Escharotic and other botanical agents for the treatment of skin cancer: A review

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A growing era of alternative medicine is upon us. All who practice medicine have a small population of patients who eschew Western medicine and prefer alternative approaches, including botanical remedies, to treat their medical problems. Many alternative practitioners advertise and sell products on the Internet. Indeed, this trend now includes a growing number of topical treatments for skin cancer, including escharotic agents.

Self-treatment of skin cancer requires a substance that will destroy tissue, usually indiscriminately. Escharotic agents are caustic, corrosive substances that produce a thick coagulated crust (an eschar) and subsequently a scar.

The following case illustrates one representative situation.

CASE REPORT

A 59-year-old man presented to our clinic with a biopsy-proven basal cell carcinoma on the left ala (Fig 1) and paresthesias of the left cheek. He had a history of several basal cell carcinomas elsewhere and had elected to treat some of those, and this lesion on the nose that included extension onto the cheek, with a topical preparation called Can-X (containing red clover, bloodroot, galangal, and sheep sorrel) approximately 1 year before presentation. After treatment, the lesion on the nose had fast become inflamed and, with time, scarred. Several months later a papule appeared within the scar on the nose that was biopsied showing basal cell carcinoma. The scar on the cheek did not change.

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The patient underwent Mohs micrographic surgery (MMS). The tumor had spread from the nose throughout the scar laterally onto the cheek, invading deeply into the subcutaneous tissue and creating a through-and-through defect into the nasal mucosa. It was cleared after 10 stages of MMS creating a defect of 4.7 by 3.5 cm (Fig 2). Pathology showed infiltrative and micronodular growth patterns with perineural spread (Fig 3) and large skip areas.

Two months later, the same patient was referred for MMS for a second lesion on the scalp, a biopsy-proven basal cell carcinoma, also previously treated with this particular escharotic agent and now recurrent. There were two pink scaly papules around a scar measuring 3.0 by 1.6 cm in total. The tumor was cleared after 8 stages, with a postoperative size of 8.5 by 8.0 cm. The tumor showed infiltrative and micronodular subtypes with large skip areas. In one section there were elongated cords and nests of tumor cells deep in the specimen along the galea, imparting an appearance of vascular invasion, although closer examination revealed that no blood vessels or nerves were directly involved by the tumor (Fig 4).

This particular escharotic agent is marketed exclusively through the Internet and claims to contain "an enzyme known to neutralize carcinogens prior to their stimulating any tumor growth. Another herb has a substance that prevents tumorous cells from multiplying once they have started."[1] It contains botanicals found in similar preparations: bloodroot, galangal, red clover, and sheep sorrel. The preparation is a deep red-brown paste, and appears tarry and granular. It has a pungent aroma. The accompanying product material suggests that its users apply it to the affected area, occlude for 24 hours, remove, and then conservatively treat the area as a wound.

DISCUSSION

This type of clinical encounter appears to be consistent with a growing trend whereby patients self-treat skin cancers (basal cell, squamous cell, and melanoma) with unregulated, often Internet-acquired escharotic agents, which may or may not contain zinc chloride,[2] the most commonly

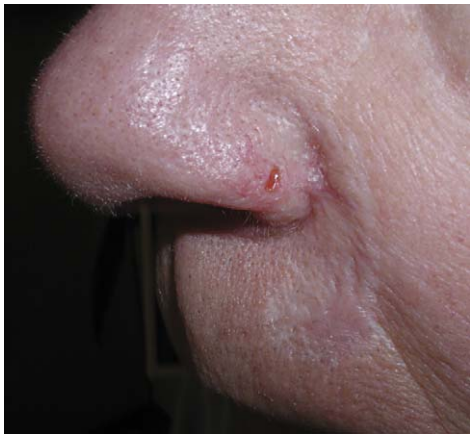

Fig 1. Preoperative picture: biopsy-proven basal cell carcinoma on left ala.

