

FONDAZIONE ISTITUTO ITALIANO DI TECNOLOGIA

A TECHNOLOGY TEASER

WOUND DRESSING MATERIALS



Released on May 2015

NEW MATERIALS

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- promotes and develops scientific and technological excellence, both directly, through its multi-disciplinary research laboratories, and indirectly, through a wide collaboration with national and international laboratories and research teams;*
- carries out advanced training programs as a part of wider multi-disciplinary projects and programs;*
- fosters a culture based on sharing and valuing results, to be used in order to improve production and for welfare-related purposes, both internally and in relation to the entire national research system;*
- creates technological understanding about components, methods, processes and techniques to be used for the implementation and interconnection of innovative products and services, in strategic areas for the competitiveness of the national production system;*
- pools research scientists operating in various research institutes and establishes cooperation agreements with high-level, specialized centers;*
- promotes interactions between basic research and applied research facilities, encouraging experimental development;*
- spreads transparent, merit-based selection mechanisms for research scientists and projects, in compliance with globally approved and established criteria.*

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EXECUTIVE SUMMARY

Two distinct technologies targeting wound management applications are currently being developed at IIT. Both technologies use exclusively natural polymers as vehicles for the delivery of active therapeutic agents that, in turn, can be both synthetic or natural.

The first technology deals with the production of flexible polymeric films of sodium alginate (NaAlg) that incorporate either the traditional antiseptic povidone iodine complex (PVPI or betadine), or essential oils as natural antibacterial and antifungal agents. The composite films are easily manageable, demonstrate remarkable flexibility, homogeneous dispersion of the incorporated active ingredients and, most importantly, have highly efficient antimicrobial and antifungal properties due to the controlled release of the active agents to the wounds. They can be easily adapted to large areas as wound dressings or to internal wound treatment for slow drug release.

The second technology deals with the production of nanofibrous mats of natural polymers that are envisioned for wound dressing. The nanofibers are produced by the electrospinning technique. The huge surface area of these fibers and the nano/microporosity of the mats are very advantageous for wound treatment. This technique has been used for the production of nanofibers of NaAlg. Although NaAlg is increasingly used in wound management, the use of nanofibers of these polymers is strongly limited by their very rapid degradation in aqueous environments. For this reason, IIT has developed a strategy for enhancing the stability and controlling the degradability of alginate-based nanofibers for up to a couple of weeks. The produced mats can incorporate the active agents described above. Finally, we have produced electrospun nanofibrous mats of the natural polymer cellulose acetate encapsulating essential oils (cinnamon, lemongrass and peppermint), as natural antimicrobial agents, that have shown a very effective inhibition of *E. coli* growth. In this case, the nanofibers do not biodegrade in contact with the wounds, but slowly release the incorporated essential oils due to their porous nature. In all cases the fibrous constructs have been proved to be highly biocompatible.

The two wound dressing technologies mentioned above are at different stages of R&D, with the alginate/PVPI composite material in a more advanced phase of development. They can represent a unique opportunity for a healthcare company to boost and extend its pipeline in wound management, or to enter a new market segment for a generic medical device company. Accordingly, IIT assets appear well positioned for an out-licensing strategy, providing the licensee partner with the ability to take care of the late stage development, CE certification, scale-up and production processes. The licensee should guarantee a high probability of market success based on a consolidated marketing & distribution organization able to reach hospitals and pharmacies with novel OTC products. A licensing strategy based on milestone payments (e.g., upfront, CE certification, completed scale-up) and subsequent royalties on net sales can be envisaged.

