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TECHNICAL REPORT

PracaSil®-Plus

In Vitro Evaluation of the Safety Profile of PracaSil®-Plus on Human Melanoma Tissue

Abstract: Melanoma is a cancerous skin condition that often leads to surgical removal of the affected tissue, which results in skin scarring. Scars may not only be aesthetically unpleasant but may also have physical consequences such as pain and psychosocial consequences (e.g., anxiety, distress). PracaSil-Plus is a proprietary anhydrous silicone topical base used for incorporation of different APIs indicated in skin regeneration and healing. The purpose of this study was to evaluate the safety profile of PracaSil-Plus on the progression of melanoma, using the MLNM-FT-A375 human melanoma tissue model. Results have demonstrated that PracaSil-Plus did not contribute to the progression of melanoma cells when compared to untreated tissues. Therefore, PracaSil-Plus may be regarded as a safe compounding base to be used by pharmacists in scar management therapy.

Introduction:

Melanoma is a cancerous condition that arises from unregulated growth of melanocytes (pigmented cells), resulting in tumor production on the skin (most common) and mucous membranes [1]. The unregulated growth of melanocytes can be divided into two phases: radial growth phase (RGP), represented by slow proliferation of cells in the epidermis; and vertical growth phase (VGP), a more advanced phase with presence of nodules [2]. Depending on the growth phase of the melanocytes and the aggressiveness of the tumor, melanoma may be classified into one of 5 stages: stage 0 is the least severe while stage 4 is the most severe. With the exception of stage 4, treatment of melanoma involves initial surgical removal of the tumor, which results in skin scarring, the imperfect but normal end point of tissue repair [1]. Unfortunately, scars cannot yet be made to disappear, and may range from a desirable fine line to a variety of abnormal scars, including hypertrophic and keloid scars. Skin scarring is often considered trivial but may also be aesthetically unpleasant and disfiguring, causing distress, anxiety and other psychosocial consequences. Scars may also have physical consequences as tenderness, itching and pain, which is functionally disabling and contributes to diminished quality of life [3-5].

Taking into account that clinical treatments do not entirely eliminate skin scarring, the therapeutic goal is to reduce, as much as possible, the severity of scars. However, not only are scars different but there is also considerable qualitative and quantitative variability in skin scarring between individuals. Consequently, clinical treatments should envisage a personalized approach and be adapted to both the scar and patient specificities [3, 6, 7]. For this reason, plastic surgery and various medication for scar treatment are commonly used to help restore the appearance of the tissue [8]. PracaSil-Plus is a proprietary anhydrous silicone base developed to be applied topically in scar and wound management therapy as a base for incorporation of different active pharmaceutical ingredients (APIs) indicated in skin regeneration and healing.

Therefore, the purpose of this study was to evaluate the safety profile of PracaSil-Plus on the progression of melanoma, using the MLNM-FT-A375 human melanoma tissue model.

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Methodology:

The safety profile of PracaSil-Plus was evaluated *in vitro* using the MLNM-FT-A375 human melanoma tissue model (MatTek Corporation), which comprises of human malignant melanoma cells
(A375), cultured and differentiated to form a multilayered skin model. This model was designed to resemble the progression of melanoma *in vivo* as melanoma cells are found in the tissue at various stages of development [9]. In this study, melanoma tissues were cultured for 7 days prior to sample application. Following tissue preparation, 50 µL of PracaSil-Plus (50 mg/50 µL) were applied topically to a set of melanoma tissues (n=2), every other day, for a period of 14 days. At the same time, another set of tissues (n=2) were left untreated and monitored throughout the study period to serve as negative control. Prior to each re-application with PracaSil-Plus, the surface of the tissues were cleaned with a sterile cotton tip. At days 0, 3, 5, 7, 9, 11, and 14 post-application, tissue cross-sections were obtained and stained using Hematoxylin and Eosin (H&E). Images of tissue cross-sections were captured and analyzed at 10x, 40x, and 100x optical magnifications using an Olympus VS120® slide scanner [10].

