

# Calcium Alginate ( $C_{12}H_{14}CaO_{12}$ )<sub>n</sub> Value in the Cicatrisation of Diabetic Foot Lesions

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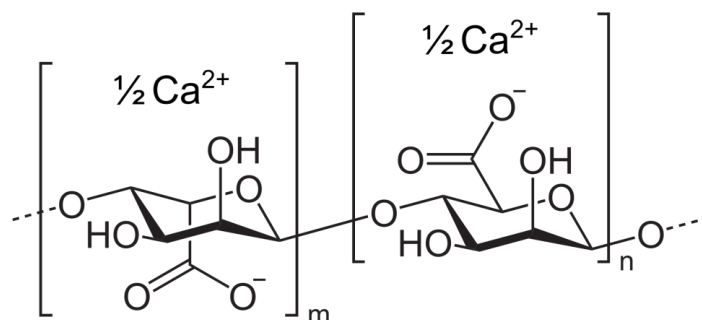
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**Abstract:** The present article explores the usage of calcium alginate in the actual management of diabetic mellitus foot ulcers. A retrospective study was performed on 305 cases of patients with diabetic mellitus foot diagnostic, admitted to Surgery Clinic II of "Sf. Ap. Andrei" Emergency Clinical Hospital, Galati, in the period between 1<sup>st</sup> October 2015 and 31<sup>st</sup> October 2019, for which calcium alginate dressings had been used. Calcium alginate ( $C_{12}H_{14}CaO_{12}$ )<sub>n</sub> dressings had been applied to all patients from the series (n=305), with favorable evolution in 97.7 % cases, the dressing being replaced at 48 hours and the average duration for injury's healing oscillating from 21 up to 50 days.

**Keywords:** calcium alginate, diabetic mellitus, lesions

## 1. Introduction

Calcium alginate (calcium  $\beta$ -D-mannopyranuronosyl-(1 $\rightarrow$ 4)-  $\alpha$ -L-gulopyranuronosyl-(1 $\rightarrow$ 4)-  $\alpha$ -L-gulopyranuronat), with chemical formula ( $C_{12}H_{14}CaO_{12}$ )<sub>n</sub>, is a gelatinous substance, with creamy aspect, indissoluble in water, created by adding watery calcium chloride to the watery sodium alginate.



**Figure 1.** The chemical structure of calcium alginate  
([https://commons.wikimedia.org/wiki/File:Calcium\\_alginate\\_skeletal.svg](https://commons.wikimedia.org/wiki/File:Calcium_alginate_skeletal.svg))

From the introduction of alginate dressings in the wound treatments 30 years ago [1-3], the medical practice has developed and new technologies and dressings have been introduced, with the purpose of improving the clinical results in the management of diabetic mellitus foot ulcerations. The calcium alginate biopolymer has been and is being used even today in order to achieve the highest performance bandages.

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Their performance is demonstrated in particular by improving the efficiency of wound healing and the incidence of their recurrences. The current tendency in the treatment of trophic ulcers is to use hydroactive dressings. In this category, those using calcium alginate enhance the hydrophilic nature of the wound dressing and create the required moisture environment [4].

If we combine the use of these types of dressings with the correct topical care of the wounds, removing the exudate we will obtain a substantial increase of the wound healing speed.

This chemical compound is capable of cross-linking with other organic and inorganic substances that can control the control and rapid healing [5].

The present article explores the usage of calcium alginate in the actual management of the diabetic mellitus foot ulcers. The dressing consists of calcium fibers and sodium alginate, which have been combined, in order to form a strong cohesive product [6, 27], resulting an extremely adsorbent non-adherent dressing which transmits oxygen and humidity vapors [7,8]. In the presence of the exudates, the fibers form a hydrophilic gel [6,27].

When the dressing is applied on a wound, significant proportions of the calcium ions are replaced by sodium ions from the wound's level, and the fibers are dilating, in order to form a gel which will fill the wound [9-17, 2].

Our retrospective study aims to highlight the indications and management of hydroactive applications which use calcium alginate in treatment of complications of diabetic mellitus foot from our Hospital experience.