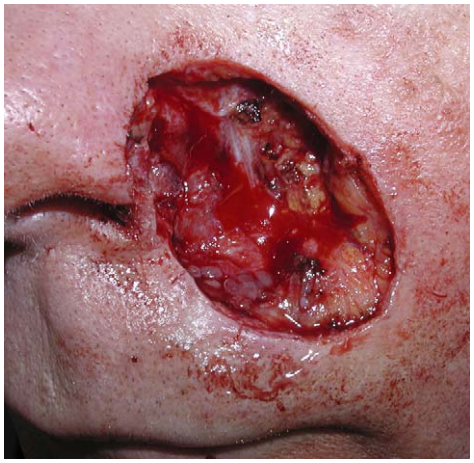

Fig 2. Postoperative picture: large defect on left ala, extending onto left cheek and cutaneous aspect of upper lip.

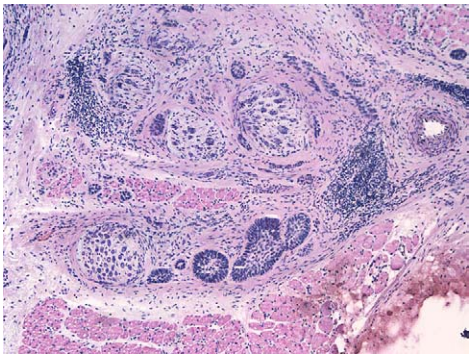

Fig 3. High-power view of perineural basal cell carcinoma (nose).

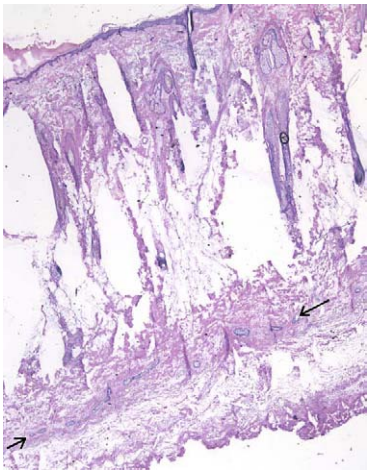

Fig 4. Low-power view of basal cell carcinoma, infiltrating along base of specimen (*arrows*) (scalp).

recognized agent used in conventional medicine. The escharotic agent in question, which does not contain zinc chloride, does not specify which of its botanical ingredients is considered active, although all have been studied to some degree. This report contains data collected from Internet sources of the plethora of available escharotic anticancer agents. Their ingredients have been assembled according to their proposed biologic activity, although many of them may have more than one effect (Table I). Most of the following data were collected using Ovid Medline and PubMed searches and cross-referencing the specific botanical or substance with "anticarcinogenic," "antineoplastic agents," or "cancer." Additional information was gathered in *The Review of Natural Products* 2004 edition, an Ovid-affiliated online textbook.[3] In many cases, there were multiple studies showing a certain biologic activity. These were not all listed. Selected, key references were instead detailed in support of that botanical's mechanism of action. It is critical that dermatologists recognize these agents and the results of their use.

Escharotic agents

Bloodroot and zinc chloride are the two compounds that are most clearly labeled as escharotic agents. Goldenseal was used traditionally as a caustic agent and has mild escharotic activity, but it will be discussed separately under agents with primarily anticarcinogenic activity.

Most dermatologists remember zinc chloride as the tissue fixative used by Dr Frederic Mohs in the early MMS.[4] Zinc chloride, in fact, was just one of many fixatives tested by Dr Mohs. Although zinc chloride in high doses caused significant necrosis (and if injected intravascularly in rats caused convulsions and death), it was safer than other tested chemicals such as arsenic trioxide, phenol, mercuric chloride, and silver nitrate.[4] It has a slow onset of action requiring 24 hours of contact, creates a relatively bloodless field, and penetrates unpredictably,

Table I. Botanical and elemental components of escharotic agents

Ingredient	Esharotic activity	Anticarcinogenic activity	Antioxidant activity	Keratolytic	Other
Zinc chloride	*	*	*		
Bloodroot	*	*			
Goldenseal	*				
Red clover		*			
Graviola leaf		*			
Bitter melon		*			
Sodom apple		*			
Lavender		*			
Frankincense		*			
Galangal		*			*
Capsicum peppers		*			*
Slippery elm		*			*
Tea tree oil		*	*		*
Silymarin		*	*		*
Willow bark		*	*		
Ginger		*	*		
Chapparel		*	*		
Birch bark		*	*		
Burdock root			*		
Sheep sorrel					*
Carbamide				*	
Apricot pits				*	*

although the depth seems to correlate fairly well with the thickness of the applied paste. Zinc chloride may be used for the debridement of chronic leg ulcers[5] and for chemosurgical debridement of osteomyelitic bone.[6] More recent research has shown that zinc chloride may prevent nuclear damage after exposure to nitrogen mustard.[7] It is a strong escharotic and among the most potent ingredients found in Table I.