Results and Discussion:

In order to assess the effect of PracaSil-Plus on the progression of melanoma, a total of 38 H&E stained tissue slides were analyzed for presence of VGP-like nodes, as well as changes in the size of the nodes and invasion of the melanoma cells into the dermal layer. On day 3 post-application, VGP-like nodes were shown in both non-treated tissues and tissues treated with PracaSil-Plus (Figure 1). Similarly, initial invasion by melanoma cells occurred on day 5 post-treatment while VGP-like nodes increased in size on day 7 for tissues in both groups. By day 9, deeper invasion of melanoma cells in the dermal compartment occurred for non-treated tissues as well as for tissues treated with PracaSil-Plus (images available upon request). Images collected on day 14 post-application revealed deeper invasion into the dermis for both tissue samples, treated and non-treated (Figure 2).

As a result, no difference was noted in melanoma cells progression between non-treated tissues and tissues treated with PracaSil-Plus. The presence of VGP-like nodes, as well as increases in nodes size and dermal invasion of melanoma cells, all appear to be synchronized when comparing PracaSil-Plus-treated and non-treated tissues. These results demonstrate that PracaSil-Plus does not contribute to the progression of melanoma and, therefore, it may be used as a topical compounding base following the surgical removal of skin tumors.

In Vitro Evaluation of the Safety Profile of PracaSil®-Plus on Human Melanoma Tissue

