Chronic wounds need an
ideal microenvironment.

AWC Medical

Wound microenvironment of chronic wounds represents a major therapeutic challenge[1]

Relevant factors that influence the healing process are:

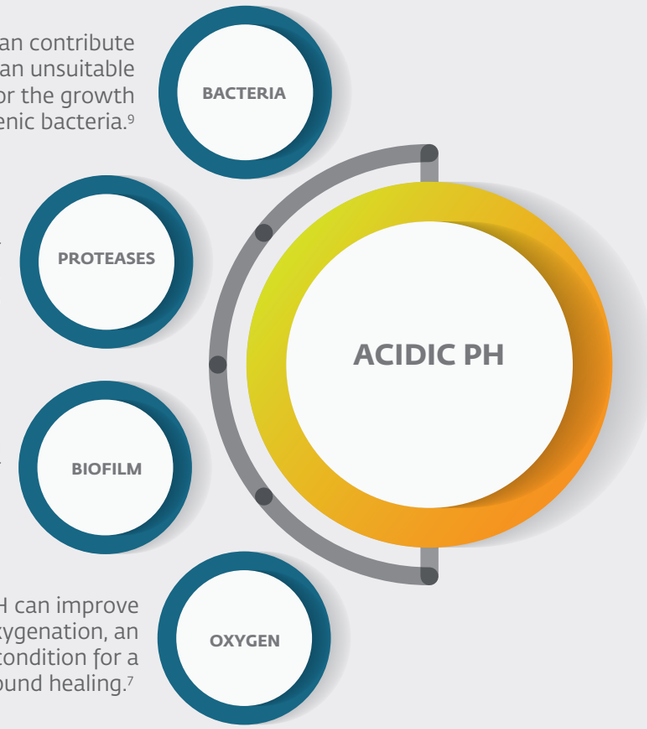
Chronic wounds provide favorable conditions for uncontrolled bacterial growth. Bacterial infection is one of the most prevalent causes for poor wound healing.[9]

Proteases (e.g. MMPs and elastase) play a key role in wound healing but excessive expression can lead to prolonged inflammation and delayed wound healing.[2]

Bacterial biofilm plays an important role in maintaining a prolonged inflammation and increasing tolerance to antimicrobials.[3]

In chronic wounds there is a substantial imbalance between the supply of oxygen and the high- energy demand of the healing tissue. Inadequate oxygenation can delay the wound healing process.[4]

An acidic environment can contribute to reboot healing in a stalled wound:



An acidic pH can contribute to creating an unsuitable environment for the growth of the pathogenic bacteria.[9]

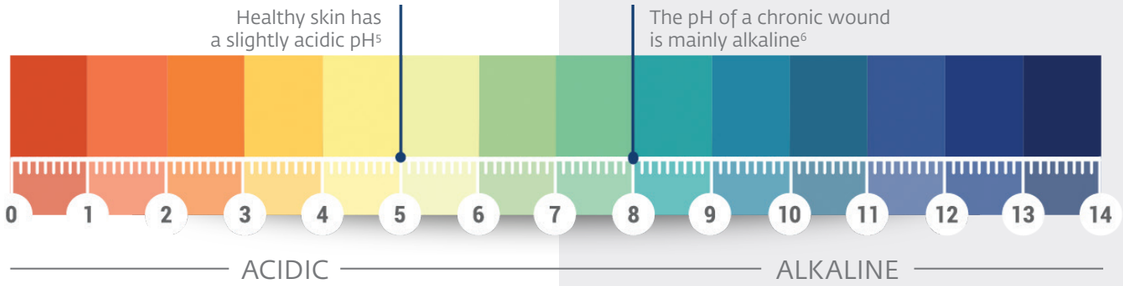
A more acidic environment can reduce the activity of MMPs promoting the physiological healing process.[9]

An acidic environment can reduce the growth rate of bacterial load in the biofilm.[8]

An acidic pH can improve the tissue oxygenation, an essential condition for a successful wound healing.[7]

The importance of pH in the wound healing

Wounds with an alkaline pH have demonstrated lower rates of healing[6]



