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# Healing Diabetic Foot Ulcers: A Comparative Study of Epitram® (Arginine Aminobenzoate) and Silvadene® Cream 1%

by

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## Executive Summary

Epitram® (Arginine Aminobenzoate) is a novel nutritive topical cream used to heal diabetic foot ulcers and to ease the dryness and discomfort associated with them. Unlike many other topical wound-healing agents, Epitram® is 100% steroid-free, alcohol-free, and antibiotic-free. It is an all-natural amino-based product that has been deemed non-toxic and non-mutagenic by an independent FDA-recommended laboratory and by the studies presented here. What distinguishes Epitram® from its predecessors is the combination of its active ingredient, 1% Allantoin, with the patented wound-healing technology, Arginine Aminobenzoate (EpiCare Limited). By stimulating surface microcirculation, this technology has been observed to promote the recruitment of immune factors to the wound, and in doing so, focuses the body's natural healing efforts on the site of injury. Not only does Arginine Aminobenzoate accelerate the re-epithelialization of the wound, but its additional benefits include debriding necrotic tissue, reducing swelling, and palliating discomfort associated with ulceration.

To further substantiate the mounting evidence that Epitram® has unique place in the topical wound-healing market, the data presented here show that Epitram® out-performs an industry standard in both wound-healing efficacy and safety in a small human trial. This report summarizes why new therapies for diabetic foot ulcers are necessary, how Epitram® differs from currently available would-healing products, and its efficacy compared to one of the treatments commonly used in diabetic wound care today.

Up to 25% of people with diabetes will suffer from diabetic foot ulcers at least once in their lifetime.[1] Ulcers may appear on the feet or on other areas of the lower leg, as shown in Figure 1. Often they limit mobility, and they are very costly. Healing diabetic foot ulcers requires rapid wound closure to reduce the risk of infection, hospitalization, and in the most severe cases, amputation. To ensure complete recovery, care should include adequate perfusion, aggressive debridement, employing topical wound-healing creams, using sterile cotton dressings to prevent contamination of the wound, and alleviating any type of pressure or friction that the wound may withstand.[2] In general, this type of care allows only 25% of diabetic foot ulcers to completely heal within 12 weeks. However, as the current study shows, selecting an optimal topical therapy, such as Epitram®, may reduce this

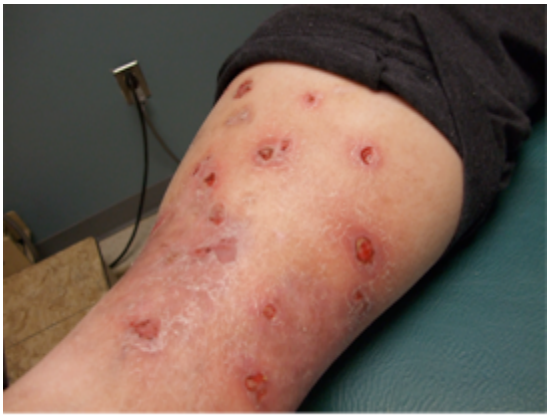


**Figure 1.** Lower-limb dry skin and ulceration.

treatment window to just 3 weeks. Consequently, patients' discomfort may be alleviated more quickly, and their financial burden may be greatly reduced.

Besides Epitram®, there are a number of different types of therapies used to treat diabetic ulcers. Some of different treatment options include silver-containing antimicrobials (Silvadene®), growth factor-containing gels (Regranex®), and tissue replacement therapies (Dermagraft® and Apligraf®). Each of these therapies is associated with significant caveats. For example, the efficacy of Silvadene® in treating wounds is inconsistent across several studies.[3-5] Furthermore, this cream has been shown to exert its effects via its antimicrobial activity since it is bactericidal against many gram-negative and gram-positive bacteria[6]. However, bacterial resistance to antimicrobial agents is a growing problem in diabetic wounds today.[7] Regranex® utilizes growth factors, which stimulate the body's endogenous healing mechanisms.[8-10] However, this therapy has been shown to increase patients' risk for mortality secondary to malignancy, and it has also been linked to the development of malignancies distant from the site of application.[11] Dermagraft® and Apligraf® are different bioengineered tissue replacement therapies that employ newborn-derived cells to stimulate growth and proliferation of dermal cells, which are involved in wound repair and tissue remodeling.[12, 13] Like most treatments that involve the use of human tissues, there are considerable costs associated with these therapies that may hinder their use in some patients.[13]