## 2. Material and method

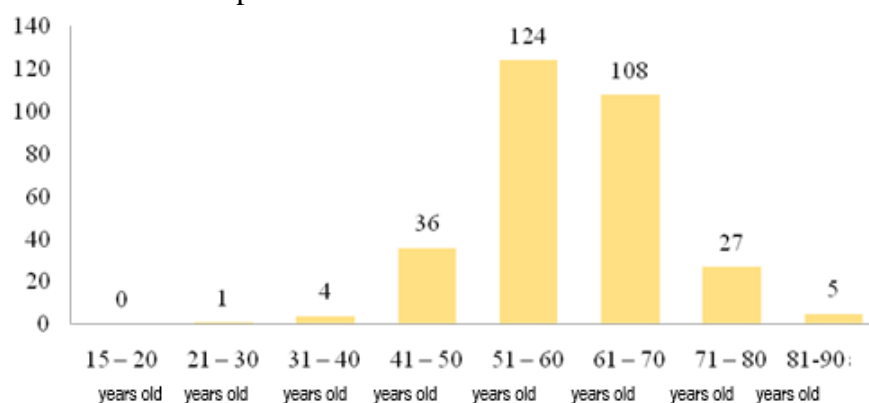
A retrospective study on 305 cases of patients with diabetic mellitus foot diagnostic was performed, patients hospitalized in Surgery Clinic II of "Sf. Ap. Andrei" Emergency Clinical Hospital, Galati, in the period between 1<sup>st</sup> October 2015 and 31<sup>st</sup> October 2019, for which calcium alginate dressings had been used. The selection criterion was represented by diabetic mellitus foot diagnostic, the date being processed from the patient's consultation sheets.

The criteria for inclusion in this study are that these patients present with injuries of the foot only, as a result of a surgical and / or spontaneous act. Based on the information obtained, a database was created, database which was used for statistical processing.

The study was approved by the Ethics Committee of "Sf. Ap. Andrei" Emergency Clinical Hospital, Galati, being considered that it is a non-interventional study which complies with the confidentiality and ethics requirements towards the patients.

## 3. Results and discussions

For the series analyzed, the minimum age included in the series was 24 years old and the maximum age being 86 years old, the average age being 60 years old, with a standard deviation of 8.576. The presence in the studied series of young patients (a 24-year old patient) confirms the particular aspects of the peripheral arteriosclerosis in patients with diabetes mellitus.



**Figure 2.** Distribution of cases per age groups

The prevalence of diabetes mellitus type 2 is expected to increase step by step, along with the extension of population ageing and life expectancy. The physiological changes which develop along with ageing make more difficult the analysis than the studies for the young patient group. Consequently, there are many questions without answer regarding the management of diabetes mellitus for senior patients.

Within the series under study (n=305), 85.6% among patients were male and 14.4% were female patients. The data obtained are similar with those from other studies performed and confirm the fact that most patients with diabetic mellitus foot are males. Regarding their origin, we have confirmed 112 cases from the rural cases studied came from rural environment (36.7%) and 193 cases from urban environment (63.3%).

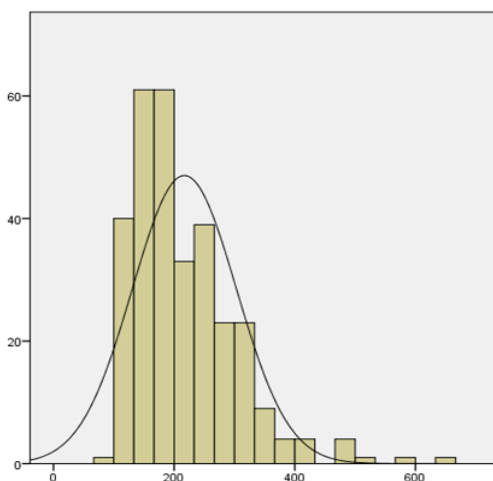
The predominance of diabetic mellitus foot cases at patients from urban environment are most probably due to an inadequate life style, characterized by an inadequate diet and by a reduced physical activity. The pain was the main reason for which the patients from the series under study came to the medical checkup. It was accompanied in 37% cases by functional impotency, in 8% by necrosis and in 4% cases of edema at the level of the affected body part.