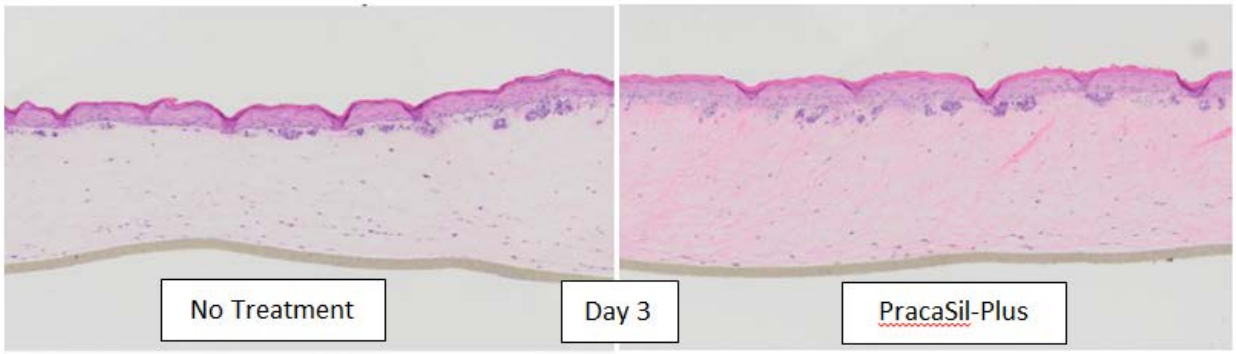

Figure 1. *Melanoma tissue model 3 days post-applicationt (40x magnification).*

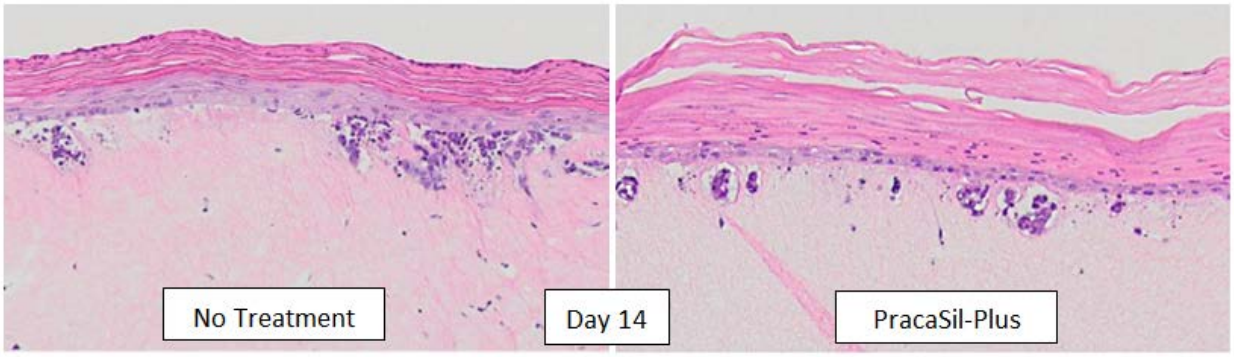

Figure 2. *Melanoma tissue model 14 days post-application (100x magnification).*

Conclusions:

Melanoma is a cancerous skin condition that often leads to surgical removal of the affected tissue, which results in skin scarring. Scar patients are likely to seek clinical treatment, particularly for abnormal scars, as skin scarring is often associated with substantial emotional and financial costs [3-5]. Compounding pharmacists may then have a critical impact in scar and wound management therapy by dispensing personalized topical formulations.

The *in vitro* evaluation of the safety profile of PracaSil-Plus has demonstrated that this topical base did not contribute to the progression of melanoma cells within the human tissue model. Topical application of PracaSil-Plus can thereby be considered safe as there were no significant differences between the progression of melanoma in tissues treated with PracaSil-Plus versus the untreated tissues.

The favorable safety profile demonstrated by PracaSil-Plus is promising data to suggest that this topical base may be safely used by compounding pharmacists for the incorporation of different APIs indicated in scar management therapy.

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JOURNAL ARTICLE

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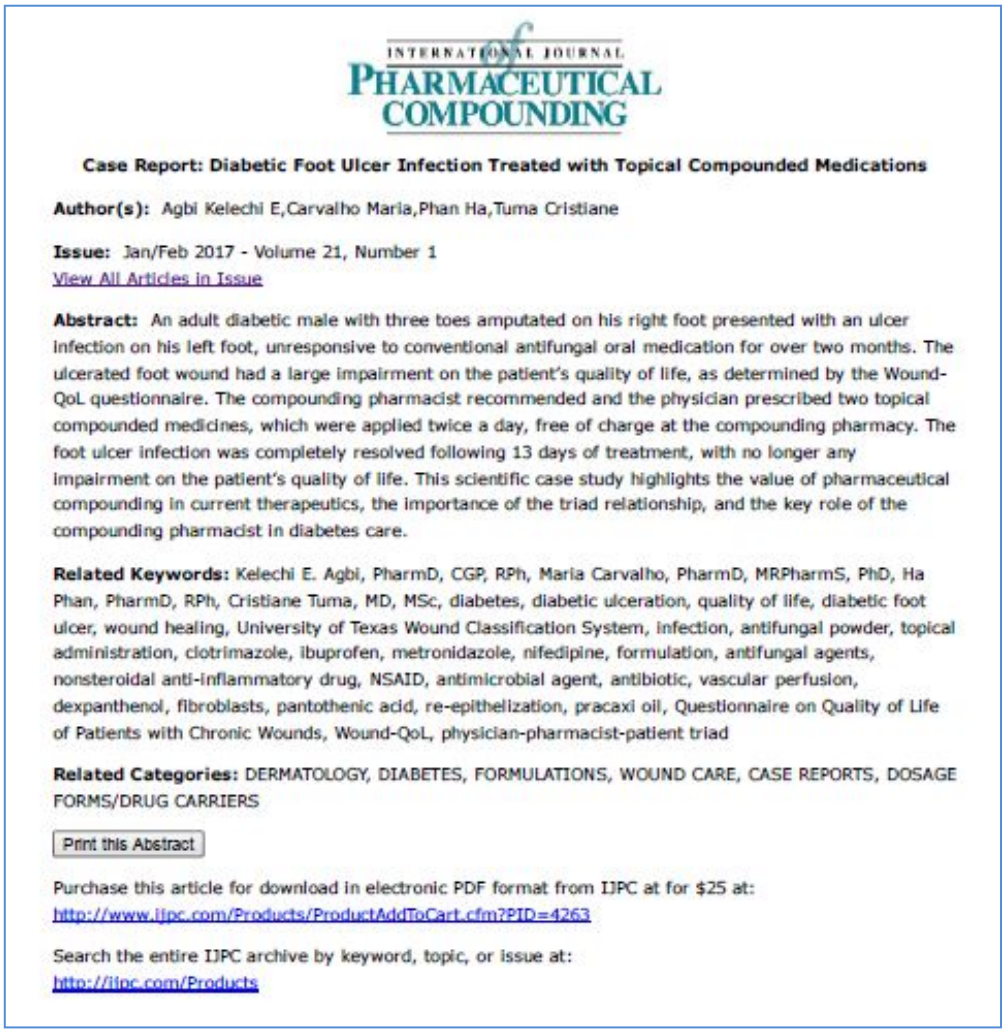
Case Report: Diabetic Foot Ulcer Infection Treated with Topical Compounded Medications