INTELLECTUAL PROPERTY

PCT International Publication #	WO 2013/140362A1 - 26 September 2013
Priority Application #	TO2012A000258 - 21 March 2012
Regional Patent Applications filed	Nationalized in EU, US, CA, JP on 21 September 2014
Applicant	Fondazione Istituto Italiano di Tecnologia
Inventors	Athanassia Athanassiou, Ilker Bayer, Ioannis Liakos, Loris Rizzello, Roberto Cingolani, Stefania Sabella, Pier Paolo Pompa
Title	Polymeric composite materials with antimicrobial and biodegradable properties and use thereof

Short Description

Povidone Iodine (PVPI) is a well-known broad spectrum antiseptic for wound treatment and irrigation. PVPI, however, is a very hydrophilic substance having poor resistance against water. Wound treatments with PVPI are, therefore, short lived. We have developed a simple and inexpensive method to directly incorporate PVPI in alginic (sodium & calcium) polymer matrices to enable its slow and controlled release into infected areas. The process also prolongs antiseptic effects of PVPI considerably. Aqueous PVPI solutions are blended with sodium alginate solutions at any proportion from which films can be cast. Droplets or continuous liquid streams of the blend solutions can be cross-linked in calcium salt solutions to form PVPI encapsulated beads and fibers.

Priority Application #	TO2015A000055 - 26 January 2015
Applicant	Fondazione Istituto Italiano di Tecnologia
Inventors	Hadi Hajiali, Ilker Bayer, Elisa Mele, Jose Heredia Guerrero, Athanassia Athanassiou
Title	Procedimento di insolubilizzazione di alginato

Short Description

This invention describes a method to produce alginate-based micro- and nanostructures, conferring them controlled stability over time in aqueous media and adjustable biodegradability. To this end, trifluoroacetic acid (TFA) and its derivatives are used.

IIT TECHNOLOGY

Antimicrobial and Biodegradable Composite Materials

The technology relates to a new antiseptic and biodegradable composite material, comprising povidone-iodine complex (PVPI) and alginate, and to medical devices produced with the use of the above mentioned composite material. PVPI is a stable chemical complex of polyvinylpyrrolidone (PVP) and elemental iodine (9 to 12%).



Figure 1. Wound area covered by PVPI and gauze (left); PVPI applied to an abrasion using a cotton swab (right)

Beside its wide use as a skin antiseptic, PVPI is also used for burns, infections, large wounds, deep tissues, or mucosa (Figure 1).

In the bandage field, products for wound dressings are particularly available using PVPI as an active antimicrobial ingredient in combination with polymeric substances, such as PEG (see for example the commercial product INADINE™ by Johnson & Johnson). Whereas PEG has the drawback to be a synthetic, non-biodegradable polymer, IIT technology provides new biodegradable substrate materials suitable for controlled release of PVPI, consisting of a matrix of sodium or calcium alginate in which PVPI is dispersed; alginate provides a healing effect, while PVPI provides an antiseptic effect.

An alginate wound dressing is a natural wound dressing material derived from different types of algae and seaweeds. These types of dressings are best used on wounds that have a large amount of exudates. They have been successfully applied to cleanse a wide variety of secreting lesions. The high absorption is achieved via strong hydrophilic gel formation. This limits wound secretions and minimizes bacterial contamination. Alginate dressings maintain a physiological moist microenvironment that promotes healing and the formation of granulation tissue. Alginates can be rinsed away with saline irrigation, so removal of the dressing does not interfere with healing granulation tissue; this makes dressing changes virtually painless. Alginate dressings are very useful for moderate to heavily exuding wounds. Brand names on the marketplace are: Sorbsan™, Tegagen™, Kaltostat™, Algosteril™ and Comfeel Alginate™.

Special aspects of IIT invention are depicted in Figure 2. The technology aims at: a) providing a medical device in the form of a self-supporting film for PVPI release, useful as antiseptic dressing for wounds; b) providing antiseptic filling systems, for internal and external use, of open wounds, particularly in the form of microcapsules; c) providing medical devices in the form of antiseptic and biodegradable surgical suture threads; these sutures have antimicrobial properties and will significantly reduce the chances of wound infection after a surgery. Moreover, such sutures are biodegradable and hence very ideal for patients who either cannot return to the hospital for suture removing or underwent internal surgery. In such cases the sutures will stay in the body tissues long enough to allow healing and then degrade themselves without leaving any unwanted material or needing another procedure; d) providing biodegradable antimicrobial

coatings or packaging materials for medical devices, since the composite material may comprise plasticizers suitable to confer to the composite material the appropriate mechanical properties for their use of interest.