Bloodroot, containing the alkaloid sanguinarine, is derived from the root of *Sanguinaria canadendid* and other poppy fumaria species. Bloodroot liquid flows from the plant when cut and coagulates into a thick paste. It is a strong escharotic and was also used at times by Dr Mohs in his escharotic paste. It has also been shown to possess antimicrobial, anti-inflammatory, and antioxidant properties. Recent studies have demonstrated its effect on inducing selective apoptosis in cancer cells,[8] perhaps through inhibition of the transcription factor nuclear factor-kB activation, inhibitor of kappa B-alpha phosphorylation and degradation.[9] Another study showed sanguinarine's ability to cause cell cycle blockade and apoptosis of prostate carcinoma cells through cyclin kinase inhibitor-cyclin-cyclin-dependent kinase machinery modulation.[10]

Anticarcinogenic agents

Red clover (*Trifolium pretense*) is a perennial herb that commonly grows in meadows throughout Europe and Asia, and has now been naturalized to grow in North America. Red flowers at the end of the branched stems contain the biologically active substances and are dried for therapeutic use. They contains isoflavones that have been shown to have photoprotective effects after topical application in hairless mice, reducing photocarcinogenesis.[11] Red clover extracts have also shown the ability to stimulate differentiation of human osteoblastic osteosarcoma cells.[12]

Goldenseal (*Hydrastis canadensis*) is a perennial herb found in the woods of the northeastern United States. It is a mild escharotic agent. It was used medicinally by Native Americans and extensively by the alternative medical community, so extensively that the wide harvesting coupled with loss of habitat led to depletion in wild populations and a listing under the Convention on International Trade in Endangered Species of Wild Fauna and Flora. It has found a niche market in hiding positive outcomes in urinalyses for illicit drugs and is now one of several adulterants sought and detected in such urinalysis evaluations. It contains several isoquinoline alkaloids that have been reported to selectively inhibit uptake of glucose by cancer cells and inhibit tumor promotion in a mouse skin carcinogenesis model.[13]

Graviola (*Annona muricata*), or soursop, is a small evergreen tree found in tropical areas in North and South America. Pond apple (*A glabra*) is a related tree in the *Annonaceae* family. The most significant studies of this family show an inhibitory

effect of two diterpenoid compounds isolated from *A glabra* on the proliferation of a human cancer cell line, a phenomenon correlated with the induction of cell apoptosis by down-regulating bcl-2 gene and up-regulating the bax gene.[14]

Bitter melon (*Momordica charantia*) and a related species, *M grosvenori*, are tropical fruit trees used in traditional medicine in China, India, and Africa. Their juice is marketed as a natural sweetener. Recently, cucurbitane glycosides isolated from *M grosvenori* inhibited a two-stage carcinogenesis test of mouse skin tumor cells.[15] With ginger, *M charantia* inhibited the development of mammary tumors and, by itself, the bitter melon extract inhibited uterine adenomyosis in virgin mice.[16]

Ginger (*Zingiber officinale*) is used in traditional medicine as an antiemetic and to treat a variety of gastrointestinal problems.[3] Two vanillyl ketones found in ginger, gingerol and (6)-paradol, demonstrated antitumor-promoting properties and suppressed superoxide production, both of which suggested potential chemopreventative activities.[17] More recently, zerumbone, a sesquiterpene found in ginger, was shown to suppress skin tumor initiation and promotion in a mouse model.[18]

Lavender (family *Lamiaceae*, with multiple species used for medicinal purposes) may be distilled to produce perillyl alcohol, which may also be produced from cherries, spearmint, and celery seeds. Perillyl alcohol has been studied as an anticarcinogenic agent, inducing the apoptosis-producing protein Bak in pancreatic ductal adenocarcinoma relative to untransformed ductal epithelial cells.[19] Perillyl alcohol has also shown chemopreventive effects in mouse lung[20] and rat esophageal tumorigenesis.[21]