(1) Kruse CR et al (2015): Wound Repair and Regeneration 23(4): 456–464
(2) Caley MP et al (2015): Advances in Wound Care 4(4): 225-234
(3) Watters C et al (2015): Chronic Wound Care Management and Research 2: 53–62
(4) Castilla DM et al (2012): Advances in Wound Care 1(6): 225-230
(5) Lambers H et al (2006): J Cosmet Sci 2006; 28: 359–370
(6) Gethin G (2007): Wounds UK, 2007:3/3
(7) Greener B et al (2005): J Wound Care 14(2): 59–61
(8) Hostacka˘ A et al (2010): Folia Microbiol. 55 (1): 75–78
(9) Basavraj S et al (2015): Wounds 27(1): 5-11

Our solution

Wound cleansing is performed to remove surface **contaminants, bacteria, non-viable** tissue and excess **exudate** from the wound bed and surrounding skin.[10]

An ideal wound cleanser should modulate the **wound microenvironment** balancing the management of key components with preservation of **tissue safety.**[11]

NEXODYN can support the physiological healing process.

- **Acidic pH: 2.5 - 3.0**
- **The pH value is preserved over the shelf life**
- **High purity** >95% of free chlorine species from hypochlorous acid (HCIO)
- **Free Chlorine species: 40-70 ppm**
- **Long stability** 30 days from first opening

NEXODYN is a FDA-cleared **hypochlorous acid-based wound cleanser**, developed for topical treatment in the field of **acute** and **chronic wound management**

The mechanical action of the fluid flowing across the lesion can help to remove biologic and inert materials such as microorganisms, biological debris and environmental dirt.

(10) McLain N and Moore Z (2015): Cochrane Database of Systematic Review, 4 (CD011167)
(11) Main RC (2008): J Wound Care 17(3): 112-114

Indications

- **Leg ulcers**
- **Diabetic ulcers**
- **Post-surgical wounds**
- **1st and 2nd degree burns**
- **Stasis ulcers**
- **Stage I-IV pressure ulcers**
- **Grafted and donor sites**

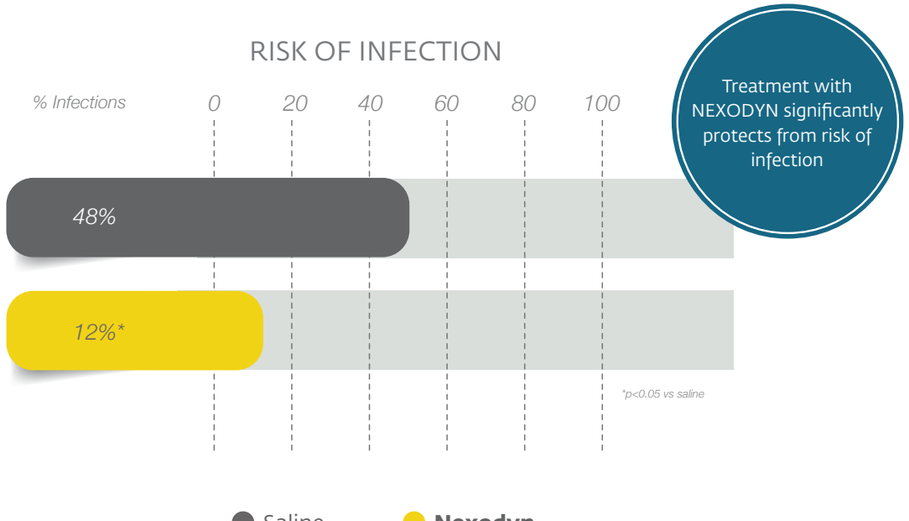
Hypochlorous acid inhibits microbial contamination within the solution. Antimicrobial preservative effectiveness has been demonstrated against the organisms in the table below in *in vitro* testing:

