

## CASE REPORT

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# Marine Isopod *Ceratothoa Oestroides* Extract: a Novel Treatment for Diabetic Foot Ulcers? Case Report of an Immunosuppressed Patient

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## ABSTRACT

**Introduction:** Diabetic foot ulcer (DFU) is a common lower-extremity complication in patients with diabetes mellitus. A novel DFU treatment is tested by using an ointment containing as healing agent olive oil isopod *Ceratothoa oestroides* extract. **Case report:** A 58 years old obese man, smoker, with a history of unregulated Type 2 Diabetes Mellitus, peripheral neuropathy and Hodgkin lymphoma was referred to Athens–Greece university hospital Laikon. The patient presented clinically with a lower extremity DFU and peripheral neuropathy with dysesthesia and disturbed sensation of hot and cold. He was treated with an ointment containing *C. oestroides* extract for five months, without any antimicrobial treatment. Therapy was evaluated by measurement of the transepidermal water loss, skin hydration, photo documentation and planimetry. At each patient's visit, DFU presented a satisfactory healing process. Five months after treatment initiation the patient had complete healing of his DFU. Blood tests after treatment revealed a significant reduction of the levels of the inflammatory markers. Ulcer cultures did not reveal any microbial development neither before nor after treatment. **Conclusion:** The administration of the *C. oestroides* extract ointment proved to be effective in this case. Although these results should be further investigated, the reported case suggests a novel option for the management of neuropathic diabetic foot ulcers, especially in patients with severe co-morbidities.

**Keywords:** Diabetic foot ulcer, *Ceratothoa oestroides*, peripheral neuropathy, Diabetes mellitus, immunosuppression.

## 1. INTRODUCTION

Diabetic Foot Ulcer (DFU) is a chronic and common complication of Diabetes mellitus. The lifetime risk of developing a foot ulcer in a patient with diabetes ranges from 15% to 25% (1, 2). Thus DFU is associated with a high economic and social burden. DFU's yearly incidence ranges from 2% to 4% in developed countries (2). DFU and diabetic nephropathy has been established as important risk factors for foot ulceration and lower-extremity amputation (3). It is well known that DFU consists a serious problem for the scientific community, since it is one of the most common and serious lower-extremity complications of Diabetes mellitus, and influences both patient's quality of life and the economy of the health system in developed countries (4, 5).

The pathophysiology of the “diabetic foot” includes important factors such as infection, destruction of the deep tissue, ulceration and

patient-related factors including age, other comorbidities that can affect wound healing and determine the ulcer (6). DFU pathophysiology comprises also high levels of cytokines, chemokines, and growth factors (7). In case of delayed treatment, a prolonged phase of inflammation takes place and a chronic DFU is established (8). DFU is very difficult to treat. A lot of treatment methods are available, however very few seem that can really contribute to heal. Pre-clinical studies with topical application of an ointment containing olive oil *C. oestroides* extract showed a significant wound healing efficacy (9). This marine isopod is a parasite found mainly in the oral cavity of sea bass and sea bream (10, 11). In order to investigate new DFU effective treating methods the oily extract of *C. oestroides* was clinically tested.

## 2. AIM

In this study is presented a case of a successful treatment of a DFU in an

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Figure 1. Diabetic foot ulcer at baseline

immunosuppressed patient using *C. oestroides* oily extract ointment.

### 3. CASE REPORT

In June 2016, a 58-year-old man, obese (BMI: 36,62 kg/m<sup>2</sup>) and smoker (8 cigarettes/day) was referred to our Diabetic Foot Clinic in General Hospital of Athens “Laiko” from Hematology clinic due to diagnosis of a DFU. The patient had a history of unregulated Type 2 Diabetes Mellitus in the last 8 years (2009) and peripheral neuropathy the last 3 years (2014). The patient had also undergone radiotherapies from April 2015 since May 2016 due to Hodgkin’s lymphoma, diagnosed in March 2015. The patient clinically presented with a lower extremity DFU in the plantar surface of the first metatarsal head of the right lower extremity, along with dysesthesia and disturbed sensation of hot and cold (Figure 1).