The highly aromatic frankincense (*Boswellia serrata*) has an obvious religious historic reference: the gift brought to baby Jesus by the wise men. Frankincense is obtained from the *Boswellia* tree through a deep, longitudinal incision in the tree trunk, from which the white, milklike juice exudes and subsequently hardens to form "tears" that are collected. It is part of the *Burseraceae* family of trees and shrubs that encompasses more than 540 species. *B serrata* gum resin is used in alternative medicine to treat osteoarthritis and inflammatory bowel disease, in addition to skin cancer in escharotic agents. In a study from 2002, boswellic acids from frankincense induced dose-dependent antiproliferative effects on several human malignant cell lines.[22] Boswellic acids have also been shown to trigger apoptosis in colon cancer cells through a caspase-8 activation pathway[23] and at low concentrations demonstrated cytotoxic activity against meningioma cells through inhibition of phosphorylation of the extracellular-signal regulated kinase 1 and 2 (Erk-1 and Erk-2.)[24]

Willow trees (*Salix alba*, *S purpurea*, *S fragilis*, *S caprea* [goat willow], and other species) are small shrubs that encompass several hundred species. Willow bark has been used in folk medicine for hundreds of years; it contains salicylate derivatives with well-known biologic effects. In 2004, Sultana and Saleem[25] published that *S caprea* applied to animals inhibited oxidative stress, ornithine decarboxylase activity, and DNA synthesis, inhibiting murine skin carcinogenesis. In addition, willow leaf extracts have shown antileukemic activity, killing blasts in acute myeloid leukemia.[26]

Silymarin, a polyphenolic flavenoid derived from the seeds of the mild thistle plant (*Silybum marianum*) contains isomers that have been shown to reduce thymine dimer positive cells and up-regulate p53-p21/Cip1.[27] This process may inhibit cell proliferation and apoptosis. Several other studies have demonstrated silymarin's anticarcinogenic properties through modulation of mitogen-activated protein kinases and cyclo-oxygenase enzymes.[28,29] Traditionally it has been used as an antihepatotoxic agent and is available as a supplement. Baumann[30] recently published an informative commentary on silymarin's properties, including its potential anticarcinogenic, antioxidant, and anti-inflammatory effects.

The sodom apple plant (*Solanum sodomaeum*, also known as devil's apple) forms a large, branching, low shrub covered with spines. It produces a yellow fruit that contains glycoalkaloids that may cause gastroenteritis and even hallucinations and confusion when ingested. *Cancer Letters* published an article in 1987 showing efficacy in the treatment of basal cell carcinomas, squamous cell carcinomas, keratoacanthomas, and actinic keratoses.[31]

Capsicum peppers (*Capsicum frutescens*) contain capsaicin, a pungent phenolic chemical with well-known neurologic and dermatologic therapeutic effects. Along with several other closely related compounds, it is responsible for the spicy characteristics found in cayenne pepper, and red and green peppers. In addition to having active biologic effects on nerves (depleting substance P) and itch, and skin (powerful irritant), it has shown anticarcinogenic activity. Capsaicin inhibited hepatocellular carcinoma SK-Hep-1 cell growth in a concentration-dependent manner through the induction of apoptosis, down-regulation of the antiapoptotic Bcl-2, up-regulation of the proapoptotic Bax, and increased caspase-3 activity.[32] Capsiate, a derivative of capsaicin, targeted a variety of pathways involved in cancer development and inflammation, and also

induces apoptosis.[33] In contrast, A/J mice with chemical-induced lung tumors showed no benefit with systemic doses of capsaicin.[34]

Birch trees (*Betula*) produce bark that has been studied as an anticarcinogenic and antioxidant. White birch tree (*B platyphylla* var. *japonica*) extracts demonstrated protective effects against hydrogen peroxide in a hamster lung fibroblast cell line and induced apoptosis in a human promyelocytic leukemia cell line. (Similar to data shown with capsaicin, there was an increased expression of Bax and activation of caspase-3.) In the same group of experiments, the birch bark extract showed potent free radical scavenging activity, increased the activities of several cellular antioxidant enzymes, and lipid peroxidation inhibition.[35] In addition, betulinic acid, a triterpene found in the birch bark, has shown the ability to induce programmed cell death with melanoma and other neuroectodermal tumor cells through mitogen-activated protein kinase activation.[36]