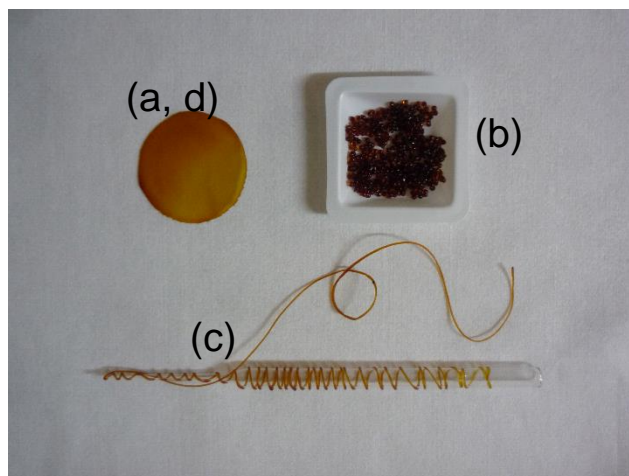


Figure 2. Films for wound dressings or biodegradable antimicrobial coatings or packaging materials for medical devices (a, d); Beads for open wound surgeries (b); Surgical sutures (c)

Slow and controlled release of PVPI into open wounds is highly desired in clinical applications due to the fact that internal wounds treated directly with aqueous solutions of PVPI complex can lead to lethal dose of iodine absorption by the wound. Preferably, the composite material does not comprise other polysaccharides beside alginate in order to avoid the formation of liquid systems with PVPI and thus give rise to deteriorations, losses or infiltrations, optionally by increasing the patient's glycemic index.

Accordingly, biodegradable free standing antimicrobial films suitable for wound dressing applications were developed by blending water dispersions of sodium alginate (NaAlg) and PVPI. The plasticity of the films was controlled by adding glycerol. Various amounts of antiseptic PVPI was incorporated into the NaAlg matrix.

Based on a review of other patents incorporating antiseptic agents such as PVPI, existing technologies do not explicitly report incorporation of PVPI in alginate polymers in the form of films, beads or fibers, but rather gel-like matrices such as polyethylene glycol (PEG), which is a synthetic and non-biodegradable polymer. Alginate has the advantage of being natural, biocompatible and biodegradable at the same time. Additionally, these alginate-PVPI blend systems can be used for diabetic ulcers or for people with diabetes, since the alginate polysaccharides are known not to enhance the diabetic conditions but rather regulate and control them.

In conclusion, the alginate-PVPI system developed at IIT is a wound dressing material that has proven antimicrobial properties in addition to its wound healing potential due to sodium or calcium alginate. Other dressings mentioned in the relevant patents from the prior art do not target antiseptic properties, but rather have been developed for use as a protective and healing assistant barrier for the wound against the external environment; however, microbial organisms are likely to grow on such dressings risking an infection to the wound and hence deteriorate the healing mechanisms of the immune system. Hence, the present sodium/calcium alginate-PVPI composites in the form of film membrane, beads and sutures can indeed overcome such microbial problems and offer an alternative to the available wound healing dressings and surgical suture procedures.

A side by side comparative study of the alginate-PVPI system developed at IIT with the standard of care INADINE™ by Johnson & Johnson has been conducted in the mouse model of full thickness skin excisional

wound. In this model, male mice (C57BL/6J, weighing 22-24 g) were individually anesthetized using an intraperitoneal injection of ketamine (10%) and xilazine (5%), and the dorsal surface were shaved and rinsed with an alcohol swab. A full-thickness excisional wound of 1 cm² was induced in each animal. Mice (n=5 per group) were dressed with IIT alginate-PVPI film or INADINE™, and then covered with TEGADERM™ (only for the first 3 days) to prevent the mice from removing the dressing. After 3 days, IIT alginate-PVPI film and INADINE™ dressings were applied once a day for two consecutive days and then left in place up to the end of experiments, while untreated wounded animals were left uncovered. Animal wounds were photographed regularly for at least 12 days (Figure 3). Wound closure was calculated as percentage based on wound size relative to the original wound dimensions.

