

A Multi-Component Topical Botanical For Wound Healing

Both within and outside of China, in animal models and in humans, investigators have used various combinations of topically applied herbal constituents for the treatment of disease, including skin complaints.

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A botanical-based ointment has been formulated, comprised of *Camellia oleifera* (Camellia oil), the dried bark of *Paeonia suffruticosa* (Tree peony bark), the root of *Coptis chinensis* Franch (Coptis), the dried root of *Rheum palmatum* (Rhubarb root), the red resin of the fruit of *Daemonorops draco* (“Dragon’s blood”—a non-specific designation), the dried root of *Lithospermum erythrorhizon* (*Lithospermum* root, Gromwell), the dried bulbs of *Fritillaria cirrhosa* (Lily bulb), the dried tubers of *Corydalis turtschaninovii* (*Corydalis*), the dried resin of *Dryobalanops aromatica* (Borneol), the dried powder of *Os draconis fossilia* (Fossilized bone) and the dried powder of *Endothelium corneum gigeriae galli* (Chicken gizzard lining).

These constituents of Winvivo (Puji) ointment have an ancient lineage in Chinese medicine. “The Divine Farmer’s *Materia Medica*” (25-220 AD) reported the dried root of *Lithospermum erythrorhizon* for medical use in. The dried bulbs of *Fritillaria cirrhosa* were referenced in the same work. The medicinal use of the red resin of the fruit of *Daemonorops draco* was recorded in “Grandfather Lei’s Discussion of Herb Preparation” (Lei Xiao, 470 AD). The dried resin of *Dryobalanops aromatica* appeared in the “Newly Revised *Materia Medica* (Su Jing, 657-659 AD). The dried tubers of *Corydalis turtschaninovii* were mentioned by Chen Cang-Qi in “Omissions from the Classic of the *Materia Medica*” (741 AD).

Both within and outside of China, in animal models and in humans, investigators have used various combinations of topically applied herbal constituents for the treatment of tibial fractures,¹ diabetic foot ulcers,² UV-induced hyperpigmentation,³ atopic dermatitis,⁴ and burn wounds.⁵ In like manner, the use of Winvivo ointment has recently been assessed with positive outcomes for wound healing in a series of American patients.⁶ The favorable properties of the constituents of the proprietary botanical ointment prompted testing the ointment in animals for safety and efficacy prior to testing more widely the effects of this non-prescription herbal preparation on the wounds of patient volunteers.

The animal work was contracted to Life Source Biomedical, an animal research laboratory housed at Moffitt Field, Sunnyvale, CA. In brief, rats were treated topically with the proprietary botanical ointment primarily to assess its systemic safety (both via percutaneous absorption and via licking behavior) but also to identify any irritant contact dermatitis. Guinea pigs were treated topically with the proprietary botanical ointment for systemic safety as well as for identification of any irritant and/or allergic contact dermatitis. Farm pigs were anesthetized and given standardized full thickness surgical skin wounds that were treated with the proprietary botanical ointment versus Polysporin ointment at some wound sites and Vaseline at other wound sites as controls. No irritant or allergic

contact dermatitis occurred. Moreover, the proprietary botanical ointment caused no identifiable adverse effect or toxicity either locally or systemically in any of these animal models. Finally, Winvivo ointment-treated wounds formed granulation tissue and re-epithelialized faster than did Polysporin- and Vaseline-treated wounds of identical area and depth. (Data on file.) These favorable outcomes encouraged the use of the proprietary botanical ointment on wounds of patient volunteers. The cases that follow document favorable clinical responses to Winvivo ointment in such patients having various kinds of wounds.