Tea tree oil (*Melaleuca alternifolia*) comes from a specific tea tree native to Australia, an evergreen shrub that can grow to 6 m and has narrow, thin, hooked leaves. Its oil has gained popularity as a broad-spectrum antibacterial, antifungal, and antiseptic agent, and notoriety as an allergic contact allergen of growing importance. Recently Calcabrini et al[37] published a study showing that terpinen-4-ol, the most active component of tea tree oil, inhibits human melanoma cells in vitro through caspase-dependent apoptosis. It may also have anti-inflammatory and antioxidant properties, as another study demonstrated suppression of superoxide production by monocytes stimulated with lipopolysaccharide.[38] Crawford et al[39] recently published a thorough review of the cutaneous effects of this oil, including its current uses and side effects profile.

Galangal (*Alpinia officinarum*, *Languas galanga*) has traditionally been used for rheumatic disease in Southeast Asian medicine and as traditional medicine in China "due to its significant therapeutic properties for spleen and stomach."[3] It has been shown to inhibit proinflammatory mediators through an inhibition of mitogen-activated protein kinase, p44/42, and nuclear factor-kB.[40] More recently, Ito et al[41] demonstrated that 1'-acetoxychavicol acetate, present in the galangal seeds and rhizomes, dramatically inhibited cellular growth of human leukemic cells by inducing apoptosis through a mitochondrial- and fas-mediated dual mechanism.

Slippery elm (*Ulmus rubra*) is a large tree native to Canada and eastern and central United States. When the inner bark contacts water, it produces thick mucilage that was used by Native Americans to build canoes and shelters. This viscous substance has been used as a demulcent, applied topically to skin or mucous membranes, in throat lozenges, as a poultice, and to soothe the gastrointestinal tract. At least one major US university's Internet page details slippery elm, its medicinal uses, available forms, and directions for use in medicinal purposes.[42] A review of the literature and Internet sources revealed two recent studies demonstrating potential anticarcinogenic activity. Lee et al[43] demonstrated antitumor activity through inhibition of proliferation and induction of apoptosis of human breast cancer cells through several mechanisms. Wang et al[44] demonstrated in vitro antiproliferative activity of *Ulmus* extract on cervical, melanoma, breast cancer, and histiocytic lymphoma cell lines. These experiments showed a mechanism of action of oligonucleosomal fragmentation and activation of caspase-3, which led to decreased expression of anti-apoptotic Blc-2 and Bcl-$_{XL}$, with increased expression of proapoptotic Bax.

Antioxidant, keratolytic, and other mechanisms

Carbamide, or urea, is a well-known keratolytic and humectant. More than 30 years ago, *Lancet* published an article entitled Urea Treatment of Skin Malignancies.[45] The authors treated 112 patients with basal or squamous cell carcinomas with injections of urea solution followed by topical urea powder used as an abrasive on the traumatized surface of the tumors. They reported 58% total cure with an additional 27% with great improvement. The authors did not hypothesize on possible mechanisms. These data have not been replicated.

Currently carbamide is included in many escharotic agents. It is not clear whether there is an anticarcinogenic benefit other than increased absorption of other ingredients through keratolysis. Similarly, apricot (*Prunus armeniaca*) pits are included in several preparations. They cause exfoliation through the friction of their granular texture, enhancing absorption, and perhaps have a more direct effect. Of note, apricot kernel ingestion is a relatively common source of cyanide poisoning, with widely variable concentrations of amygdalin, which is then hydrolyzed to hydrogen cyanide. Laetrile, a semisynthetic derivative of the apricot-derived amygdalin, was used extensively and with much controversy in the 1970s and 1980s in the treatment of different cancers. Proponents hypothesized that laetrile would be metabolized by β-glucosidase, releasing toxic cyanide, and that this reaction would be selectively prevalent in tumor tissue.