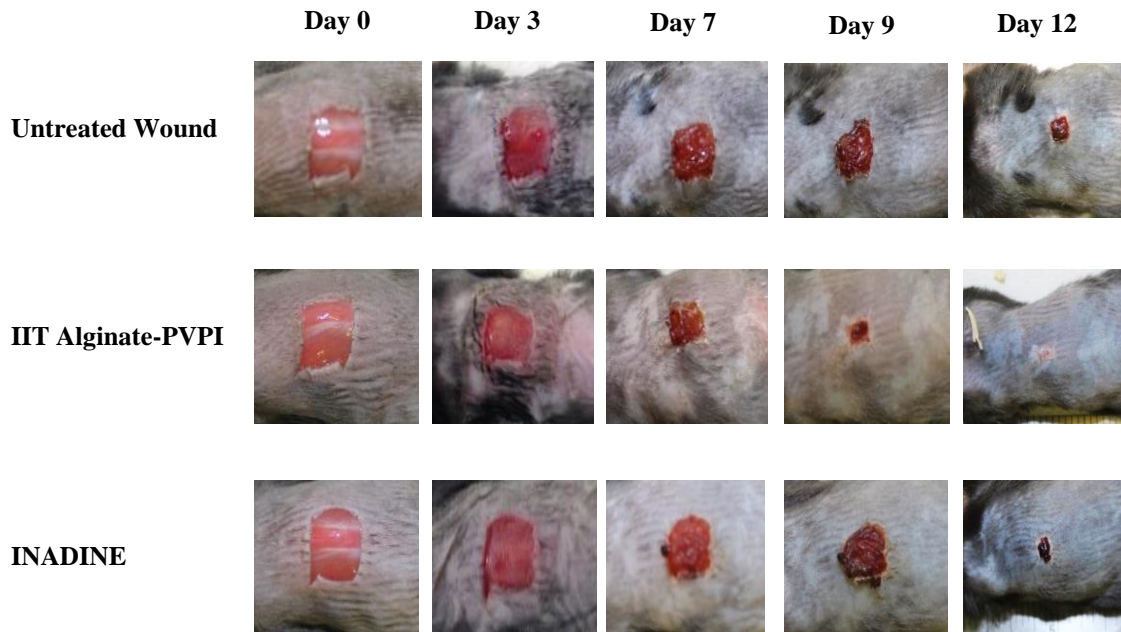


Figure 3. Pictures of the skin wound from the three groups of animals at various time points after surgery

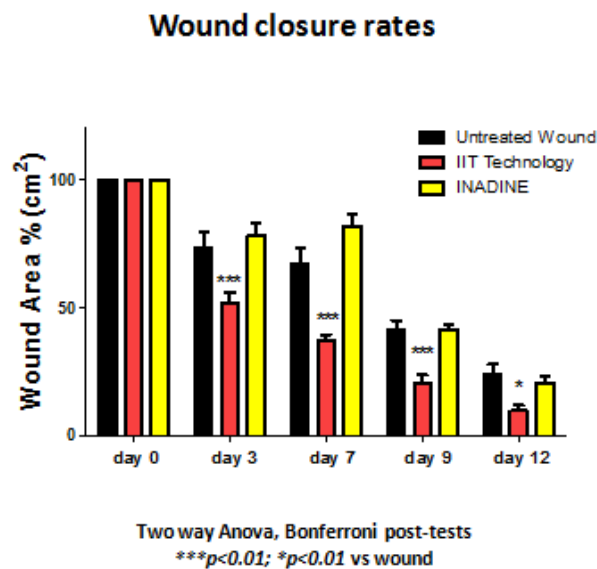


Figure 4. Wound closure rates represented as percentage of reduction in wounded area at different times after surgery