Due to the many complications associated with currently available wound-healing therapies, there is an immediate need for newer agents that are even more effective and 100% non-toxic. Epitram® is one such therapy that has proven to be effective and safe after being subjected to a battery of toxicology tests and to human trials in patients with diabetic ulcers. To convince physicians and strategic development opportunities that Epitram® out-performs currently available wound-healing therapies, its safety and efficacy were determined in the comparative study summarized in this report. A prospective, single-center study evaluated the effects of Epitram® and Silvadene® on Wagner Class I diabetic foot ulcers in 28 patients. The goal of these studies was to define the 12-week healing rate of diabetic foot ulcers using each of these treatments. The mean closure time for patients who received Silvadene® was 34.83 days. For patients treated with Epitram®, the mean closure time was only 20.40 days, 14 days less than a treatment commonly used in wound healing. Importantly, no complications arose with Epitram® treatment in this study. Therefore, the study authors conclude that Epitram® accelerates wound healing, and it is an extremely effective means to treat Wagner Class I diabetic foot ulcers.

## Scope of the Problem

Diabetic foot ulceration and subsequent lower-limb amputation are two of the most dreaded complications by diabetes patients.[2] The prevalence of foot ulcers in people with diabetes mellitus ranges from 4 to 10% with a lifetime incidence of up to 25%.[1] Ulceration commonly results from a combination of ischemia and diabetic peripheral neuropathy (DPN), a condition that causes dry skin, pain, and numbness in the hands and feet of up to 80% of people with diabetes.[14, 15] Consequently, their feet are vulnerable to even minor traumas

like repetitive pressure and friction[16]. Foot ulcers, which are frequently located on the tips of the toes or in the plantar region (Figure 2), are often preceded by calluses caused by such mechanical load on the lower limbs. When calluses are not removed, hemorrhage and tissue necrosis occur under the callus, and as a result, an ulcer forms.[2] Without treatment, these lesions close slowly or not at all. If the wound is or becomes ischemic, surgical intervention usually is necessary.[16] The ultimate treatment goal for patients with diabetic foot ulcers is to obtain rapid wound closure to reduce the risk of infection, hospitalization, and progression to severe infection requiring limb amputation.

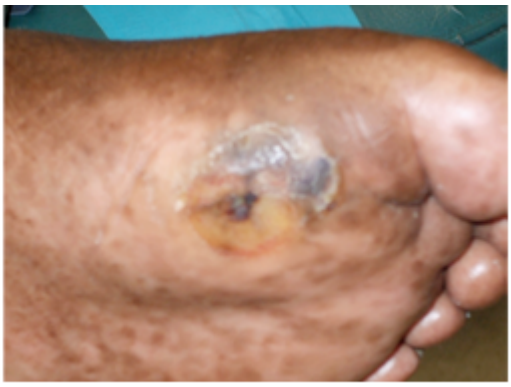


**Figure 2.** Diabetic foot ulcer- plantar in location.

Despite the high prevalence and incidence of diabetic ulcers, the progression from ulceration to amputation may be preventable with proper treatment.[2] However, more than 60% of non-traumatic lower-limb amputations are performed on patients with diabetes, who are 10 times more likely to receive an amputation than the general population.[17] Mostly, diabetic foot and lower-leg ulcers are to blame since they underlie many amputations. Current estimates indicate that treating a single diabetic foot ulcer costs as much as $28,000; having an amputation increases that figure to more than $50,000.[18, 19] The annual economic impact of diabetic foot ulcers on the United States is upwards of $1.6 billion,[19, 20] and amputations add another $1 billion to that burden.[19] Fortunately, progression of these ulcers can be preventable with proper therapeutic intervention. New therapies such as Epitram® play a role in healing more ulcers before it is too late to spare patients from undergoing amputation. Furthermore, by closing wounds at a quicker pace, agents like Epitram® will save Americans countless numbers of dollars currently spent on treatments for wounds as they progressively worsen.

