(Achillea millefolium),* contains anti-inflammatory ingredients including chamazulene. Known for its anti-inflammatory and anti-pruritic activity, it is used externally in the form of compresses and bath additives.

Oak bark

Oak bark *(Quercus alba)* contains a mixture of tannins including catechins, oligomeric proanthrocyanidins and ellagitannins. Due to their astringent, vasoconstrictive and cooling properties they make excellent soothing compresses.

Aloe Vera

The use of aloe as a medicinal can be traced back to 333 BC, and there are over 180 aloe species identified. It is widely used for the treatment of burns and wounds. The active component is a polysaccharide that forms a protective and soothing coating when applied to the skin. The ability of aloe to accelerate wound healing was demonstrated in a study with patients who had full-face dermabrasion[20]. Aloe vera was also found to be effective in the treatment of psoriasis[21] and it has been used as a biologically active vehicle for certain ingredients.

Calendula

Calendula *(Calendula officinalis),* derived from the marigold plant, is quite widely used in topical skin and hair preparations as a soothing ingredient. Its anti-inflammatory effects are a result of triterpene flavonoids and saponins[22]. It has been used topically as an antiseptic agent and applied to poorly healing wounds.

Capsaicin

Capsaicin inhibits substance P, a peptide transmitter involved in pain transmission, cutaneous vasodilation, and the inflammatory process. Capsaicin has also been found to be effective in the treatment of plaque-type psoriasis[23,24]. It is worth noting that the first few applications of topical capsaicin often result in burning and stinging.

These symptoms diminish with continued use. However, in both studies noted, the dropout rate was significant due to these reactions.

Other anti-inflammatory herbs

Walnut leaf *(Juglans regia),* extracted from the dried leaves of the English walnut, contains ellagitannins, whose astringent properties can be soothing to weeping lesions when used as compresses. There are many other topically applied anti-inflammatory herbs that are used mostly in Europe and Asia, such as mallow *(Malva sylvestris),* wild pansy *(Viola tricolor),* and fenugreek seeds *(Trigonella foenum-graecum)* that contain several anti-inflammatory saponins.

Bioflavenoids

The bioflavenoids, including quercetin and hesperidin, inhibit histamine release and mast cell degranulation, and support capillary integrity[13,14]. Quercetin (found in high levels in onions) inhibits phospholipase A2 and lipoxygenase enzymes. This results in the inhibition of proinflammatory prostaglandins and leukotrienes.

Essential fatty acids

The essential fatty acids are those fatty acids that are not synthesized or are poorly synthesized by humans. Historically, a diet rich in land animal fats results in much higher levels of arachidonic acid with a concomitant increase in proinflammatory prostaglandin synthesis. Conversely, a diet rich in fish will have the opposite effect, increasing anti-inflammatory prostaglandins. Several studies demonstrate marked clinical improvement in atopic patients using dietary supplementation with either eicosapentanoic acid (EPA), or gamma-linoleic acid (GLA)[15,16,17]. The most effective fatty acids include EPA, docosahexanoic acid (DHA) from fish oils, and GLA from plant oils such as borage, black currant, and evening primrose, since they bypass the desaturation enzyme steps. It generally takes several months of fatty acid supplementation before improvement is noted. There are anecdotal reports about the application of evening primrose oil to chapped, irritated skin, leading to clinical improvement and healing.

Conclusion

As our familiarity with herbal ingredients increases and we employ our known scientific methodology to study them physiologically, our ability to treat patients satisfactorily, with fewer side effects will be enhanced. Many more herbs are being studied for their therapeutic as well as preventative roles in traditional medicine, thus narrowing a gap that has been present for many years.