A significant number of patients, respectively 82 (27%) had upon admission to the hospital necrosis lesions without any painful symptomatology. This happened probably due to advanced diabetic mellitus neuropathy. This fact confirms once again the major role of neuropathy in the development of the complications of the diabetic mellitus foot and the fact that the lesions may remain unobserved for a long time due to the loss of sensitivity in the affected area.

The surgery was performed on 205 patients, representing a percentage of 79%. A number of 55 patients, representing a percentage of 21%, received pharmacological medical treatment. The most primary surgeries performed were amputations (148 cases - 59%), followed by incision, debridement and necrectomy (86 cases - 34%).

44 patients benefited from bacteriological examination of the secretions from the wound, representing a percentage of 14% of the total number of patients diagnosed with diabetic foot. Of these, in 42 cases (95%) the bacteriological examination was positive and in two cases (5%) the bacteriological examination was negative. The most common pathogens identified on the bacteriological examination of wound secretions were *Staphylococcus aureus* (26%) and coagulase - negative staphylococcus (24%), followed by enterococci (17 %).

Another clinical features of the patients were infected wounds, deep mixt ulceration and edema. Among them, 96% of patients had type diabetes mellitus type 2 (294 cases) and 4% of patients with diabetes mellitus type 1. It is noted that the majority of patients hospitalized with the diagnosis of diabetic mellitus foot had diabetes mellitus type 2, these being usually patients over 50 years old, with longer disease duration and with associated conditions that have favored the complications [33, 34].



**Figure 3.** Histogram for glycemia values at admission

For the patients included in the series, the minimum value of the blood sugar level at the moment of being admitted to hospital was 90 mg/dL, the maximum value of 645 mg/dL, with an average value of 216.85 and a standard deviation of 86.25. For the studied series, 99% of the patients presented at the moment of being admitted to hospital values of the blood sugar level over of the maximum allowed limit, indicating its inadequate control.

The prolonged exposure to hyperglycemia plays a major role in the onset and development of arteriosclerosis and in the pathogenesis of the micro- and macrovascular disorders which are present in patients with diabetes mellitus. It represents the main risk factor in the development of chronic complications of this condition.

The results of the study are in agreement with the data from the literature according to which patients with unbalanced diabetes mellitus have a very high risk of developing and progressing the chronic complications associated with this condition.

The evolution of the lesions is complicated by the presence of other comorbidities. For example, in the case of the presence of a chronic varicose disease, its complications are the basis of the appearance of mixed trophic lesions. Phlebitis, thrombophlebitis may appear complicated or diabetic foot treatment and undue difficulty.

In general, trophic lesions of the toes were more frequent than the plantar ones with a ratio of 3/1.

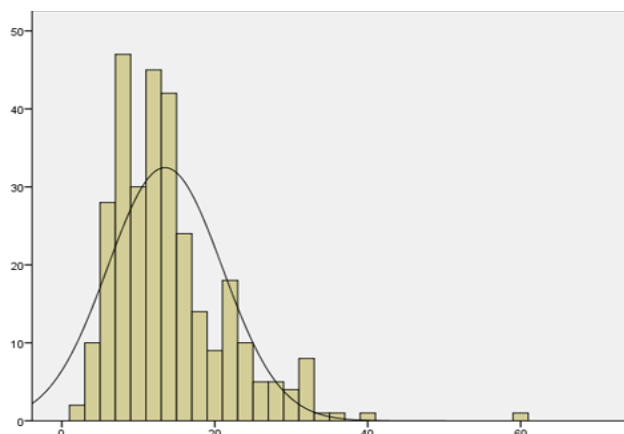
Calcium alginate dressings were applied to all patients in the series ( $n = 305$ ), with a favorable evolution in 97.7% cases, only in 7 cases the lesions being advanced required surgical treatment. The dressings were replaced at 48 h, and the average wound healing time ranged from 21 to 50 days (23 in case of patient D.M., presented in Figure 4).



**Figure 4.** Aspect of wound cicatrisation after hallux amputation by using calcium alginate dressings: a)-after 3 days;b)-after 7 days; c)-after 14 days; d)-after 20 days

For the patients included in the group, the minimum duration of hospitalization was 2 days, the maximum duration of hospitalization was 60 days with an average hospitalization of 13 days and a standard deviation of 7,493 (Figure 5).