Conventional care for diabetic ulcers that are not infected includes debridement, applying a topical wound healing agent, and reducing weight shearing forces.[2] With this type of care, most ulcers heal within 12 weeks. Good control of one's diabetes including optimizing glycemic control, also positively affects wound healing. This report summarizes a prospective study that evaluated the safety and efficacy of a new wound-healing agent, Epitram®, which should reduce the likelihood of diabetic ulcers progressing to require limb amputation. The present study compares Epitram® (Arginine Aminobenzoate) with Silvadene® cream 1%, in 28 patients with diabetic foot ulcers.

| Wagner Classification System | |
|---|---|
| **Stage 0** | Preulcerative lesion, healed ulcers, presence of bony deformity |
| **Stage I** | Superficial ulcer without subcutaneous tissue invovlement |
| **Stage II** | Penetration through subcutaneous tissue that may expose bone, tendon, ligament, or joint capsule |
| **Stage III** | Osteitis, abscess, or osteomyelitis |
| **Stage IV** | Gangrene of the forefoot |
| **Stage V** | Gangrene of the entire foot |

## Diabetic Foot Ulcer Classification

Several wound classification systems exist but one of the most well-established and common schemes used to grade foot ulcers is the Wagner Classification System, which is shown in the table to the left. The Wagner system stages foot ulcers based on a number of clinical and prognostic factors including wound depth and the presence of osteomyelitis or

gangrene.[15, 21] As the stage number increases from 0 to V, so does ulcer severity. Stage 0 ulcers consist of preulcerative lesions and healed ulcers while Stage V ulcers have progressed and encompass the entire foot with gangrene. Accordingly, patients who have late-stage ulcers have an increased number of amputations, and are therefore associated with poorer prognoses.[21]

In the current study, the efficacy of Epitram® is tested in Wagner Stage I diabetic neuropathic foot ulcers. Therefore, patients presented with ulcers that were superficial and had no subcutaneous tissue involvement.

## Filling a Void

There are several different types of therapies currently used in topical heal wound care. However, none of them provide patients with effective relief of their symptoms with no additional risk to the patient. Some of the commonly used products are silver-containing antimicrobials (Silvadene®), growth factor-containing gels (Regranex®), and tissue replacement therapies (Dermagraft® and Apligraf®). Despite the plethora of agents available, none have proven to be consistently effective in treating diabetic wounds. Furthermore, many are associated with high costs and serious toxicities, which cause some patients to discontinue treatment with these agents. Therefore, patients are forced to either switch to less effective treatments or forego treatment for their ulcers altogether. Given the significant limitations of current treatment options, a large void in the diabetic wound treatment market exists. Therefore, there is a need for newer treatments, like Epitram®, which are consistently efficacious, cost-effective, and all-natural, to fill this void and safely and effectively treat debilitating and costly diabetic foot ulcers.

**Silvadene® (silver sulfadiazine)**

Silvadene® (silver sulfadiazine) is an FDA-approved cream used as an adjunct to prevent and treat wound sepsis in patients with second- and third- degree burns. While it is not specifically indicated to treat diabetic foot ulcers, it is used widely by clinicians to treat these and other skin lesions. Silvadene® is a silver-containing sulfonamide antibiotic that is spread over wounds. The silver reacts with moisture from the wound fluids to release silver ions, which exhibit antimicrobial activity against bacteria and fungi.[22] Silvadene® has two main functions: creating physical barrier so that nothing contaminates the wound and serving as a broad antimicrobial agent. While Silvadene® has been shown to allow injured tissue to heal properly, it does not do so at an accelerated rate.