Wound closure was analyzed as the percentage of the reduction in wounded area at day 0, 3, 7, 9, and 12 (Figure 4). IIT alginate-PVPI film treated animals showed more significant wound closure than INADINE™ and untreated-wounded animals at each time points considered. Specifically, the size of the wound was decreased more rapidly in the IIT alginate-PVPI film treated group compared to the other groups. Interestingly, wound closure was achieved within 12 days only in the IIT alginate-PVPI film treated group. These results indicate that the full thickness wounds were more rapidly healed in the IIT Technology film treated group and suggest that IIT alginate-PVPI film treatment should be even more effective in reducing the size of the wound compared to INADINE™.

Overall, the novelty of this technology can be summarized as PVPI has been encapsulated into alginate-based natural polymers for the first time, forming a mechanically stable antiseptic material suitable for controlled drug release. This allows stable encapsulation of PVPI liquid in alginate-based polymers in any desired quantity expanding use of PVPI liquids in the biomedical field. The same technology can be used for the encapsulation of antibacterial and antifungal essential oils in the alginate films instead of PVPI.

Electrospun nanofibres for Wound Dressing

Electrospinning, namely the extrusion of polymer fibres by means of high electric fields (Figure 5), is an interesting technology for the development of innovative biomedical devices for wound care. In fact, in this sector the ultrafine size of the electrospun fibres guarantees:

- mechanical flexibility and consequently excellent conformability of the non-woven mat to the wound site;
- complete coverage of the injured tissue and protection against infections and dehydration, as well as thermal insulation;
- permeation of gases, transport of nutrients, retention of moisture and absorption of exudates, thanks to the high porosity of the electrospun mesh;
- adhesion, proliferation and differentiation of cells during tissue regeneration;
- delivery of drugs (e.g. antioxidant, anti-inflammatory and antimicrobial agents) to the wound.

IIT technology uses polymers derived from **natural sources**, such as alginate, cellulose and chitosan, for the production of functional nanofibers with controlled size, morphology and degradation rate. These biopolymers offer remarkable advantages in terms of biocompatibility, biodegradability and environmentally friendliness.

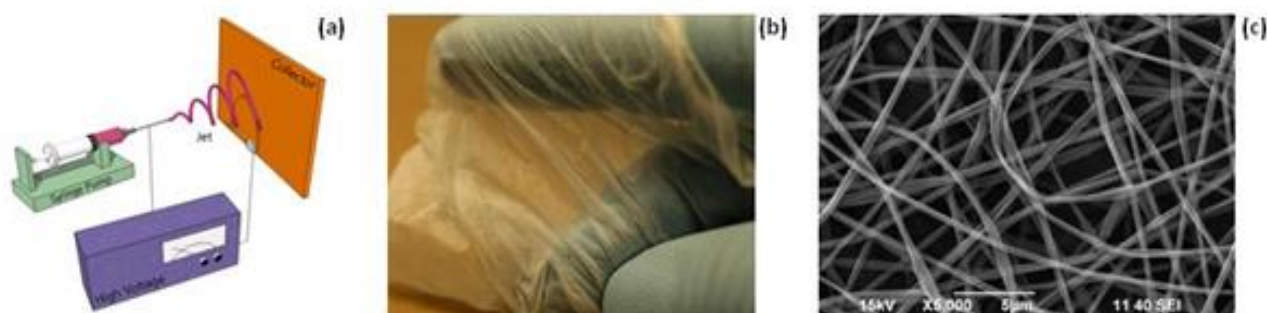


Figure 5. (a) Electrospinning apparatus consisting of a syringe pump for the delivery of the polymer solution and a plate for the collection of the fibres. The high voltage is applied between the metallic needle and the collector. (b) Photograph of an electrospun mat and (c) corresponding scanning electron microscope (SEM) image.