CASE 1: A 76-YEAR-OLD MAN WITH ULCERATED CROANGIODERMATITIS

The patient developed muted red edematous papules and nodules as well as pitting edema limited to the legs while on chemotherapy for diffuse large B-cell non-Hodgkins lymphoma, centroblastic variant. The chemotherapy consisted of rituximab, doxorubicin, vincristine, cyclophosphamide, prednisone, and dexrazoxane. The lymphoma regressed, but the eruption persisted. A trephine biopsy revealed proliferation of capillaries, diapedesis of red blood cells, edema, hemosiderin deposition, and fibrosis. Clinical and pathologic correlation established a diagnosis of acroangiokeratosis (pseudo-Kaposi's sarcoma). Ongoing systemic medicines consisted of Coreg, Avandia, Edecrin, Diltiazem, and Coumadin. He also used Combivent and Albuterol inhalers. The acroangiokeratosis gradually improved over the ensuing five years with graduated compression stockings at 20-30mm Hg from toes to knees and triamcinolone acetonide ointment 0.025% qhs to the affected skin.

The patient fell and hit the anterior aspect of the left leg. The injured skin sloughed, leaving a 39 x 30mm ulcer at the trauma site. The proprietary botanical ointment BID to the ulcer was started and compression stockings were continued. One week later, the ulcer measured 35 x 27mm; at two weeks, 30 x 23mm; at three weeks, 25 x 21mm; at four weeks, 21 x 17mm. The patient was then lost to follow-up.

CASE 2: AN 84-YEAR-OLD WOMAN WITH A WOUND FROM TRAUMA TO ELASTOTIC SKIN

The patient, maintained on Toprol XL, Lasix, Hydrochlorothiazide/Triamterene, KCl, warfarin, and Oscal with vitamin D, presented with a non-healing wound on the posterior aspect of the left forearm. About seven weeks prior to being seen, she had torn her markedly fragile, sun-damaged skin while removing a bandaid. The wound was initially treated with Polysporin ointment without apparent improvement. After four weeks of such treatment, the wound, measuring 40 x 27mm, was complicated by itching, redness, and inflammatory papules, representing allergic contact dermatitis to Polysporin ointment. The Polysporin ointment was stopped



Fig. 1. A 60-year-old man with a 5.3 x 4.4cm wound on the forearm due to curettage and electrodesiccation. Appearance of Winvivo ointment is shown on upper half of wound.

Fig. 2. Granulation and re-epithelialization of the healed wound within 15 days.

and replaced by the proprietary botanical ointment applied daily. Seven days later, the wound measured 25 x 19mm and the dermatitis had disappeared; by Day 16 of treatment, the wound measured 17 x 6mm; by Day 23, the wound had completely healed.

CASE 3: A 60-YEAR-OLD MAN WITH A WOUND FROM CURETTAGE AND ELECTRODESICCATION

The patient presented with a patch on the lateral aspect of the right forearm that had been followed without intervention for 15 years. Five years prior to the current presentation, the lesion had been described as red to deep purple with scabbing and a clearing center. No diagnostic impression was given in the record. At presentation, the lesion displayed irregular areas of redness and pinkness, apparent scarring, small crusts, and poor circumscription, measuring approximately 53 x 40mm. Shave biopsy revealed a superficial basal cell carcinoma. Curettage and electrodesiccation were done, leaving a 53 x 44mm defect (Fig. 1). The proprietary botanical ointment, applied daily, was started. The wound healed completely after 15 days of treatment (Fig. 2).

CASE 4: A 68-YEAR-OLD MAN WITH A WOUND FROM CURETTAGE AND ELECTRODESICCATION

The patient had a history of mild hyperglycemia, hyperuricemia, hypertension, stented coronary artery disease, renal calcium stones, hypercholesterolemia, mild congestive heart failure, and mild sleep apnea. He presented with a 21 x 15mm rough red patch on the left side of the back and concurrently with a 24 x 23mm rough red patch on the right side of the back. Biopsies were not definitive but had features suggesting incipient squamous cell carcinomas in situ. It was elected to treat both patches with curettage and electrodesiccation, leaving a 23 x 19mm defect on the left side of the back and