| Silvadene® (silver sulfadiazine) |
|---|
| **Indications** |
| Adjunct for prevention and treatment of would sepsis in patients with 2 nd- and 3rd- degree burns |
| **Mechanism of Action** |
| Topical antimicrobial agent; bactericidal for many gram -positive and gram -negative bacteria as well as yeast |
| **Adverse Events** |
| Decreased white blood cell count, skin necrosis, erythema multiforme, skin discoloration, burning sensation, rashes, interstitial nephritis |
| **Systemic Absorption** |
| Depending on the extent of tissue damage, reactions to sulfanimides (hematologic complications, dermatologic and allergic reactions, hepatitis, GI tract abnormalities, CNS reactions, toxic nephrosis) |

One of the major problems with Silvadene® is that its efficacy is inconsistent. One prospective randomized trial compared it to a biologically active tripeptide copper complex (TCC) cream and also to a placebo in 86 patients. Each patient presented with venous ulcers of at least 3 months duration. Silvadene® healed significantly more wounds (21%) than the placebo (1%; $p$=0.08), which was not significantly different from the number of wounds healed by

the TCC cream (0%). A different study reported that Silvadene® was not as efficacious as the authors of the first study claimed. In 60 participants the efficacy of Silvadene® was compared to a control treatment that consisted of a plain non-adherent dressing, for venous leg ulcers. There was no significant difference between the two groups for number of wounds healed at 12 weeks, 63% and 80%, respectively ($p$=0.16).[4] Furthermore, a different study that defined the time it took to achieve complete wound healing compared Silvadene® with hydrocolloid dressings in 51 patients with at least 2 chronic leg ulcers. Again, no significant difference was found in healing times between Silvadene® and the dressings, 15 and 16 weeks, respectively (no $p$-value given).[5]

In addition to the inconsistent efficacy of Silvadene®, this topical cream is also associated with significant adverse events. A major side effect that has been reported is transient leukopenia, which is a decreased white blood cell count.[6] Other less frequent side effects include skin necrosis, hypersensitivity reactions, skin discoloration, burning sensations, rash, and kidney disorders.[6] In addition, patients with ulcers that have greater tissue damage may absorb more of the compound systemically. As a result, various systemic sulfonamide-related adverse events such as dermatologic and allergic reactions, hematological abnormalities, gastrointestinal reactions, hepatitis, central nervous system reactions, and toxic kidney disease may also occur.[6]

Another growing caveat to using a bactericidal agent like Silvadene® to treat diabetic foot ulcers is bacterial resistance. The most frequently encountered type of bacteria in diabetic foot ulcers is *Staphylococcus aureus* (*S. aureus*). Resistant strains of this type of bacteria have garnered attention lately since they are becoming increasingly prevalent in hospitals and clinics. Often, they are referred to as methicillin-resistant *S. aureus*, or MRSA.[23] Because the efficacy of Silvadene® is at least partially attributed to it being an antibiotic, it is possible that it will become less and less effective in treating diabetic wounds in the future. Therefore, it is particularly important to use topical therapies that can handle MRSA-containing diabetic ulcers; antibiotic-containing topical agents may not be sufficient.

**Regranex® (becaplermin)**

Regranex® (becaplermin) is the only FDA-approved treatment for diabetic ulcers that contains growth factors, which stimulate cell proliferation and growth. Specifically, Regranex® is a recombinant human platelet-derived growth factor (hPDGF), which is involved in the body's native tissue repair process. Growth factors help ulcers heal by participating in all three aspects of the wound healing process: inflammation, new tissue formation, and wound remodeling.[24]

| Regranex ® (becaplermin) |
|---|
| **Indications** |
| Treatment of lower extremity diabetic neuropathic ulcers that extend into or beyond the subcutaneous tissue and have adquete blood supply |
| **Mechanism of Action** |
| Functions like endogenous PDGF, which stimulates chemotactic recruitment and proliferation of cells involved in wound healing |
| **Adverse Events** |
| Rash and increased rate of mortality secondary to malignancy at site of application |
| **Systemic Absorption** |
| Minimal |

