Is Nitric Oxide the Next Big Thing in Wound Care?

Nitric Oxide (NO) has numerous benefits for wound healing but has challenges associated with its delivery. Several companies are addressing those challenges and creating an exciting opportunity in wound care.

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Nitric oxide (NO) was named "Molecule of the Year" by the journal *Science* in 1992, and six years later, three US scientists were awarded the Nobel Prize for Physiology and Medicine for their efforts to prove that NO, an endogenous gas and free radical, could have crucial biological effects. One of the well-known medical uses of NO is via nitroglycerin, a precursor to NO, to prevent and treat chest pain (angina). It works by relaxing blood vessels, which decreases the amount of work the heart has to do. NO has been identified for its value in chronic wound healing for many years because of its function in vasodilation, relaxing blood vessels and increasing blood flow, as well as its broad-spectrum antimicrobial and antibiofilm activity.

No products have yet reached the market for chronic wounds; however, *SmartTRAK* has noted increasing activity related to the benefits of NO for wound healing. In fact, an article was published earlier this year entitled "Emerging Strategies for Nitric Oxide Production and Their Topical Application as Nano Dressings to Promote Diabetic Wound Healing." The article identified four primary modes in which NO benefits the diabetic wound healing process: providing antimicrobial properties, promoting angiogenesis, regulating inflammation and promoting tissue regeneration and remodeling. This article will discuss the challenge of bringing NO products to market, the commercial and clinical activity to date, and the surge in intellectual property related to this potentially exciting new technology/product offering.

The Challenge

Research has shown that when NO is appropriately activated and sustained in the body, it improves oxygen and nutrient delivery and is anti-pathogenic, aiding in the wound healing process. Several years ago, 3M (now Solventum) researchers published an article, "Nitric oxide levels in wound fluid may reflect the healing trajectory," in which their data analysis

demonstrated that the amount of NO metabolites in a wound can discriminate between worsening and progressing wounds. Low levels of NO can be attributed to age and/or concomitant disease, creating a challenge for the wound to overcome the inflammation stage, resulting in the creation of a chronic wound.

A solution could be a device to supply the wound with additional NO; however, the delivery of NO has significant challenges due to its short half-life and its tendency to instantaneously react with ambient oxygen to form nitrogen dioxide (NO 2), which in turn can further complicate the storage, transportation and wound site application of NO. In addition, the diffusion of NO directly into the wound poses additional challenges.

Despite the challenges associated with NO, the market potential in wound care is significant, with the initial opportunity to exceed $1.0B in the antimicrobial segment, and several manufacturers have NO technologies in different stages of research, development and commercialization. Companies closest to bringing a NO-based product to market include Convatec, NOxy Health Products and Nytricx.

Commercial Activity

In April 2023, Convatec acquired 30 Technology's wound care platform for a total consideration of up to $220MM (£176MM). The UK-based company developed a NO-generating technology platform representing a unique natural antimicrobial and antibiofilm mode of action. In April of this year, Convatec announced the EU and UK regulatory approval of ConvaNiox, a multimodal NO-generating antimicrobial and antibiofilm dressing. The dressing will be available for DFU patients in France, Germany, Italy, Poland, Spain and the UK later this year as part of an initial market launch. Convatec will be pursuing FDA regulatory clearance for the product in the US.

In contrast, NOxy Health Products is taking a more ambitious route by pursuing full IND approval—a longer and more resource-intensive regulatory path. This strategic decision is driven by the potential to unlock a broader set of indications, secure differentiated reimbursement and establish a high barrier to entry for future competitors. In addition to the IND pathway, NOxy's portfolio is broad enough to support additional, near-term regulatory pathways as well. This dual strategy positions the company for both early market entry and durable long-term leadership, with the potential for expanded clinical impact across multiple indications.

