

# COMPARING THE EFFECT OF COLACTIVE PLUS AG DRESSING VERSUS NITROFURAZONE AND VASELINE GAUZE DRESSING IN THE TREATMENT OF SECOND-DEGREE BURNS

## COMPARAISON DE PANSEMENTS COLACTIVE® PLUS AG ET NITROFURAZONE/ VASELINE DANS LE TRAITEMENT DE BRÛLURES DU 2ÈME DEGRÉ

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**SUMMARY.** Wound care quality and speed of burn healing are important factors that affect the treatment, prognosis and complications of burns. Burn care is challenging, and the ideal method controversial. The aim of this study was to compare the effects of a new dressing (ColActive dressing) in the treatment of superficial second-degree burns versus traditional dressing including Vaseline and Nitrofurazone. This was a randomized clinical trial study involving 25 cases. A superficial second-degree burn area was divided into two parts in each patient; randomly, traditional dressing was used on one area, and ColActive plus Ag dressing on the other. Every 3 days, after removing the dressings and washing the wounds, wound surface area was evaluated by medical photographic records and J image software. Wound surface area in the two groups was compared before dressing and on the 3rd, 6th, 9th and 12th day afterwards. The difference was not significant before dressing, but significant on the 3rd, 6th, 9th and 12th post-operative day. The difference was significant in both groups, but it was more prominent in the ColActive group ( $p < 0.001$ ) than in the traditional group ( $p < 0.05$ ). Considering the results of this study and good results in previous case reports, ColActive may be more effective than traditional dressing. We suggest a more comprehensive study for a longer period with a larger number of cases to compare other important variables such as scar quality, cost, and pain in the two dressings.

**Keywords:** Nitrofurazone, Vaseline, ColActive Plus Ag, second-degree burn

**RÉSUMÉ.** La qualité des soins locaux et la vitesse de cicatrisation sont d'importants paramètres affectant le traitement, le pronostic et les complications des brûlures. La méthode idéale reste encore à trouver. Le but de cet étude est de comparer un nouveau pansement (ColActive®) au traditionnel nitrofurazone/vaseline sur les brûlures du 2<sup>ème</sup> superficiel. Il s'agit d'une étude randomisée portant sur 25 patients. Les zones de 2<sup>ème</sup> superficiel étaient divisées en 2 recevant, après tirage au sort, l'une ColActive® Plus Ag, l'autre nitrofurazone/vaseline. Après nettoyage, les photographies des brûlures étaient évaluées en utilisant Image J, à l'entrée et à J3, 6, 9 et 12. Les différences étaient significatives à J3, 6, 9, 12 avec une valeur de p plus prononcée ( $< 0,001$ ) dans le groupe ColActive® Plus Ag que dans le groupe contrôle ( $< 0,05$ ). Considérant ces résultats en faveur de l'utilisation de ColActive® Plus Ag, nous suggérons une étude plus globale, sur un nombre plus élevé de patients, comparant aussi la qualité cicatricielle, le coût et la douleur.

**Mots-clés :** nitrofurazone, vaseline, ColActive® Plus Ag, brûlure, 2<sup>ème</sup> degré

### Introduction

Burn injuries are a major public health problem in the world.<sup>1</sup> According to the International Society of Burns, burn is defined as an injury to the skin or other body tissue caused mainly by acute thermal trauma, such as hot liquid, fire, radiation, electricity or friction.<sup>2</sup> According to the World Health Organization (WHO), there were 300,000 deaths worldwide due to burns in 2012, with 96% of these deaths occurring in developing countries.<sup>3</sup>

Boyer classified burns as first- second- and third-degree, according to the tissues affected. Treatment differs according to burn depth. Second-degree burns are those that damage the epidermis and part of the dermis.<sup>1</sup> Superficial second-degree burns

involve epidermis and superficial layers of dermis. The treatment of these burns is conservative.

Burn wound bed preparation is the most important factor affecting the healing of the wound. The care of superficial second-degree burns is controversial, and the ideal method for topical burn care is unknown. The quality of the scar following burns depends on the duration of healing. The aim of care of these burns is to decrease the healing period.