Agbi, K.E., Carvalho, M., Phan, H. and Tuma, C. (2017) 'Case Report: Diabetic Foot Ulcer Infection Treated With Topical Compounded Medications', *International Journal of Pharmaceutical Compounding*, 21 (1), p. 22-27.



INTERNATIONAL JOURNAL of PHARMACEUTICAL COMPOUNDING

Case Report: Diabetic Foot Ulcer Infection Treated with Topical Compounded Medications

Author(s): Agbi Kelechi E,Carvalho Maria,Phan Ha,Tuma Cristiane

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Abstract: An adult diabetic male with three toes amputated on his right foot presented with an ulcer infection on his left foot, unresponsive to conventional antifungal oral medication for over two months. The ulcerated foot wound had a large impairment on the patient's quality of life, as determined by the Wound-QoL questionnaire. The compounding pharmacist recommended and the physician prescribed two topical compounded medicines, which were applied twice a day, free of charge at the compounding pharmacy. The foot ulcer infection was completely resolved following 13 days of treatment, with no longer any impairment on the patient's quality of life. This scientific case study highlights the value of pharmaceutical compounding in current therapeutics, the importance of the triad relationship, and the key role of the compounding pharmacist in diabetes care.

Related Keywords: Kelechi E. Agbi, PharmD, CGP, RPh, Maria Carvalho, PharmD, MRPharmS, PhD, Ha Phan, PharmD, RPh, Cristiane Tuma, MD, MSc, diabetes, diabetic ulceration, quality of life, diabetic foot ulcer, wound healing, University of Texas Wound Classification System, infection, antifungal powder, topical administration, clotrimazole, ibuprofen, metronidazole, nifedipine, formulation, antifungal agents, nonsteroidal anti-inflammatory drug, NSAID, antimicrobial agent, antibiotic, vascular perfusion, dexpanthenol, fibroblasts, pantothenic acid, re-epithelization, pracaxi oil, Questionnaire on Quality of Life of Patients with Chronic Wounds, Wound-QoL, physician-pharmacist-patient triad

Related Categories: DERMATOLOGY, DIABETES, FORMULATIONS, WOUND CARE, CASE REPORTS, DOSAGE FORMS/DRUG CARRIERS

Second-degree Skin Burn Injury Following a Domestic Incident

SUMMARY: Burns caused by heat in domestic kitchens have a high incidence worldwide and commonly result in open wounds and skin scarring. This case study demonstrates the successful treatment of a second-degree skin burn with PCCA formulas 12781 (naltrexone 0.5% and aloe vera 0.2% in Spira-Wash) and 12830 (pentoxyfilline 1% in PracaSil-Plus). According to the patient's self-assessment, the 4 primary treatment domains (global satisfaction, effectiveness, convenience and side effects) were all rated over 80 /100. It is suggested that these formulas may be recommended as a viable personalized treatment option in skin burns.