References

1. Arora RB, Kapoor V, Basu N, Jain AP. Anti-inflammatory studies on *Curcuma longa* (turmeric). *Indian J Med Res* 59(8):1289-95 (1971 Aug).
2. Srivastava R. Inhibition of neutrophil response by curcumin. *Agents Actions* 28(3-4):298-303 (1989 Nov).
3. Srimal RC, Dhawan BN. Pharmacology of diferuloyl methane (curcumin), a non-steroidal anti-inflammatory agent. *J Pharm Pharmacol* 25(6):447-52 (1973 Jun).
4. Srivastava R, Srimal RC. Modification of certain inflammation-induced biochemical changes by curcumin. *Indian J Med Res* 81:215-23 (1985 Feb).
5. Okimasu E, Moromizato Y, Watanabe S, et al. Inhibition of phospholipase A2 and platelet aggregation by glycyrrhizin, an antiinflammation drug. *Acta Med Okayama* 37(5):385-91 (1983 Oct).
6. Ohuchi K, Kamada Y, Levine L, Tsurufuji S. Glycyrrhizin inhibits prostaglandin E2 production by activated peritoneal macrophages from rats. *Prostaglandins Med* 7(5):457-63 (1981 Nov).
7. Teelucksingh S, Mackie AD, Burt D, McIntyre MA, Brett L, Edwards CR. Potentiation of hydrocortisone activity in skin by glycyrrhetinic acid. *Lancet* 335(8697):1060-3 (1990 May).
8. Evans FQ. The rational use of Glycyrrhetinic Acid in dermatology. *Br J Clin Pract* 12:269-74 (1958).
9. Taussig SJ. The mechanism of the physiological action of bromelain. *Med Hypotheses* 6(1):99-104 (1980 Jan).
10. Korting HC, Schafer-Korting M, Hart H, Laux P, Schmid M. Anti-inflammatory activity of hamamelis distillate applied topically to the skin. Influence of vehicle and dose. *Eur J Clin Pharmacol* 44(4):315-8 (1993).
11. Merfort I, Heilmann J, Hagedorn-Leweke U, Lippold BC. In vivo skin penetration studies of camomile flavones. *Pharmazie* 49(7):509-11 (1994 Jul).
12. Della Loggia R. Chamomile extracts exerted anti-inflammatory effects when applied topically in animal models of inflammation. *Plant Med* 56:657-8 (1990).
13. Middleton E Jr, Drzewiecki G, Krishnarao D. Quercetin: an inhibitor of antigen-induced human basophil histamine release. *J Immunol* 127(2):546-50 (1981 Aug).
14. Emim JA, Oliveira AB, Lapa AJ. Pharmacological evaluation of the anti-inflammatory activity of a citrus bioflavenoid, hesperidin, and the isoflavenoids, duartin and claussequinone, in rats and mice. *J Pharm Pharmacol* 46(2):118-22 (1994 Feb).
15. Berth-Jones J, Thompson J, Graham-Brown RA. Evening primrose oil and atopic eczema. *Lancet* 345(8948):520 (1995 Feb).
16. Schalin-Karrila M, Mattila L, Jansen CT, Uotila P. Evening primrose oil in the treatment of atopic eczema: effect on clinical status, plasma phospholipid fatty acids and circulating blood prostaglandins. *Br J Dermatol* 117(1):11-9 (1987 Jul).
17. Bahmer FA, Schafer J. [Treatment of atopic dermatitis with borage seed oil (Glandol)—a time series analytic study]. *Kinderarztl Prax* 60(7):199-202 (1992 Oct).
18. DerMarderosian A, editor. *The review of natural products. facts and comparisons* Publishing Group (2000).
19. Herbal Index at onhealth: http://www.onhealth.com/ch1/resource/herbs/
20. Fulton JE Jr. The stimulation of postdermabrasion wound healing with stabilizing aloe vera gel-polyethylene oxide dressing. *J Dermatol Surg Oncol* 16(5):460-7 (1990 May).
21. Syed TA, Ahmad SA, Holt AH, Ahmad SA, Ahmad SH, Afzal M. Management of psoriasis with Aloe vera extract in a hydrophilic cream: a placebo-controlled double-blind study. *Trop Med Int Health* 1(4):505-9 (1996 Aug).
22. Brown DJ, Dattner AM. Phytotherapeutic approaches to common dermatologic conditions. *Arch Dermatol* 134(11):1401-4 (1998 Nov).
23. Ellis CN, Berberian B, Sulica VI, et al. A double-blind evaluation of topical capsaicin in pruritic psoriasis. *J Am Acad Dermatol* 29(3):438-42 (1993 Sep).
24. Bernstein JE, Parish LC, Rapaport M, Rosenbaum MM, Roenigk HH Jr. Effects of topically applied capsaicin on moderate and severe psoriasis vulgaris. *J Am Acad Dermatol* 15(3):504-7 (1986 Sep).

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Conclusion

Efforts to control prescription prices have, to date, focused on negotiating better pricing through group purchasing and other actions at the margins. The key to controlling pricing will be partnership of physicians with industry and pharmacy to prescribe appropriate medications, keeping costs in mind. Physicians must recognize the implication that spiraling prescription costs have for our patients and the health care system, and play a lead role in advocating the use of cost-effective medications.