Regranex has been shown to be efficacious in several studies. One double-blind multicenter trial compared it to a placebo in 118 patients. Complete wound healing occurred in 48% of patients in the Regranex arm but in only 25% of those taking placebo ($p$=0.01).[10] A larger double-blind, randomized, phase 3 clinical trial enrolled 382 patients with diabetic ulcers to test the proportion of wounds closed and the rate of healing achieved by Regranex®. A closure rate of 50% was reported in patients using Regranex® while patients using a placebo treatment only had a 35% closure rate ($p$=0.007). Healing

time was also much shorter in patients treated with Regranex® than in those given a placebo, 86 and 127 days, respectively ($p$= 0.013).[10]

While Regranex® has been shown to have good clinical efficacy, it has the potential to be extremely detrimental to patients. Therefore, it is not widely used by clinicians due to poor clinical experience and also a very high cost.[9] Up to 2% of patients experience rashes with continued use of the product.[24] Many other adverse events relate to the underlying ulcer, not the treatment (e.g. osteomyelitis, wound infection, etc.) have also been reported but were fairly common in patients using a placebo treatment as well.[24] The most serious issue associated with Regranex® is its reported role in cancer and in fatality secondary to malignancy. This agent is contraindicated for patients with any known malignancy since the hPDGF acts like it does endogenously, and therefore promotes cell proliferation and growth, key factors in the development of many cancers.[11] Furthermore, it also has been shown to be associated with an increased risk of developing malignancies distant from the site of insult in patients who have used three or more tubes of Regranex®.[11] Therefore, patients are strongly advised to use Regranex® only when its benefits will outweigh its potentially life-threatening risks.

**Dermagraft® and Apligraf®**

Dermagraft® and Apligraf® are similar types of tissue replacement therapies that are FDA-approved to treat diabetic foot ulcers.[12, 25] These agents serve as a bioengineered skin substitutes provide a scaffold onto which human fibroblasts and extracellular matrix components can grow.[13] When applied to a wound, the human-derived fibroblasts proliferate and secrete collagen, proteins, cytokines, and growth factors, which create a three dimensional skin substitute. As such, they have been shown to allow ulcers to re-epithelialize and heal.

Dermagraft®, an example of this type of tissue replacement therapy, heals wounds more quickly than some other wound healing agents. In a randomized, controlled, multicenter trial, 214 patients with diabetic ulcers were all given saline-moistened dressings to treat their wounds. For the control arm of the study, 112 participants also received Dermagraft® applications to test its efficacy. Of the wounds treated with dressings alone, 19.6% achieved closure. The Dermagraft® cohort had 29.5% wound closures ($p$=0.065). While there is no significant difference in the overall response to treatment, patients treated with Dermagraft® did experience faster wound closure than those treated with dressings alone ($p$=0.04). In addition, adverse events related to Dermagraft® application have been reported to be minimal and generally pertain to the wound itself.[26]

A significant limitation of Dermagraft® and other bioengineered skin therapies such as Apligraf®, include their prohibitively high cost. While some argue that this tissue replacement therapy reduces total costs of ulcer care due to its quick and effective wound closure capacity, others suggest that because it is expensive and difficult to use, there is no financial benefit in the end.[12] Therefore, many patients may opt out of receiving this type of treatment.

**Epitram® (Non-greasy cream/emulsion of 5.0% Arginine Aminobenzoate, 1% Allantoin and Dihydroxybenzene Polyphenolic acid)**

Epitram® is a novel, all natural, non-greasy cream used to treat diabetic foot ulcers. Unlike many other topical wound-healing agents, Epitram® is non-steroidal and non-antibiotic. Therefore, there have never been any reports of side effects from its use. Also setting it apart from currently available therapies is its advanced patented technology, Arginine Aminobenzoate. This technology provides many benefits to wound healing. First and

foremost, it is reported in the present study to be even more efficacious than at least one of the most commonly used wound-healing ointments, Silvadene®.