The care principles of burn wounds (wound bed preparation) include the same principles as chronic wound care, which are briefly summed up with T.I.M.E (tissue non-viable or deficient, infection or inflammation, moisture control, epidermal growth), and include early excision, biological control of amount of exudates, prevention of tis-

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sue desiccation and adequate moisture in the wound environment.<sup>4</sup>

The nature of a chronic wound is similar to the burn wound environment in the amount of MMP levels. T.I.M.E for chronic wound care is equivalent to modern and organized care in burn wounds. Applying the principles of chronic wound care to burn wounds has improved patient survival and prognosis.

An ideal dressing should contain a suitable environment including growth factors and MMPs, at the least create exudates, provide appropriate microbial burden and adequate moisture, lead to less pain and be economical and available.<sup>5-8</sup>

Different companies have provided several compounds for dressing wounds. One compound that has recently been introduced is ColActive Plus Ag.<sup>9</sup> It is claimed that this dressing includes components such as collagen, silver ion, CMC (Carboxy Methyl Cellulose), EDTA (Ethylene Diamine Tetracetic Acid) and Alginate and, therefore, is very effective in the care of wounds, chronic and burn wounds in particular. Some case studies report good results following the application of this dressing to chronic wounds such as diabetic foot ulcer, pressure ulcer, venous ulcers, ulcers caused by blood diseases, partial-thickness burn wounds and acute wounds.<sup>10-19</sup>

The most important compound within ColActive dressing is collagen. The effectiveness of other dressings including collagen has been reported in numerous clinical trials on several chronic wounds, second-degree burns, acute wounds and location of donor areas.<sup>20-27</sup> In our centre, the experience of applying this dressing on second-degree burns has been successful.<sup>28</sup>

Considering all this evidence, it seems that this compound is effective in the treatment of burn wounds. However, our review of the available literature did not find any reliable study on the use of this dressing, apart from some case reports.

Nowadays, therapeutic strategies to restore burned tissue are mostly unsatisfactory from an aesthetic and functional point of view. Thus, new therapeutic strategies to reduce the damage caused by burns are necessary.<sup>29,30</sup>

Therefore, this study was designed to evaluate the effectiveness of this compound in the treatment of superficial second-degree burns versus traditional dressing including Vaseline and Nitrofurazone.

## Material and methods

This was a randomized clinical trial study to compare two kinds of dressing in patients with superficial second-degree burns, who were referred to the Shahid Motahari Burn Hospital in Tehran, Iran, from August to December 2015. Twenty-five cases were enrolled in the study. The proposal was explained to the patients, and they chose to participate voluntarily. Informed consent was taken from patients, their parents or their legal guardian. The study was approved by the Ethical Committee of Iran University of Medical Science of the Islamic Republic of Iran (IR.IUMS.REC.1349-24669).

Patients of both sexes, aged between 5 to 40 years, who were referred in the first 24 hours after burn trauma, were included. Exclusion criteria included underlying disease, electrical or chemical burn, and inhalation injury.

A superficial second-degree burn area was divided into two parts in every patient. This was clinically performed by an experienced burn surgeon. Randomly, traditional dressing [Nitrofurazone (Iran Najo Company) and Vaseline

(Salem Company, Iran)] was used on one area and ColActive plus Ag (composed of collagen, sodium alginate and silver ion and EDTA) on the other. For dressing, each area was washed by the conventional method with normal saline. One area was dressed with Nitrofurazone and Vaseline Gauze and the other area with one sheet of ColActive plus Ag as primary dressing. The Gauze was applied on top of primary dressings in both areas and fixed by bands or Surgifix on the face.

The Vaseline and Nitrofurazone dressing was changed once daily, and the other at least once every 3 days. This was done by an experienced burn nurse. Then every 3 days, after the dressings had been removed and the wounds washed, the patients were evaluated by an experienced burn surgeon, who was blind to the type of dressing used, and photographs of the wounds were taken. Wound surface area was evaluated by medical photographic records and J image software. A burn surgeon evaluated the amount of epithelialization and wound healing every 3 days and the remaining wound surface area was measured by image J software (National Institutes of Health, Bethesda, Maryland, USA). Wound infection was evaluated clinically and by culture. The wounds were assessed by two separate surgeons and infectious disease specialists. Wound culture taken during the dressing change was sent for bacterial wound culture testing. There was no sign of wound infection in our patients.

Statistical analysis was conducted by SPSS-16 and using the t test, and results for the two groups were compared.