Fig. 3. A 57-year-old woman with deep fissures on the thumbs in association with psoriasis. **Fig. 4.** The Winvivo ointment-treated fissures on one thumb and the clobetasol propionate ointment-treated fissures on the other thumb healed equally in 5 days.

a 23 x 22mm defect on the right side of the back with both defects extending to the upper reticular dermis based upon bleeding patterns. One of the wounds was treated with the proprietary botanical ointment BID and the other was treated with Polysporin ointment BID. Neither patient nor physician knew which wound received which topical agent because the patient's wife, a nurse, applied the agents in a blinded manner. The course of healing was complicated by a generalized morbilliform eruption deemed secondary to azithromycin that had been started for bronchitis 13 days after the surgery. Until the diagnosis of drug eruption was made, the topical agents were not applied—a lapse of five days. For the eruption, the patient took prednisone, tapering from an 80mg daily dose to zero over a period of 25 days. Despite the delay of wound healing due to the course of prednisone, the wound that was treated with the proprietary botanical ointment healed two weeks before the wound that was treated with Polysporin ointment.

CASE 5: A 64-YEAR-OLD MAN WITH ATOPIC DERMATITIS AND DEEP DIGITAL FISSURES

The patient presented with confluent red oozing and crusted skin markedly involving the right popliteal fossa and mildly involving the left popliteal fossa as well as nummular eczematous patches on the neck. Culture of the oozing skin produced a heavy growth of Group B beta-hemolytic streptococci. Complete blood count was normal other than an absolute eosinophil count of 682 (normal 15-500) cells/mL. IgE of 127 (normal <114) kU/L and Eosinophil Cationic Protein of 15 (normal 2-10) mg/L. The clinical findings coupled with the laboratory findings combined with a history of seasonal allergic rhinitis indicated a diagnosis of atopic dermatitis. The patient was initially placed on a tapering dose of prednisone, starting at 1mg/kg/day as well of desoximetasone ointment. Due to a history of penicillin allergy, patient was placed on Ciprofloxacin

500mg P.O. BID. When examined a month later, the sites previously involved had greatly improved but patient had developed deep fissuring of the thumb, index, and middle fingers of the left hand. He used a Chinese cream of unknown composition for the ensuing two weeks without improvement of the fissures. The prior Chinese cream was stopped in favor of the proprietary botanical ointment, which he applied BID. The fissures healed by the end of three weeks.

CASE 6: A 57-YEAR-OLD WOMAN WITH PSORIASIS AND DEEP DIGITAL FISSURES

The patient had been troubled with psoriasis, markedly involving the hands but mildly on the feet, for more than 30 years. The psoriasis had also been expressed as red scaly patches on the face and as plaques on the back and thighs. The fissuring on the hands was painful and disabling. Prior applications of mometasone furoate cream followed by triamcinolone ointment 0.1% were not helpful. She reported a history of asthma and emphysema as well as hypertension. Systemic treatment was limited to benazepril HCl and hydrochlorothiazide. The patient requested systemic treatment. A PPD was negative. Complete blood count, liver and renal function tests, and standard chemistry panel were all normal. A A1298C mutation of methylene tetrahydrofolate reductase rendered use of methotrexate an unattractive option. Adalimumab was started as well as hydrocortisone valerate ointment to the facial psoriasis and clobetasol propionic ointment limited to fissures on the hands. By week 12 of adalimumab, psoriasis on the trunk and thighs had responded nicely, but the fissures on the hands persisted. Adalimumab was discontinued in favor of ustekinumab, which was started four weeks later. The psoriasis on the trunk and thighs remained well controlled, but new deep and painful fissures appeared on the ends of the thumbs (Fig. 3). The proprietary botanical ointment BID was started to the fissures on one thumb and clobetasol propionate ointment BID to the fissures on the other thumb. Within five days, the fissures on both thumbs had healed (Fig. 4).