Epitram® exerts its therapeutic effects via Arginine Aminobenzoate, which increases the DNA synthesis of an endogenous growth factor called human Epidermal Growth Factor (hEGF). In doing so, Epitram® takes advantage of the physiological attributes of growth factors, which are to positively influence tissue repair and remodeling. Importantly, several studies have shown that creams containing hEGFs accelerate wound closure by reestablishing cellular integrity, an essential part of healing.[8, 27-29] Similarly, in preliminary studies, Epitram® has been shown to considerably increase the rate of wound healing by stimulating the proliferative phase of tissue regeneration. Other phenomena observed include an increase in surface microcirculation at the site of Epitram® application, which increases blood flow to the site of insult, and antimicrobial effects against both gram positive and gram negative bacteria.

| Epitram® (Arginine Aminobenzoate) |
|---|
| **Indications** |
| Treatment of lower extremity diabetic neuropathic ulcers (pending FDA -approval) |
| **Mechanism of Action** |
| Functions like endogenous hEGF, which stimulates epidermal and possibly dermal tissue repair. |
| **Adverse Events** |
| None |
| **Systemic Absorption** |
| Unknown |

A chief reason that Epitram® has such an outstanding safety profile is because it is an all-natural product. Not only is its patented ingredient an amino-based compound, but the other components of the cream are all-natural as well. Its ingredients include safflower oil, apricot kernel oil, mixed tocopherols, glycerin, coconut oil, borage oil tea tree oil, lanolin, camphor, sandal wood oil, lecithin, grapefruit extract, aloe vera and Dihydroxybenzene polyphenolic acid. All of these ingredients are Generally Recognized as Safe (GRAS) and therefore have no known toxicities. Its non-toxic and non-mutagenic attributes have been confirmed in an independent laboratory. Unlike currently available therapies used to treat diabetic foot ulcers, none of the significant complications such as bacterial resistance, secondary malignancies, and high cost are associated with Epitram®.

## Testing the Ointment

### Study Design

The potential role of Epitram® in treating diabetic foot ulcers was evaluated in a prospective, single-center, open-label study of 28 patients with a history of diabetic-related ulcers. The objective of the study was to evaluate the safety and efficacy of Epitram®, and to determine the time (in days) needed for complete wound closure of the target ulcer. The primary endpoint of the study was the 12-week healing rate of the diabetic ulcers. Complete wound healing was defined as the full epithelialization of the wound with the absence of drainage.

Patient inclusion criteria required that the patient:

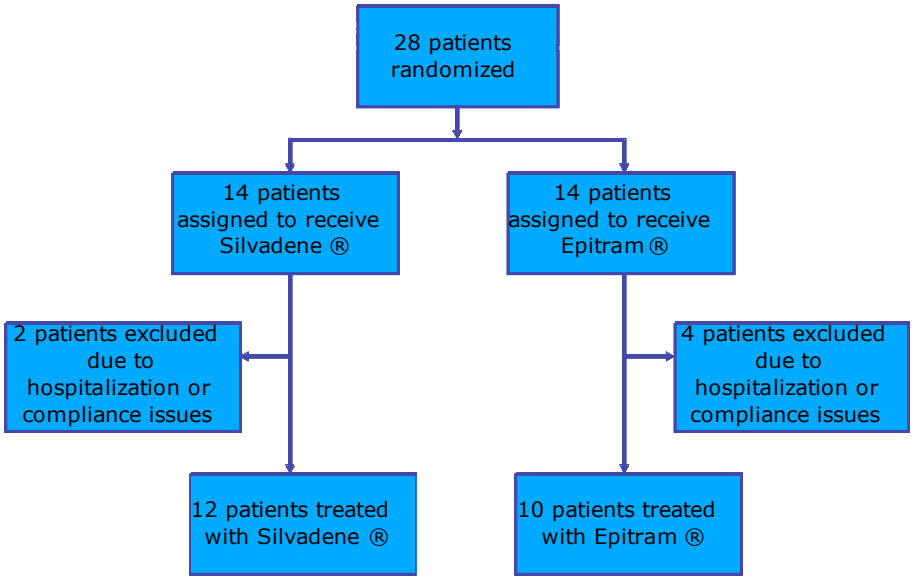
- Was at least 18 years of age
- If female and of reproductive age was not pregnant and was using contraception
- Had a diabetic foot ulcer located between the tibia and the foot