Bactericidal activity tests	**Results**
Time Kill Assay **PSEUDOMONAS AERUGINOSA**	**>99.9999%** (>6.11 Log_{10}) reduction of *Pseudomanas aeruginosa* after 15 second exposure time
Time Kill Assay **ESCHERICHIA COLI**	**>99.9999%** (>5.55 Log_{10}) reduction of *Escherichia coli* after 15 second exposure time
Time Kill Assay **PROPIONIBACTERIUM ACNES**	**>99.9999%** (>6.9 Log_{10}) reduction of *Propionibacterium acnes* after 1 minute exposure time
Time Kill Assay **EXTENDED-SPECTRUM BETA LACTAMASE (ESBL) PRODUCING ENTEROBACTERIACIAE**	**>99.9999%** (>6.23 Log_{10}) reduction of *ESBL-producing Enterobacteriaciae* after 15 second exposure time
Time Kill Assay **MULTI-DRUG RESISTANT (MDR) STAPHYLOCOCCUS AUREUS**	**>99.9999%** (>5.44 Log_{10}) reduction of *MDR-Staphylococcus* after 15 second exposure time
Time Kill Assay **VANCOMYCIN RESISTANT (VR) ENTEROCOCCUS FAECALIS**	**>99.9999%** (>5.87 Log_{10}) reduction of *VR-Enterococcus faecalis* after 15 second exposure time
Time Kill Assay **EXTENDED-SPECTRUM BETA-LACTAMASE (ESBL) PRODUCING PROTEUS MIRABILIS**	**>99.9999%** (>5.99 Log_{10}) reduction of *ESBL-producing Proteus mirabilis* after 15 second exposure time
Time Kill Assay **MULTI-DRUG RESISTANT (MDR) ESCHERICHIA COLI**	**>99.9999%** (>5.92 Log_{10}) reduction of *MDR-Escherichia* after 15 second exposure time
Time Kill Assay **CANDIDA ALBICANS**	**>99.9999%** (>5.01 Log_{10}) reduction of *Candida albicans* after 15 second exposure time

Clinical profile

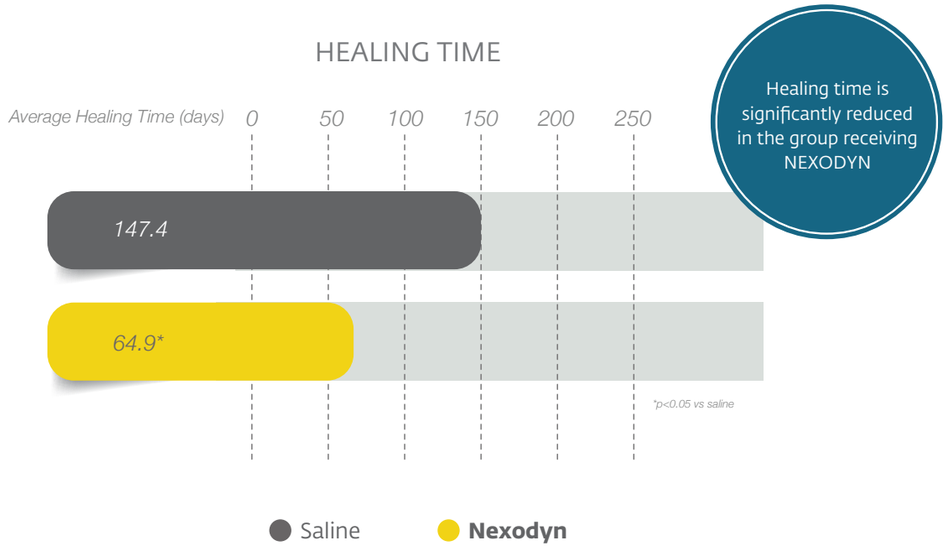
Efficacy

Nexodyn efficacy compared to saline solution



Treatment with NEXODYN significantly protects from risk of infection

A significant and clinically relevant reduction of infection cases was found in the group using NEXODYN [12]



Healing time is significantly reduced in the group receiving NEXODYN

A significant healing time reduction (56%) was found in the group using NEXODYN [12]

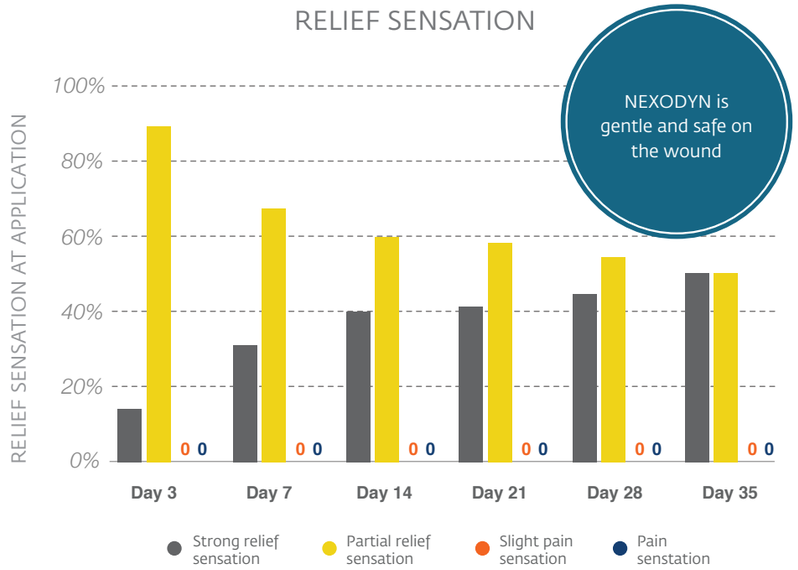
The integration of Nexodyn on top of standard treatment has been assessed in the management of post-surgical, non-ischemic and non-infected lesions of the diabetic foot.