Submitted by: D.H. John Kim, PharmD, FAARFM, President at Robinson Drug Compounding Center, Mendham, NJ

Introduction:

A burn is an injury to the skin or other organic tissues primarily caused by heat (thermal burns). Although preventable, burns are a global public health issue accounting for an estimated 180,000 deaths annually[1]. In 2016, there were 486,000 burn injuries in the USA requiring medical treatment[2]. The majority of the incidents occur in the home and workplace; children and women are usually burned in domestic kitchens[1]. Burns are classified as first-degree (superficial), second-degree (partial thickness), or third-degree (full thickness), depending on how deep and severely they penetrate the surface of the skin[3]. Post-inflammatory hyperpigmentation of the skin (melanosis) may occur following a thermal burn (Figure 1).

The purpose of this case study is to discuss the management of a second-degree skin burn injury following a domestic incident with a combination of topical compounded medications.

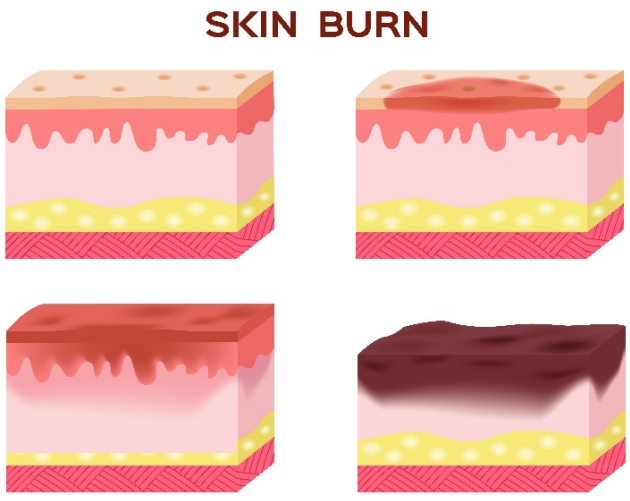

Figure 1. *Schematic representation of the skin burn stages (adapted from Gritsalak Karalak/Shutterstock.com).*

Case Report:

An adult male was severely burned on the right forearm and hand while opening a container with hot soup under pressure. The patient was admitted to the emergency room for immediate assistance and applied Silvadene® Cream 1% with dry burn dressing for 3 days to absorb all the fluids produced by the burn. Figures 2a and 2b show the patient's second-degree burn 12 hours following the domestic incident. Then for a period of one week the patient applied PCCA formula 12781 (Table 1), which includes naltrexone 0.5% and aloe vera 0.2% in PCCA Spira-Wash Gel. Natrexone, an opioid receptor antagonist, is known to accelerate fibroblast proliferation and wound healing[4]. Aloe vera, derived from the tropical cactus of the genus aloe, has been traditionally used for its efficacy in the treatment of burn wounds[5]. Spira-Wash is a proprietary gel designed to promote a moist wound environment, ideal for the healing process. Figures 2c and 2d show the patient's second-degree burn 7 days and 10 days following the domestic incident, respectively.

For 5 additional days, the patient combined the naltrexone formula with PCCA formula 12830 (Table 2), which includes pentoxifylline 1% in PCCA PracaSil-Plus. Pentoxifylline, a xanthine derivative, inhibits the production of collagen and reduces the proliferation of fibroblasts in post-burn hypertrophic scars[6-7]. PracaSil-Plus is a proprietary silicone base containing pracaxi oil developed for the incorporation of different active pharmaceutical ingredients (APIs) indicated in skin regeneration and healing[8]. From day 16 onwards, the patient applied the pentoxifylline formula alone, every day until two months post-injury. Figures 2e and 2f show the patient's second-degree burn 14 days and 2 months following the domestic incident, respectively.