Alginate Nanofibers with controlled degradation rate

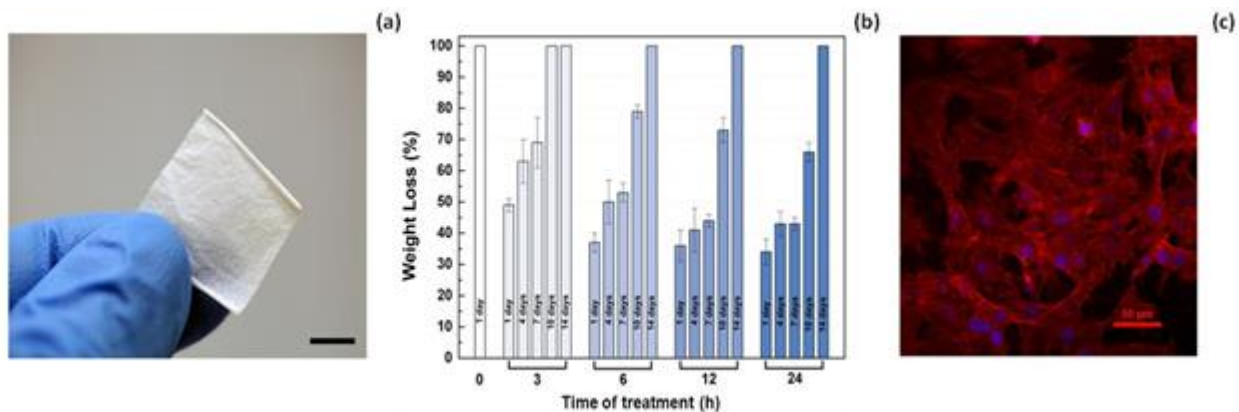


Figure 6. (a) Photograph of the nanofibrous scaffold; scale bar = 0.5 cm. (b) Analysis of the biodegradation properties of the alginate nanofibres after the acidic procedure at different time intervals (3, 6, 12 and 24 hours). The weight loss of the samples was measured after 1, 4, 7, 10 and 14 days of PBS incubation under physiological conditions (37°C, pH 7.4). (c) Fluorescence micrographs of DAPI (nucleus) and phalloidin (actin filaments) stained fibroblast cells, cultured on the treated alginate nanofibres.

Alginate is a polysaccharide derived from brown algae that exhibits excellent biocompatibility, low toxicity, non-immunogenicity, and relatively low cost. It finds application in tissue engineering for skin, nerve, bone and cartilage regeneration, and in the drug delivery systems. Due to its high water solubility, the corresponding nanofibers are poorly stable in aqueous environments, and their real applicability in biomedical sectors is strongly limited. IIT has developed and patent protected the know-how to stabilize alginate nanofibers in aqueous environments. Nanofibers of sodium alginate with a diameter of 80 nm are fabricated by the electrospinning technique and then treated with trifluoroacetic acid (TFA). The acid soaking induces a chemical modification of the nanofibers' structure while maintaining their shape and network organisation (Figure 6a). By acting on the duration of the TFA treatment (from 3 to 24 h), the degradation rate of the electrospun alginate constructs can be controlled under physiological conditions (in buffer saline solution at 37 °C). As shown in Figure 6b, the alginate fibers not exposed to TFA completely dissolved after 1 day (100% weight loss). On the contrary, the TFA-treated samples are characterized by a slower degradation. For instance, when the TFA procedure is extended up to 12 and 24 hours, the degradation time of the electrospun samples is of 14 days, with a high structural stability in the first 7 days (weight loss of around 43%). Moreover, the treated fibrous scaffolds are highly biocompatible (Figure 6c). Therefore, cytotoxic compounds are not contained within or released from the electrospun mats.