The New England Journal of Medicine in 1980 published an important negative study, in which not only was there no therapeutic benefit from treatment with amygdalin, but several patients showed symptoms of cyanide toxicity.[46]

Sheep sorrel (*Rumex acetosella*), also known as sour grass because of its particular taste, is commonly found growing on lawns, in meadows and in fields. For hundreds of years, sheep sorrel has appeared in historic archives in both North America and Europe as a remedy for cancer. Ovid Medline and PubMed searches did not reveal any studies of its mechanism of action or benefit in treatment of cancer or skin disease.[47,48]

Chapparel (*Larrea divaricata*) is a wild shrub found in the Southwestern United States and Mexico and also has a long history of medicinal uses by Native Americans and in modern alternative medicine. It contains nordihydroguaiaretic acid, an antioxidant that was many years ago used as a food industry additive. Despite anecdotal reports of chaparral tea benefiting patients with cancer, in vivo tests failed to show any significant anticancer activity.[49] More recently, *Larrea* extract has been studied in rat mammarian carcinoma, demonstrating in vivo antitumoral activity[50] and in human breast cancer, colon cancer, and melanoma cell lines, showing variable inhibitory activity.[51] Given the contradictory clinical findings in the 1960s and 1970s, basic science research may continue to shed light on possible mechanisms and therapeutic avenues.

Burdock root (*Arctium lappa*) is a perennial or biennial herb with hard, fibrous, longitudinally wrinkled gray-black roots. The roots and leaves have been used in traditional medicine for cancer treatment and a wide variety of other ailments, in addition to being promoted as aphrodisiacs. *A lappa* improved hepatic outcome in rats fed liquid ethanol and injected with carbon tetrachloride, both histopathologically and using biochemical parameters.[52] In a separate, earlier study, it also showed significant free radical scavenging activity in rats similarly treated with carbon tetrachloride.[53] In addition, one study demonstrated paradoxical actions of *A lappa*, showing a protective effect in one carcinogenesis model while possessing weak co-carcinogenic influences in another model.[54]

Conclusion

McDaniel and Goldman[2] documented the multiple Internet sites dedicated to the use and sales of escharotic agents for treatment of a variety of cancers. It is apparent that many of the components of these agents have biologically active properties, with antioxidant, antimitotic, or other anticarcinogenic mechanisms of action. What is universally lacking, however, is legitimate human data beyond anecdotes. In addition, it is particularly troubling to read some of the disclaimers and discussions featured at many of these Internet sites. The following passages were found on different representative Internet pages while researching this topic:

> FDA (Food and Drug Administration) Required Disclaimer For Sites That Do Not Endorse Chemotherapy:
> This web site is for educational purposes only. It is not intended as a substitute for the diagnosis, treatment and advice of a qualified licensed professional. This site offers people medical information and tells them their alternative medical options, but in no way should anyone consider that I am "practicing medicine." I assume no responsibility for how this material is used. Also note that my web site frequently updates its contents, due to a variety of reasons. Therefore, some information may be out of date. My statements regarding alternative treatments for cancer have not been evaluated by the FDA.[55]

> Discussion of The Use of the Term "Cure":
>
> The FDA does not like people to use terms like: "cure cancer" or "cancer cure" or "cure for cancer," etc. The reason is obvious, orthodox medicine rarely cures cancer, but alternative treatments usually do cure cancer. Thus, it is necessary for me to say that if you define "cure" to mean that the cancer can never come back, even if the person lives on aspartame and trans fatty acids, then obviously nothing "cures" cancer. However, if your definition of "cure" means that you have killed virtually all of the cancer cells, and built up the immunity system so that it can fight future cancer cells as they develop, then alternative medicine can "cure" cancer. The latter definition of "cure" is the one I use on my website.[55]

In between these two paragraphs, the Internet site features a commentary on the "unbelievable damage done by orthodox medicine" and the opinion that "it is totally insane that scores of millions of dollars a year are given to the 'cancer charities,' which are nothing but puppets, deception partners, and public relations arms of the pharmaceutical companies and medical mafia, while at the same time the many people who really want to cure cancer have to do it in their spare time and use their own money."[55]

Other statements "guarantee 100% success in the removal of dermal or epidermal malignant lesions, including basal cell, squamous cell epitheliomas, and even melanomas—regardless of type or size."[56]

Statements such as these may influence those who search the Internet in hope of a cure, leading to cases such as ours. Such is, it seems, the pattern of alternative medicine as preached and advertised on

the Internet. Testimonials, unsubstantiated claims of cures, and claims regarding failures of orthodox, evidence-based, Western medicine abound. What is clear, however, is that as a whole the unregulated botanical preparations have an unreliable content of active ingredient,[57,58] despite their claims.