Fifty patients dismissed by the center were observed until complete re-epithelialization or up to 6 months. Visits were perfomed every month, while homecare treatment with Nexodyn for 25 patients was prescribed at each dresssing change. The outcomes were compared with a similar population receiving saline solution, the center's standard of care in this setting[12]

Adapted from (12) L. Abbruzzese et al (2015): Poster [EP283] EWMA 2015

Tolerability

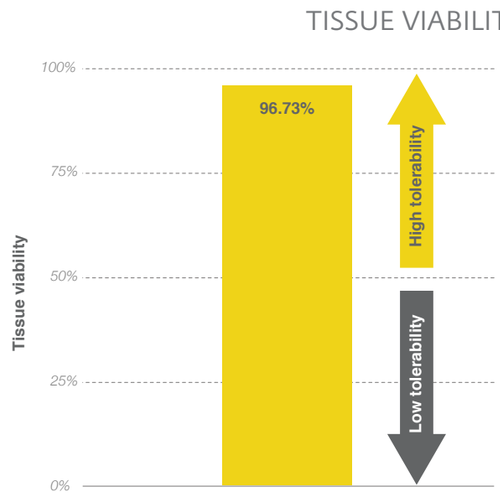
Evaluation of Nexodyn tolerability



NEXODYN is gentle and safe on the wound

After each application of Nexodyn, patients felt a sensation of relief.

A therapeutic scheme consisting of Nexodyn plus a non-adherent gauze and a multipurpose absorbent dressing has been used to evaluate the safety and the performance in critically colonized or locally infected chronic lower leg ulcers. Thirty patients were evaluated weekly for a total of 5 weeks, during which Nexodyn was used once daily until the wound was critically colonized or locally infected. When wounds were not infected, the medication was changed every other day (excluding the weekends).[13]



Tissue viability is preserved with NEXODYN

Citotoxicity was not observed following application of Nexodyn suggesting good skin compatibility.

In vitro metabolic activity assay on 3D-reconstructed human epidermis (measured after 24 h treatment with Nexodyn).[14]

(13) R. Strohal et al (2018): Adv Skin Wound Care 31(4): 163–171
(14) Adapted from D'Atanasio N et al (2015): Wounds 27(10):265-273

How to use NEXODYN™

Applying NEXODYN™ on wounds is **fast** and **simple**

1 At each application, the whole lesion area should be abundantly sprayed with Nexodyn.

2 The solution should be allowed to dry. No rinsing required.

3 A second application of Nexodyn can be consecutively repeated, if necessary.

4 The solution should be allowed to dry. No rinsing required.

5 Shortly after last cleansing with Nexodyn™, standard therapy can be applied as required.

Contraindications: Do not use in case of hypersensitivity to any component of the product (hypochlorous acid, chlorine and hypochlorite ion)

NEXODYN
Nexodyn™ Antimicrobial Wound Care Solution

NEXODYN™
Antimicrobial Wound Care Solution
3.5 fl. oz. (100 ml) spray
12 bottles/case
Product code: 21204

This document is addressed to HCPs only

The data presented in this material relate to medical devices that are referred to by different product names, according to the market concerned. The products that are the subject of the presentation are produced using the same technology of Nexodyn Antimicrobial Wound Care Solution, which has been FDA-cleared for marketing in the US. Please note that the clinical use of the products as described in this material may not be in accordance with the indications for use cleared by FDA. US clinicians should, therefore, check the cleared indications statement for the product before prescribing

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