References

1. Health expenditures ease a bit; drugs lead cost-of-care increase. *Managed Care* 8(8):13-4 (1999 Aug).
2. Hensley S. Prescription costs become harder to swallow. Providers and payers get a big dose of reality with explosive spending and patient demand for new drugs. *Mod Healthc* 29(34):30-4 (1999 Aug).
3. Smith ES, Fleischer AB Jr, Feldman SR. Nondermatologists are more likely than dermatologists to prescribe antifungal/corticosteroid products: an analysis of office visits for cutaneous fungal infections, 1990-1994. *J Am Acad Dermatol* 39(1):43-7 (1998 July).
4. Cardinale, V. *1999 Drug Topics Red Book,* Montvale, N.J.:Medical Economics, 1999. Ed.103rd.

Update on Drugs

Class	Name/Company	Approval Dates and Comments
Vaginal Atrophy	**Estradiol Vaginal Ring** *Estring* Pharmacia and Upjohn	The US FDA approved this drug in January 2000, for the treatment of urogenital symptoms associated with post-menopausal vaginal atrophy.
Urticaria	**Fexofenadine HCl** *Allegra* Aventis Pharmaceuticals	The US FDA approved this drug in February 2000, for the additional treatment of uncomplicated skin manfestations of chronic idiopathic urticaria in adults and children ≥ 6 years of age
Pediculocides	**Piperonyl Butoxide/ Pyrethrins** *Rid Mousse* Soltec Research	The US FDA approved this emulsion/aerosol foam in March 2000, for the treatment of head, pubic (crab), and body lice.
Anticancer	**Temoporfin** *Foscan* Scotia	An NDA was submitted to the US FDA in October 1999, for this photodynamic therapy product. Also in October 1999, Scotia filed this product for centralized approval in the EU for head and neck cancer. The Netherlands will act as rapporteur and Denmark as co-rapporteur.

Drug News

Dear Doctor Letter *Re: Methotrexate*	Lederle Pharmaceuticals issued a Dear Doctor letter in November 1999, regarding labelling changes for methotrexate products. Revised labelling warns that rare reports of bone and soft tissue necrosis have occurred following radiation therapy in patients receiving this drug. There have also been rare reports of painful plaque erosions when methotrexate was used to treat psoriasis. The drug interactions section now recommends that patients who receive this drug with potentially hepatotoxic agents be closely monitored for possible increased risk of hepatotoxicity. The Overdosage section notes that routine hemodialysis and hemoperfusion are ineffective in lowering methotrexate blood levels and corrective measures may include high-flux dialysis equipment.
DRUG WARNING: *Re: MuTong* (Stephania, Clematis, Akebia, Aristolochia)	Aristolochic acid, a known nephrotoxin present in Chinese herbs known as MuTong, has been identified as the cause of renal failure in two women who were taking the drugs for excema, according the a report in the November 1999 issue of the *Dermatology Times*. As a result, this drug has been banned in the UK and a drug warning was issued by HPB - Ottawa. The kidney disease suffered by these two patients is a progressive fibrosis that leads to end-stage renal failure. Both patients had been taking the drug for more than 2 years. It is not known how long it takes the herb to cause kidney problems. MuTong refers to a number of herbs including *Stephania, Clematis, Akebia* and *Aristolochia,* which are used interchangeably in traditional Chinese medicines.
Drug Recall *Re: Antiseptic Sterile Skin Preparations*	The US FDA announced in March 2000, that Clinipad Corp. of Rocky Hill, Connecticut in the US is voluntarily recalling their antiseptic sterile skin preparations because of a potential for bacterial contamination. The products are distributed under the names: *Clinipad, Clinidine, Cliniguard, EX Prep,* Cooper Instrument Corp., Moore Medical Corp., and Rausher. They are used to control and prevent infection.
Topical Anesthetic *Re: EMLA cream*	According to Dr. John Goldsmith of New Zealand in an internet release from *Medsafe,* the dosage recommendations for lidocaine-prilocaine *(EMLA)* cream should be followed carefully and the cream should be used with care in infants up to 12 months of age. Adverse effects, particularly methaemoglobinaemia, can occur in this age group.
OTC Product *Re: Docosonol*	Avanir Pharmaceuticals signed a letter of intent in December 1999, with SmithKline Beecham for rights to market Avanir's *Docosonol* 10% cream in the OTC market as a treatment for recurrent oral-facial herpes or cold sores. *Docosanol's* FDA approval as an OTC product is pending.

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