Nytricx received $1.1MM in funding from the Department of Defense (DOD)/US Army to develop a dressing that provides homeostasis in traumatic injuries with a NO-driven antimicrobial dressing combined with a rapid blood clotting agent. The company will now progress (with additional funding being sought from the National Institutes of Health (NIH), Department of Defense (DoD) and Biomedical Advanced Research and Development Authority (BARDA) into final development of the NO containing dressing. The company's commercialization plan is to apply for FDA clearance of its NO-releasing wound dressing via a De Novo regulatory pathway.

These companies are also working to further validate their NO technologies through different studies and clinical activity.

Clinical Activity

At this year's spring SAWC meeting, Convatec presented two posters related to further analysis of the ProNOx1 randomized controlled study (RCT) that was published in 2018, and NOxy Health presented a case series. One additional company, Nytricx, presented pre-clinical data in collaboration with the University of Miami.

Convatec

CR-047: A post-hoc analysis of the ProNOx1 RCT of a NO-generating wound dressing (NOGD) compared to standard of care (SoC) was performed on 124 patients with diabetic foot ulcers (DFUs). This analysis aimed to determine the impact of NO-generating wound dressing on DFU healing outcomes in patients receiving antibiotics at commencement and/or during the study. Mean percentage area reduction (PAR) was 4.5-times greater in this NOGD population than in the SoC population. Full (100%) PAR was 37% in this NOGD population compared to 15% in this SoC population.

CR-043: A post-hoc analysis of the ProNOx1 RCT of a NO-generating wound dressing compared to SoC was performed on 149 patients with diabetic foot ulcers (DFUs). The primary objective was to determine the impact of utilization of NOGD on complete wound healing that is dependent on the presence or absence of wound infection/laboratory diagnosed microbial contamination and wound age. Healing rates in infected/contaminated DFUs at 12 weeks were 36% versus 21% for NOGD and SoC arms, respectively. At 12 weeks, healing rates in DFUs 12 weeks of age were 46% versus 24% for NOGD and SoC arms, respectively. Healing rates for DFUs >12 weeks of age were similar between both groups.

Convatec continues to build the clinical evidence pipeline for this technology.

NOxy Health

CS-067: A registry-based study assessing the application of NOxy Health's over-the-counter NO delivery foam in 21 skilled nursing facilities to treat various wound etiologies and severities, including DFUs, pressure ulcers, venous leg ulcers and arterial ulcers. Results showed that 81% of 79 cases healed in a mean time of 14 days.

NOxy Health is also running a Phase 1 clinical study of NOX1416 as an adjunct to SoC in the treatment of chronic, non-healing DFUs. The study will enroll 40 patients and assess the safety and efficacy of NOX1416 (a foam-based gaseous NO product where NO is delivered topically through a microbubble foam) in the treatment of non-healing DFUs. The primary outcome is the

number of patients with Methemoglobin > 5% and adverse events at 12 weeks. Estimated study completion is June 2025.

Nytricx

LR-021: A study of the anti-microbial efficacy of silicone-based NO-releasing wound dressings developed by Nyticx in a dermal porcine wound model using 108 dermal wounds and determined that NO rapidly decreased wound bacterial count significantly, suggesting an important advance in the treatment of infected wounds.

In addition to Convatec, Noxy Health and Nyticx, several companies have published and issued patents related to the use of NO for the treatment of chronic wounds that could potentially make NO the next big thing in wound care.

A Surge in Intellectual Property

SmartTRAK monitors published and issued patents on a daily basis. Smart dressings and negative pressure wound therapy devices have dominated the intellectual property activity; however, in the past year, *SmartTRAK* has noted significant activity related to the delivery of NO for the treatment of chronic wounds. See Figure 1.

As shown in Figure 1, NOxy Health has the lead in intellectual property with eight patents published or issued in the past year. The company is based in Montana and was established in 2019.

Following Noxy is NitricGen, which has two issued and one published patent related to the generation of NO in controlled and accurate amounts. *SmartTRAK* reached out to NitricGen and learned they are no longer pursuing NO in wound care. They are focused on inhaled indications and have licensed their technology to Beyond Air Inc.

Smith+Nephew, a global market leader in Advanced Wound Care, follows with two published and one issued patent, both related to multi-layer dressings for the delivery of NO.