CASE 7: AN 83-YEAR-OLD MAN WITH A DERMABRASION WOUND

The patient had a 4 x 3.5mm shiny papule on the right nasal sidewall toward the nasal tip. The papule was biopsied. Pathology examination showed a nodular basal cell carcinoma into mid-reticular dermis. Above but neighboring the first lesion was a subtle 6 x 6mm plaque, biopsy of which revealed a second nodular basal cell carcinoma. The carcinomas were removed by Mohs micrographic surgery. The defect size of the distal wound measured 14 x 9mm and the defect above it measured 13 x 10mm. The combined defects were repaired using a melial transposition flap. In order to blend the edges of the healed flap with the

surrounding skin, dermabrasion was done. The dermabrasion produced a wound that extended to the base of the papillary dermis, as determined by the bleeding pattern (Fig. 5). The proprietary botanical ointment BID was started. Seven days later, the wound had healed completely (Fig. 6).

CASE 8: A 72-YEAR-OLD MAN WITH A DERMABRASION WOUND

The patient presented with a 7 x 7mm irregularly rolled lucent centrally delled tumor on the left malar ridge. A trephine biopsy revealed a nodular basal cell carcinoma extending into the deep reticular dermis. Five weeks later, the carcinoma was excised. The wound was closed, using a lateral to medial rotation flap and Z plasty. After a delay of almost eight months, the patient elected to improve the appearance of the scar by dermabrasion. Because the scar had healed with an almost canyon-like depression, the dermabrasion was taken to the level of the mid reticular dermis, determined visually by the focal depth of the wound and by bleeding pattern. Treatment of the large and deep wound was started with the proprietary botanical ointment BID. The wound was completely healed 10 days later.

CASE 9: A 56-YEAR-OLD MAN WITH WOUNDS FROM SHAVE REMOVALS

The patient, in excellent general health, presented with four small, banal pigmented nevi on the back and requested their removals. The four nevi were uniformly removed through the upper reticular dermis, using a Bard-Parker #15 blade. Wound measurements were as follows: wound 1: 9 x 7mm; wound 2: 7 x 6mm; wound 3: 10 x 8mm; wound 4: 9 x 8mm (Figs. 7-10). The patient's wife applied Polysporin ointment daily to two of the wounds and the proprietary botanical ointment daily to the other two wounds. Patient and physician were blinded as to which wounds received which preparation. The wounds treated with the proprietary botanical ointment showed earlier granulation and more rapid re-epithelialization than those treated with Polysporin ointment, and by the end of three weeks, the wounds treated with Polysporin ointment had not yet healed (Fig. 8), whereas those treated with the proprietary botanical ointment had completely healed (Fig. 10).

DISCUSSION

The cases provide evidence that Winvivo ointment enables or enhances wound healing. Case 1 describes healing of a large and deep ulcer from traumatized acroangiodermatitis. Proliferation of capillaries, diapedesis of red blood cells, edema, hemosiderin deposition, and fibrosis on biopsy suggested a component of stasis. Stasis-associated, lower extremity ulcers are notorious for chronicity, yet the combination of compression and the proprietary botanical ointment was accompa-



Fig. 5. An 83-year-old man with a dermabrasion wound on the nose. Fig. 6. The wound was treated with Winvivo ointment and healed in 7 days.

nied by steady, rapid healing during the time that patient was under observation. Case 2 describes rapid healing of a traumatic wound complicated by allergic contact dermatitis. Using only the proprietary botanical ointment, the wound and the dermatitis healed. Cases 3 and 4 show the proprietary botanical ointment induced rapid healing of large wounds resulting from curettage and electrodesiccation. Case 4 demonstrates improved healing using the proprietary botanical ointment irrespective of the poor health of that patient. Case 5 illustrates healing of fissures using the proprietary botanical ointment in the setting of a defective skin barrier well known to be a defining characteristic of atopic dermatitis. Another Chinese balm of unknown composition was not helpful. Case 6 describes healing of deep digital fissures in a patient with psoriasis. Ustekinumab might have allowed healing of the fissures without the use of any topicals, but it is more likely that the proprietary botanical ointment and Clobetasol propionate ointment contributed separately and equally to the healing, noting that the proprietary botanical ointment lacks the potential complications of an ultrapotent corticosteroid. It is emphasized that the proprietary botanical ointment did not contribute to the healing of fissures as though the ointment were healing psoriasis. It does not have this capacity, noting that the ointment had no impact on psoriasis in other patient volunteers. Rather, the proprietary botanical ointment appeared to contribute to the healing of fissures as wounds.