Patient exclusion criteria stipulated that patients did not:

- Suffer from hemophilia
- Receive treatment with topical steroids, immunosuppressants, anticoagulants, or cytotoxic chemotherapy in the last 30 days or anticipate requiring any of the above during the study duration
- Have HIV or AIDS
- Suffer from acute or chronic bacterial, viral, or fungal diseases that would interfere with ulcer healing
- Have a known history of poor compliance with medical treatment
- Participate in other concurrent clinical studies

Before study initiation, ulcers were graded in severity and measured at baseline to compare with follow-up visits. Subjects were then randomized to receive either Silvadene®, a currently available gold standard treatment for diabetic ulcers, or Epitram®.

**Figure 3. Study Design**




**Methods**

Of the 28 patients enrolled in this study, 15 were females and 13 were males. All provided consent to be included in the study, and HIPAA authorization was obtained for all participants prior to enrollment. The two treatment cohorts were comparable with no pronounced differences in patient demographics or baseline wound characteristics.

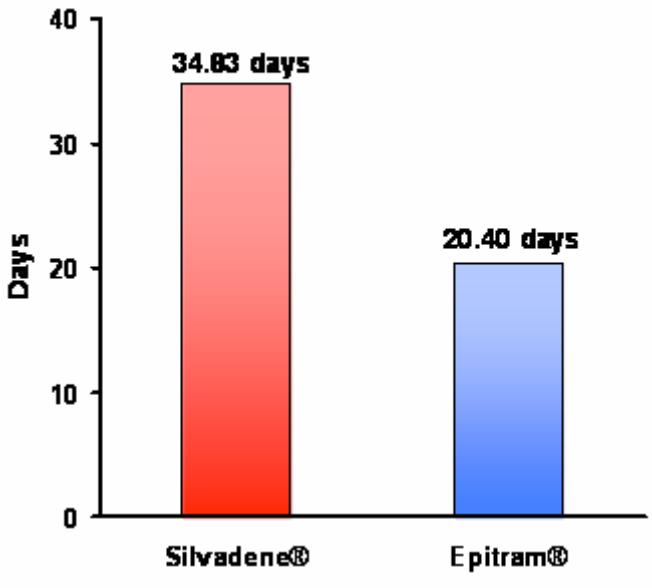
The patients' ulcers included in the study were Wagner Stage I Diabetic foot ulcers. As such, they were relatively small and fresh, and any ulcer that manifested signs of infection was excluded from the study. The median duration of the target ulcers was 12 days. Prior to treatment with either Silvadene® 1% cream or Epitram®, all patients had sharp wound

debridement. The onset of the study was July 1, 2007, and it ended on December 31, 2007.