SaNOtize has developed NO-releasing compositions for a nasal spray and a foot cleanser that locally release NO concentrations with potential antimicrobial effects against viruses, bacteria and fungi.

Two companies not included in the above figure are Convatec, which acquired a NO-generating wound dressing technology, and Nytricx. *SmartTRAK* had the privilege of talking with both companies at the Symposium on Advanced Wound Care (SAWC) Spring Poster session this past May.

Figure 1. Recently Published or Issued Patents Related to the Use of Nitric Oxide in Wound Care

Intellectual Property Activity from Jan 2024 thru April 2025				
Affilitiation	**Title**	**Published**	**Issued**	**Number**
Albert Einstein	Approach to Sustained Production and Delivery of Nitric Oxide and S-Nitrosthiols	x		2.024E+10
Imagine Pharma	Compositions and Methods for Treating Wounds	x		2.024E+10
Marquette Univ	Composite Materials Containing Sturctural Polymers and Photoreactive NO...		x	11986562
NitricGen	Apparatus and Method for Generating Nitric Oxide in Controlled and Accurate Amounts		x	12139401
	Apparatus and Method for Generating Nitric Oxide in Controlled and Accurate Amounts	x		2.024E+10
	Apparatus and Method for Generating Nitric Oxide in Controlled and Accurate Amounts		x	11945719
Noxy Health	Nitric Oxide Containing Foam Formulation For Topical Medical Use	x		2.025E+10
	Nitric Oxide Formulation Delivery Device and Method of Use	x		2.024E+10
	Nitric Oxide Topical Application Apparatus and Methods		x	12150953
	Topical Pharmaceutical Skin Composition for the Delivery of NO in Combination With Other	x		2.024E+10
	Nitric Oxide Topical Application Apparatus and Methods	x		2.024E+10
	Nitric Oxide Delivery Device for Healing Skin Wounds	x		2.024E+10
	Nitric Oxide Formulation Delivery Device and Method of Use	x		2.024E+10
	Adhesive Nitric Oxide Delivery Bandage for Skin Condition Healing			2.024E+10
Regents Univ of MI	Two-part Nitric Oxide Generating Topical Composition		x	11998513
SaNOtize Corp	Nitric Oxide Releasing Compositions		x	11945719
	Nitric Oxide Releasing Compositions		x	12252398
	Nitric Oxide Releasing Compositions	x		2.024E+10
Smith + Nephew	Wound Dressing Apparatuses and Methods for Nitric Oxide Delivery	x		2.024E+10
	Wound Dressing with One or More Composite Layers	x		2.025E+10
	Wound Dressing		x	12290627
Solventum/Systagenix	Nitric Oxide Producing Collagen/ORC Dressing		x	12234228
TO2M Corp	Multilayer Device for Supplying Nitric Oxide	x		2.024E+10
Univ of Georgia	Mesoprous Nitric Oxide-Releasing Silica Particles, Methods of Making and Uses Thereof	x		2.024E+10
Univ of NC	Extended Nitric-Oxide Polymers via Funcationalized Nanoparticles		x	12257314
Univ of North Texas	Nitric Oxxide Donor and Anti-oxidant Compounds"		x	12234228

Sources: SmartTRAK Business Intelligence. US Patent & Trade Office.

Convatec's intellectual property is listed below.

- WO2014188174 – Dressing system (two-layer system comprising a layer containing a nitrite and a hydrogel that contains hydrogen ions)
- WO2014188175 – Transdermal delivery system (two-layer system comprising a layer containing a nitrite and a hydrogel that contains hydrogen ions, with a pharmaceutically active agent in either layer)

Nytricx has three issued patents listed below and seven other pending published applications.

- US Patent – Surfaces and coating compositions having antifouling, antithrombotic and antibacterial properties and methods of making. 11,370,934
- US Patent – NO releasing surfaces for decreased fouling, thrombosis and infection of medical devices. 12,016,974
- US Patent – Disinfection device. D1,066,723