The development of an injectable hydrogel for use in wound dressing of the diabetic mellitus foot lesions has given promising results regarding its efficiency in laboratory mouse models. It is a type of dressing prepared by incorporating active nanoparticles of sodium alginate, pectin and calcium chloride.



**Figure 5.** The distribution of cases according to the duration of hospitalization

The use of nanoparticles is highly effective and causes the proliferation of human dermal fibroblasts. Laboratory analyzes showed an increase in the expression of genes associated with inflammation and macrophages, correlated with a favorable cytocompatibility. In the first stage there was an inflammatory response together with the polarization of the M2 macrophage and in the second stage it was extremely efficient in the appearance of the epithelialization buds and wound closure [28- 30].

Sayag et al. (1996) compared an alginate bandage with a dextranomer paste in a controlled study in 92 patients with skin ulcers. They found a minimum 40% reduction in wound size in the alginate group in four weeks, while the dextranomer group took eight weeks to achieve similar size reductions [21].

Schmidt (1986) suggested that calcium alginate may activate or stimulate the wound healing process, as it appeared to promote the growth of fibroblasts in mice. These findings were confirmed by Doyle et al. (1996), who suggested that calcium alginate has an effect on cell proliferation and migration, which was thought to be mediated by the release of calcium ions in the wound bed [12].

Studies in the literature indicate that the residues of alginate fibers remain in the wound for a variable period of time after the dressing has been removed [22-26].

Morgan (1997) describes the alginates like:

- interactive, i.e. produce a medium above the wound, which allows the optimum healing;
- bioactive, i.e. intervene in the cure process by promoting the optimum conditions for wound healing.

The hydrogel-based dressings containing calcium alginate have excellent absorption and moisture microclimate characteristics. However, its poor mechanical characteristics lack of antibacterial properties limits their applicability. Instead there is on the market the hydrogel with biomimetic properties, improved biomechanical characteristics and antibacterial qualities. They use free radicals for synthesis, intensified bacterial cellulose (TOBC) and about 0.0001% by weight  $Zn^{2+}$  added. Such a hydrogel has much improved antimicrobial and biological properties compared to traditional dressings, but the production costs remain high [31- 33].

It is important that the wound must not be ever “clogged” by a dressing, because this might lead to lesion's increasing in profoundness, as the liquid collects under the dressing [18-21].

The basic principles of any dressing are the microbiological tightness. Thus, the development of antimicrobial dressings becomes a necessity. The classic hydro-active dressings based on calcium alginate must be enriched with antimicrobial protection or used in parallel with other specialized dressings in this direction. The antimicrobial action of some counter-cations such as sodium, triethylammonium, tributylammonium and dihexylammonium is scientifically demonstrated. Their efficiency can be quantified by testing their hydrophilicity, linearity, branching structure, molecular weight and loading density. These substances include tributylammonium alginate (TBA-Alg), which has high anti-hemolytic and antibacterial properties, correlated with a cytotoxicity of less than 1 mg / mL (-1). Laboratory testing of tributylammonium alginate dressings has shown to accelerate reepithelialization of infected wounds [35- 37].





## 4. Conclusions

It is essential to ensure the corresponding usage of the dressing, and this can be obtained only by a complete understanding of the lesion's healing process and the way in which the dressings can improve this process. Hydro-active and bioactive bandages for wound dressing require among other features such as high antibacterial action, haemostatic properties, proper mechanical resistance, permeability to water vapor and to allow good gas exchange. These are required to ensure improved blood flow, free radical filtration and an acidic environment in the wound bed. New products appear to have non-toxicity characteristics are non-allergic, biodegradable, biocompatible, biostable. They use a lightweight biological adhesive removed or non-adhesive. Calcium alginate ( $C_{12}H_{14}CaO_{12}$ )<sub>n</sub> in combination with other biomaterials and biomolecules has excellent potential to become a dressing as close to ideal. The correct selection and individualization of the treatment according to the particularities of each case are the key to success in controlling the ulcerative complications of the diabetic foot.

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