**Results**

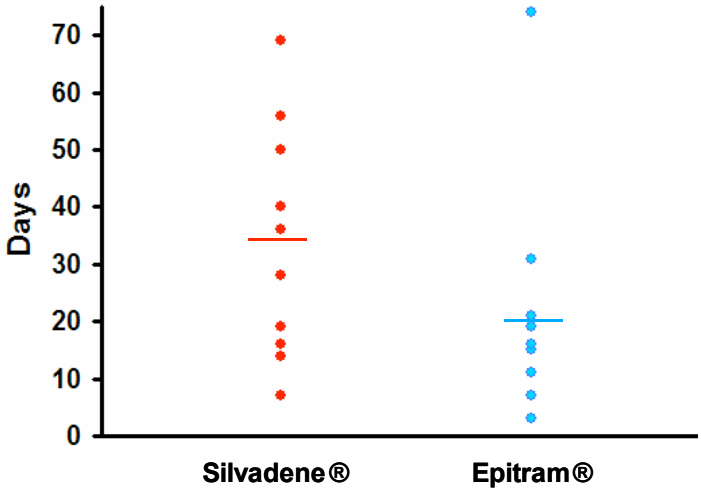
As shown in Figure 3, 28 patients were initially enrolled in this study. Half of the patients were randomized to either the treatment or the control group. Five patients were excluded from the study due to hospitalization and/or surgical procedures that occurred during the course of the study. One other patient was excluded due to compliance issues. Therefore, 22 patients were included in the study. Twelve patients received topical treatment with Silvadene® and 10 were treated with Epitram®. After randomization, the ulcers were calculated to have a median area of 2.9cm$^2$ in the Epitram® cohort and 1.9cm$^2$ in the Silvadene® treatment group. The depths of the ulcers were 0.5mm and 1.6mm in the Epitram® and Silvadene® groups, respectively.

**Figure 4. Mean Time to Wound Closure**




As shown in Figure 4, the mean time to wound closure was 20.40 days in patients treated with Epitram® and 34.83 days in patients treated with Silvadene®. These results suggest that Epitram® provides a 2 week advantage over Silvadene® (t-test; $p$=0.130) in wound closure rate. These same results are also depicted in Figure 5. This graph shows the length of time it took for the wound to close for each evaluable patient who received treatment. As you can see, the majority of the patients using Epitram® achieved complete wound closure in less than 20.40 days, the mean time to wound closure calculated in this study. In contrast, patients treated with Silvadene® had more variation in their time to would closure duration, which is consistent with previously published reports of its unreliable efficacy. Importantly, no patients experienced any side effects in the Epitram® arm of the study.

**Figure 5. Time to Wound Closure By Patient**



**Conclusions**
As the results indicate, Epitram® accelerates diabetic wound closure time compared with one of the most widely used FDA-approved therapies, Silvadene®. In most patients treated with Epitram®, wounds were completely healed in less than 3 weeks. The authors acknowledge that due to the small sample size of this study, a significant *p-value* of less than 0.05 was not achieved. However, the study authors believe that the trends shown on the graphs are indicative of the outstanding efficacy of this product. Therefore, the authors conclude that Epitram® is an effective means to treat patients with Wagner Class I diabetic foot ulcers. The authors also deem this product safe since no adverse toxicities were experienced by any patients.

## Why is this Important?

The most important treatment goal for patients with diabetic foot ulcers is to achieve the most rapid wound closure possible. With the use of Epitram®, a novel therapeutic agent that accelerates diabetic wound healing, reaching this goal is now possible. In addition to its outstanding efficacy, this product also has an impeccable safety record since no side effects have ever been reported with its use.

The results summarized in this report will significantly impact the future early management of patients with early-stage diabetic foot ulcers. Here it is documented that a 100% steroid-free, antibiotic-free, and alcohol-free nutritive foot cream is even more efficacious than an industry standard that has been used to treat diabetic wounds for years. Of the many wound healing products available, none are associated with zero complications like Epitram®. A chief consideration that may be of utmost importance in the near future is the fact that Epitram® not only heals wounds rapidly but that it does so without the use of any antibiotics. Increasingly, bacterial resistance to many of the commonly used therapies is creating problems for many clinicians involved in managing patients with diabetic wounds. Furthermore, Epitram® is non-mutagenic, and therefore life-threatening secondary malignancies are not a problem with this product. Finally, Epitram® is extremely cost effective and as such, will not place an undue burden on patients or physicians interested in the economical treatment of diabetic ulcers. The emergence of an all-natural product like Epitram® may soon shift the way in which clinicians choose early treatments for patients with diabetic wounds.

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