## Results

In this study, 25 patients with superficial second-degree burns were evaluated. Nineteen patients (76%) were male and 6 patients (24%) were female. Mean age was 14.2±3.1 years. Clinically, there was no infection in the 2 groups. Wound surface area in the two groups was compared in the days before dressing and on the 3rd, 6th, 9th and 12th day afterwards. The difference was not significant before dressing, but significant on the 3rd, 6th, 9th and 12th post-operative day. The wound surface area was evaluated by Image J software. The difference was significant in both groups, but it was more prominent in the ColActive group ( $p<0.001$ ) than in the traditional group ( $p<0.05$ ), as shown in *Table I*.

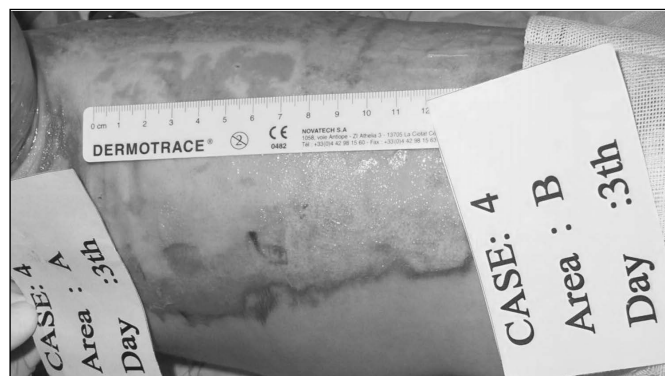
**Table I** - Comparison of wound surface area in traditional and ColActive groups

Time of evaluation	Traditional group (cm <sup>2</sup> )	ColActive group (cm <sup>2</sup> )	T-test (P value)
Before dressing	45.6±9.6	44.1±6.3	0.814
3 <sup>rd</sup> day after dressing	28.2±4.1	15.1±4.9	0.029
6 <sup>th</sup> day after dressing	20.4±5.8	6.7±3.3	0.004
9 <sup>th</sup> day after dressing	14.6±7.6	3±2.1	<0.001
12 <sup>th</sup> day after dressing	11.1±5.8	0.5±1.3	<0.001
Repeated measure test (P value)	P<0.05	P<0.001	

The healing ratio of burn wound area in the 2 groups was also compared. On every day, the difference between the 2 groups was significant. This difference was more prominent from the 9<sup>th</sup> to the 12<sup>th</sup> day, which indicates that ColActive dressing is more effective in the final days of dressing, as shown in *Table II* (Figs. 1, 2 and 3).

**Table II** - Comparison of ratio change of wound surface area with traditional and ColActive dressing

Time of evaluation	Change ratio in Traditional group	Change ratio in ColActive group	P value
3 <sup>rd</sup> day after dressing	38.1%	65.7%	0.016
6 <sup>th</sup> day after dressing	27.6%	55.6%	0.025
9 <sup>th</sup> day after dressing	19.7%	55.2%	0.003
12 <sup>th</sup> day after dressing	23.9%	83.3%	0.001

**Fig. 1** - Traditional dressing and ColActive dressing on first day**Fig. 2** - The same wound on the 3rd day**Fig. 3** - The differences between wound surface area on the 9<sup>th</sup> day

## Discussion

Thermal burn injuries and their consequences are still a major health problem in the world, especially in developing and less developed countries. However, identifying the ideal method to facilitate their healing process is challenging for modern medicine. Many dressings have been introduced by different companies, but the ideal dressing is unknown.

In this study, ColActive plus Ag dressing was compared with traditional dressing including Vaseline and Nitrofurazone. ColActive Plus Ag dressing contains collagen, silver ion, CMC, EDTA and Alginate. All these compounds have been previously applied in different dressings and their effectiveness and safety have been demonstrated. ColActive plus Ag alone includes all these compounds but in different forms, which may increase its effectiveness.