Second-degree Skin Burn Injury Following a Domestic Incident

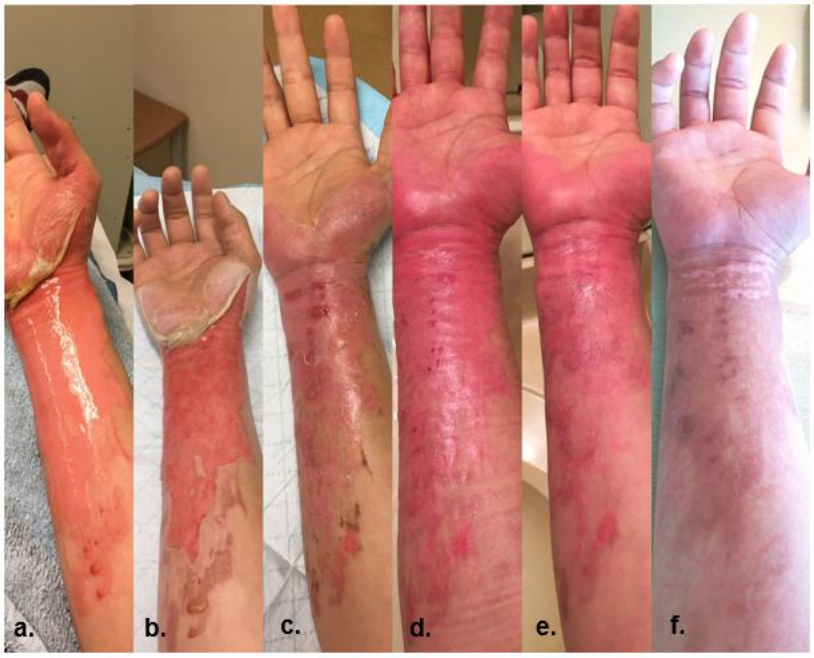

Figure 2 (a-f). *Digital images of the patient's burn injury on the right arm: (a,b) 12h post-injury; (c) 7 days; (d) 10 days; (e) 14 days; and (f) 2 months post-injury.*

Rx: *PCCA Formula 12781*
Naltrexone HCl 0.5%
Aloe Vera 0.2%
Base, PCCA Spira-Wash

Rx: *PCCA Formula 12830*
Pentoxifylline 1%
Base, PCCA PracaSil-Plus

Tables 1 (above) and 2 (below). *PCCA formulas used to manage the patient's second-degree skin burn injury.*

Methodology:

The Treatment Satisfaction Questionnaire for Medication (TSQM) was the research instrument used to evaluate the patient's level of satisfaction or dissatisfaction with the topical compounded medications. The version used was the TSQM 1.4 which comprises 14 questions that rate the treatment's effectiveness, side effects, convenience and the patient's global satisfaction. The majority of the questions are scaled on a five- or seven-point bipolar scale. The TSQM is a generic measure, as opposed to the disease-specific questionnaires, and it is psychometric sound and valid[9].

Results and Discussion:

The patient answered all questions of the TSQM following 2 months of treatment with the compounded medications. Very good treatment outcomes were reported since all questions were rated with a high score: 100 for side effects (meaning no side effects), 92.9 for global satisfaction, 88.9 for effectiveness and 83.3 for convenience. These outcomes are consistent with the visual improvements observed in Figure 2.

Conclusions:

Burns caused by heat in domestic kitchens have a high incidence worldwide and commonly result in open wounds and skin scarring. Immediate treatment is therefore important to promote wound closure and to limit skin scarring. Compounded medications offer the flexibility to combine multiple drugs in topical bases developed for specific skin conditions, such as PCCA Spira-Wash Gel (wounds) and PracaSil-Plus (scars). This case study demonstrates the successful treatment of a second-degree skin burn with PCCA formulas 12781 (naltrexone and aloe vera) and 12830 (pentoxyfilline). It is suggested that these formulas may be recommended as a viable personalized treatment option in skin burns.

References: *Please contact us to access the full list.*

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