Cases 7 and 8 describe rapid healing of dermabrasion wounds using the proprietary botanical ointment. Based upon historical time frames for healing of dermabrasion wounds, the proprietary botanical ointment is estimated to have quickened healing by approximately 30 percent. Case 9 demonstrates, in a doubly blinded manner, early granulation tissue, enhanced re-epithelialization, and early healing in wounds treated with the proprietary botanical ointment as compared with those treated with Polysporin ointment.



Figs. 7-10. A 56-year-old man with four wounds on the back from shave removals of pigmented nevi.

Cutaneous wound healing is a complex process which nonetheless may be viewed as involving three phases, specifically: the inflammatory phase, the proliferative phase, and the remodeling phase.⁷ The inflammatory phase requires the secretion of growth factors, inflammatory mediators and signaling pathways that enable collagen deposition, angiogenesis, and wound contraction.^{8,9} The proliferative phase includes fibroblastogenesis/collagen deposition, angiogenesis/granulation, and re-epithelialization, and its suppression of these phases impairs wound healing.¹⁰

The mechanisms by which the proprietary ointment improves wound healing is conjectural, but some modes of action have been identified for constituents of the balm. The Camellia oil vehicle of the proprietary ointment contains >80 percent oleic acid, and although oleic acid itself does not appear to speed wound healing,¹¹ it is known to enhance penetration of pharmacologic agents into the skin.¹² Other components of Camellia oil include the antioxidants sesamin, sasanquasaponin, and flavonoids, which may reduce reactive oxygen species and inhibit lipid peroxidation. Paeonol, one of the chief components of the dried bark of *Paeonia suffruticosa*, induces vasodilatation in part by nitric oxide generation and in part by inhibiting vasoconstrictors including angiotensin II, vasopressin, and endothelin-1.¹³ Vasodilatation improves oxygenation, which promotes myofibroblast differentiation and wound contraction, speeding wound closure.¹⁴

The proliferative phase of wound healing requires both fibroblastic and keratinocytic cell migration along with production of ground substance and collagen from the former cells as well as keratin and lipids for barrier formation from the latter cells. Lithospermum induces both

migration of dermal fibroblasts and of cultured human keratinocytes following creation of scratch wounds. Further lithospermum increases synthesis of phospholipids, sphingolipids, and neutral lipids in keratinocytes,¹⁵ noting that among the sphingolipids, ceramides are a major and essential component of the skin barrier.

None of the patients complained of painful wounds. This effect may be due to the paste-like vehicle in which the Winvivo components are incorporated. It may also be due to verticinone, a component of *Fritillaria*. Verticinone, an isosteroidal alkaloid, reduces inflammatory pain and it also reduces Paclitaxel-induced neuropathic pain in mouse and rat models.¹⁶ None of the wounds became infected. This benefit may be the result of the antimicrobial activities of *Coptis* root,¹⁷ *Rhubarb* root,¹⁸ *Lithospermum* root,¹⁸ and *Daemonorops draco* resin.¹⁹

The above cases demonstrate the benefit as well as some of the mechanisms of action of the herbal constituents of Winvivo ointment in wound healing. In addition to its beneficial effects in wound healing, preliminary observations indicate potential benefit of the proprietary botanical ointment in the treatment of atopic dermatitis and irritant contact dermatitis. Still other applications are yet to be explored based upon the pharmacologic actions of these herbs. ■

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