Alginate and carboxymethylcellulose (CMC) have been used in some wound dressings. Alginate and CMC exert an antimicrobial effect due to their gelling properties. Sodium alginate and CMC fibres absorb water and swell, so the spaces between the fibres are closed and bacteria are trapped. Also, the addition of CMC and alginate introduces unique characteristics to the matrix that optimize moisture in the wound bed.<sup>31</sup>

Some dressings include specific antibacterial agents (e.g. silver ions) in their formulation in order to further protect the wound bed from undesired microbial contaminations.<sup>32</sup> Silver-based therapies in the form of silver-impregnated wound dressings and Ag<sup>+</sup> salt solutions have been used to treat acute and chronic wounds. Ionized silver (Ag<sup>+</sup>) is the bioactive form of silver that is capable of reacting with a broad spectrum of biomolecules, including DNA, amino acid residues, and compounds with sulfhydryl groups. Ag<sup>+</sup> elicits cytotoxic effects in microorganisms by inducing physical cell wall damage, enhancing membrane permeability, disrupting ATP production and DNA replication, and generating reactive oxygen species (ROS). Silver is unionized in many dressings but is ionized in ColActive dressing, which may make it faster acting and its application less painful.

Collagen is a natural component of the dermal matrix produced by fibroblasts, and functions as protective scaffolding for migrating epithelial cells in the regenerating skin. Collagen gives the skin its tensile strength and is essential for all phases of wound healing. It attracts fibroblasts and keratinocytes to the wound and encourages debridement, angiogenesis and re-epithelialization.<sup>33</sup>

Collagen dressings stimulate new tissue growth and encourage deposition and organization of newly formed collagen fibres and granulation tissue in the wound bed. The matrix metalloproteinases (MMPs) are zinc-dependent endopeptidases. They are capable of degrading all kinds of extracellular matrix proteins. The collagen in the collagen-based dressings bind to the MMPs found in the extracellular fluid of the wounds and is an alternative collagen source, leaving the body's natural collagen available for normal wound healing.<sup>33</sup> Native collagen does not have any exposed receptor, and should be denatured in wound for its effectiveness. Collagen is native in most dressings except in dressings such as ColActive Plus Ag, ColActive plus, Bio Step and Bio Step Ag, where it is denatured.<sup>34</sup> Therefore, the collagen is faster-acting in these dressings.

Zinc is a cofactor that is required for MMP activity. Ethylene diamine tetracetic acid (EDTA) is a chelating agent that binds to zinc ion with a very high affinity. EDTA permanently deactivates MMPs by binding to the zinc ions of these proteases.<sup>35,36</sup> Therefore, ColActive inhibits MMPs through two means; collagen and EDTA.

In this study, we found that speed of epithelialization was faster with this dressing than with the conventional dressing during all application durations. For example, on the 6<sup>th</sup> and 12<sup>th</sup> day after dressing,  $6.7 \pm 3.3 \text{ cm}^2$  and  $3 \pm 2.1 \text{ cm}^2$  wound surface area in the ColActive group was not epithelialized, compared with  $20.4 \pm 5.8 \text{ cm}^2$  and  $11.1 \pm 5.8 \text{ cm}^2$  in the conventional dressing group. The difference was more prominent in the final days of application. In other words, after the 2<sup>nd</sup> week, this dressing

was more effective than the conventional dressing. The greater effectiveness of this dressing in the first days of application may be due to compounds such as CMC and Alginate, but the increased difference in the final days of application compared with the first days of application may be due to compounds such as collagen and EDTA that inhibit proteases such as collagenase. The concentration of MMPs increases as the wound becomes chronic, but the application of dressings that include collagen decreases MMP concentration. On the other hand, it has been proven that in chronic wounds, as the concentration of MMPs decreases, wound healing improves. This finding has been reported in case reports on a number of chronic wounds, such as diabetic, venous and other types of ulcer.<sup>10-19</sup> This corresponds with our own findings in the final days of application, when the wound became chronic; ColActive dressing was more effective, which may be due to the effects of collagen and EDTA on some proteases such as collagenase.

Due to many confounding factors, we could not compare the cost of the two dressing methods. ColActive is more expensive than traditional dressing, but considering the lower frequency of dressing and faster healing of wounds, it may generally be more cost effective in the long term. The effects of this dressing on scar quality were not compared because of the short period of study, but they may turn out to be better in the ColActive group because of the shorter healing period.

## Conclusion

Considering the findings of this study as well as good results in a number of previous case reports, ColActive may be more effective than traditional dressing. We suggest that a more comprehensive study over a longer period and with a larger number of cases be carried out in order to compare other important variables, such as scar quality, cost, and pain in the two dressings.

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