In response to Internet marketers' claims of cure and that their products are safe and effective, the US Federal Trade Commission (FTC), the FDA, and Health Canada (the Canadian federal health department) united to create Operation Cure. All—a law enforcement and consumer education campaign.[59] The operation has pursued actions against several companies that fraudulently marketed health products on the Internet. These actions have resulted in settlements including fines, removal of unsubstantiated claims, and warnings about potential dangers of the product.[60] The FTC's Operation Cure. All Internet page includes a link to an Internet form to file a complaint, in addition to a link to an access page in Spanish.[57] The FDA has independently issued several warning letters to Internet marketers of escharotic agents.[61]

There is a long and tumultuous history of the use of botanicals for the treatment of cancer, and in general medicine. The May 2004 edition of *Dermatology Times* reviewed the early history of escharotic agents, originally popularized by Perry Nichols as a treatment for skin cancer.[62] Later, Harry Hoxsey advocated for and performed treatment with escharotic agents for various skin cancers.[63] With significant surrounding controversy, the FDA reprimanded him. Both Nichols and Hoxsey operated through clinics (termed sanatoriums,) treating cutaneous malignancies with escharotic agents (without pathologic or surgical confirmation) and internal malignancies with oral botanical mixtures. Both refused to disclose the ingredients in their preparations. It was later learned that the topical escharotics contained zinc chloride, bloodroot, and other botanicals. Through all of the turmoil, it remains clear that there is at some level a legitimate role for botanicals in medical therapy; digitalis, vinca alkaloids, and even acetic acid have clear, well-defined roles in conventional medicine. In the case of the escharotic agents, however, one is faced the use of unproven, uncontrolled, caustic substances that have biologic activity. Their use may result in lack of efficacy and serious consequences.

We have seen the patient from the case in follow-up on several occasions and examined the scars on his trunk from previous treatments with this particular escharotic agent for presumed superficial basal cell carcinomas. The scars are large, some hypertrophic, and cosmetically displeasing. In several cases, however, there is no evidence of tumor recurrence. It is likely that this escharotic agent (and presumably others like it) do have some degree of efficacy, even if the outcome is suboptimal and the mechanism poorly understood. Our experience suggests that the deeper, infiltrative, or sclerosing tumors may not be treated as reliably with the escharotic agent, resulting in tumor recurrence within a scar. The case illustrated two aggressive and unusual features of basal cell carcinoma, perineural spread and tracking along a fascial plane (galea), which in turn led to large defects and complicated closures. In both cases, there was a significant disparity between the clinical preoperative size of the lesion and the final defect size. It is not clear whether the escharotic agent changed the behavior of the cancer, killing some tumor cells while selecting for others with more aggressive behavior. Although it could be argued that the patient simply did not apply the esharotic agent sufficiently to eliminate the entire tumor, there is no evidence to support more curative dosing. Furthermore, the patient applied the medication according to the product's recommendations, with resultant recurrence. Regardless of the mechanism, this experience suggests that the use of escharotic agents may not only delay curative treatment but mask occult tumor recurrence, leading to more invasive definitive treatment with a higher likelihood of complications.

Escharotic agents used to treat skin cancer are advertised and sold through the Internet and most contain botanical substances that have biologic activity on human cells. These effects may be organized into true escharotic activity, anticarcinogenic activity, antioxidant activity, and keratolytic activity, although many agents show several mechanisms of action. The fact that there is research evaluating the mechanisms of action is encouraging. The lack of substantial, evidence-based, nonanecdotal data in the face of growing use for cutaneous malignancies, however, is troubling. We hope this report informs others of this product and its potential effects, and the exploding world of alternative "cancer cures" featured on the Internet.

(During revision of this manuscript, www.canxproducts.com, the Web site selling this particular escharotic agent, was taken offline. This action appears to be in response to a published letter from the FDA to the marketers of this escharotic agent, published online at http://fda.gov/foi/warning_letters/g5120d.htm. The letter explicitly defines this escharotic agent as a drug and not a supplement and, hence, subject to FDA regulations. It also asserts that the makers of this product fail to provide adequate directions for use. It details the deficiencies of the

product and the Web site to comply with federal laws and regulations. The letter finishes by communicating that the manufacturers "should take prompt action to correct the listed violations. Failure to do so may result in regulatory action without further notice. Possible actions include seizure, injunction, and/or prosecution.")[64]

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