Blood tests revealed high levels of inflammatory markers as Erythrocyte Sedimentation Rate (ESR)=85mm/h, C-Reactive Protein (CRP)=16.5mg/L (normal values:<3.14mg/L) and Glycated hemoglobin A1c (GHbA1c) = 9,3%. Ulcer cultures did not reveal any microbial development. He received treatment with topical application of a novel ointment that was based on the olive oil extract of *C. oestroides* and prepared in the laboratory of the Pharmaceutical Technology, unity of Cosmetology-Dermatopharmacology, of the National and Kapodistrian University of Athens. Additionally, efforts were made to ameliorate his glucose levels and instructions were given for offloading and quit smoking. The patient had been followed up every month for five months by clinical evaluation and photo-documentation and by



Figure 2. Diabetic foot ulcer after five months of treatment with the isopod extract.

measuring transepidermal water loss, skin hydration, and planimetry.

The transepidermal water loss (TEWL) was measured by the Tewameter TM 210 (Courage and Khazaka Electronic GmbH, Cologne, Germany) evaluating humidity rate on the skin surface (in g/h/m<sup>2</sup>) and so indicating skin barrier function, the level of skin hydration by the Corneometer CM 820 (Courage and Khazaka Electronic GmbH, Cologne, Germany) (12, 13), the extent of the DFU by photo documentation (camera Sony Cyber-shot H300) measuring its dimensions using the image-analysis program AutoCAD (Autodesk Inc., San Rafael, California, U.S) the wound surface by planimetry taking imprint of the wound and evaluating the surface by a two dimension (2D) program applying the Gauss method according to the equation  $2E = \sum \Psi v \cdot (X_{v+1} - X_{v-1})$ .

During treatment, a significant clinical improvement of the ulcer was observed (Figures 1, 2). The DFU reduced from 5,5 cm<sup>2</sup> at baseline to 1,1cm<sup>2</sup> at four months after treatment initiation, and in five months DFU was healed. (Figures 2, 3). TEWL rate was gradually reduced in contrast to the level of hydration that was gradually increased in the surface of the DFU (Figure 4). Additionally, five months after initiation of treatment, a significant improvement in inflammation indices was also observed: ESR = 42mm/h and CRP = 9mg/L. It has to be noted that ulcer cultures did not reveal any pathogens during treatment.

### 4. DISCUSSION

The wound healing ability of this treatment can be considered very high (Figures 1, 2), despite patient’s comorbidities unfavorable to healing process such as immunosuppression, Hodgkin’s lymphoma, unregulated diabetes, obesity, peripheral neuropathy, smoking status and wound anatomical area. It is worth noting that no administration of antibiotics was needed. The use of this novel treatment with *C. oestroides* extract contributed significantly to the progressive reduction of the ulcer size (Figure 3). Transepidermal water loss follows the pattern of wound healing. It begins from very high values arriv-

ing after wound closure almost to the normal, showing the re-establishment of skin barrier (Figure 4). Same for hydration skin rate which begins by low and arrives almost to normal values after wound healing (Figure 4). Both clinical evaluation as well objective measures were in accordance showing complete wound healing. DFU is very difficult to be managed and treated, especially in patients with other serious comorbidities such as immunosuppression (14). Antibiotic therapy, DFU dressings, leg offloading and frequently used alternative treatments such as Vacuum Assisted Closure (VAC), growth factors, hyperbaric oxygen and fibroblast/keratinocyte therapies (5, 16, 17) can help to the management of a DFU (15, 16). These treatment methods are approved as additional therapies and are not included in the guidelines of the International Working Group on the Diabetic Foot (18). Apparently, DFU requires a novel treatment approach, which will result in total healing.

## 5. CONCLUSION

Olive oil extract of *C.oestroides* contributed significantly to the successful management of a DFU in a very difficult case. Further studies are needed to confirm these findings.

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