Sodium alginate nanofibers have been used to treat skin inflammations and burns. Tests on animal models (mice) reveal that sodium alginate fibers possess significant anti-inflammatory properties. A region of the skin of shaved animals was exposed to UV-B light and the level of the inflammatory cytokines (IL-6 and IL-1 β) was detected after different time points (6, 24, 32, 48, and 96 hours). Surprisingly, as shown in Figure 7, after 24 hours the animals treated with the electrospun mats exhibit a production of IL-6 (Figure 7A) and IL-1 β (Figure 7B) that is 4 and 10 times smaller than the untreated ones and comparable with the naïve mice (not exposed to UV light), respectively.

The effect of the alginate nanofibers is even more evident after 48 hours, when the level of IL-6 and IL-1 β for the treated animals is more than 7-25 times smaller than the untreated group, respectively. Moreover, the anti-inflammatory activity of the electrospun nanofibers is comparable, if not even better, with that of commercially available biomedical devices based on alginate microfibers (Tegaderm™, 3M).

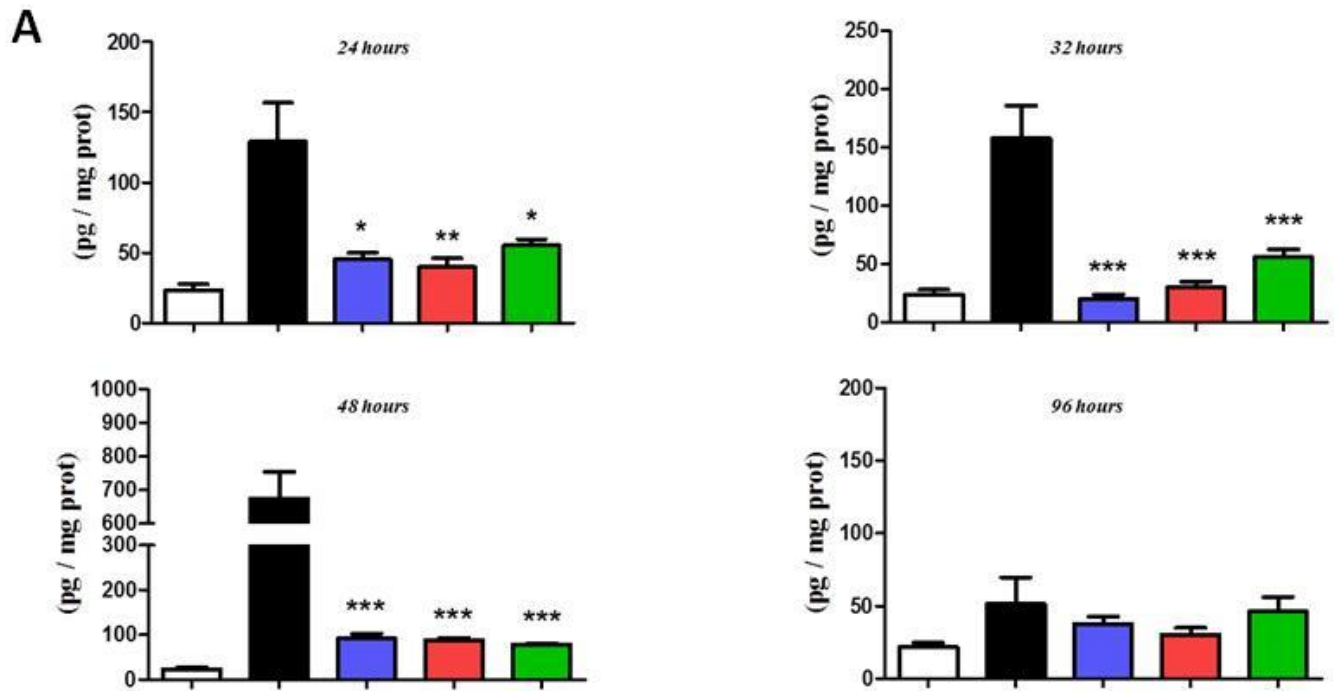
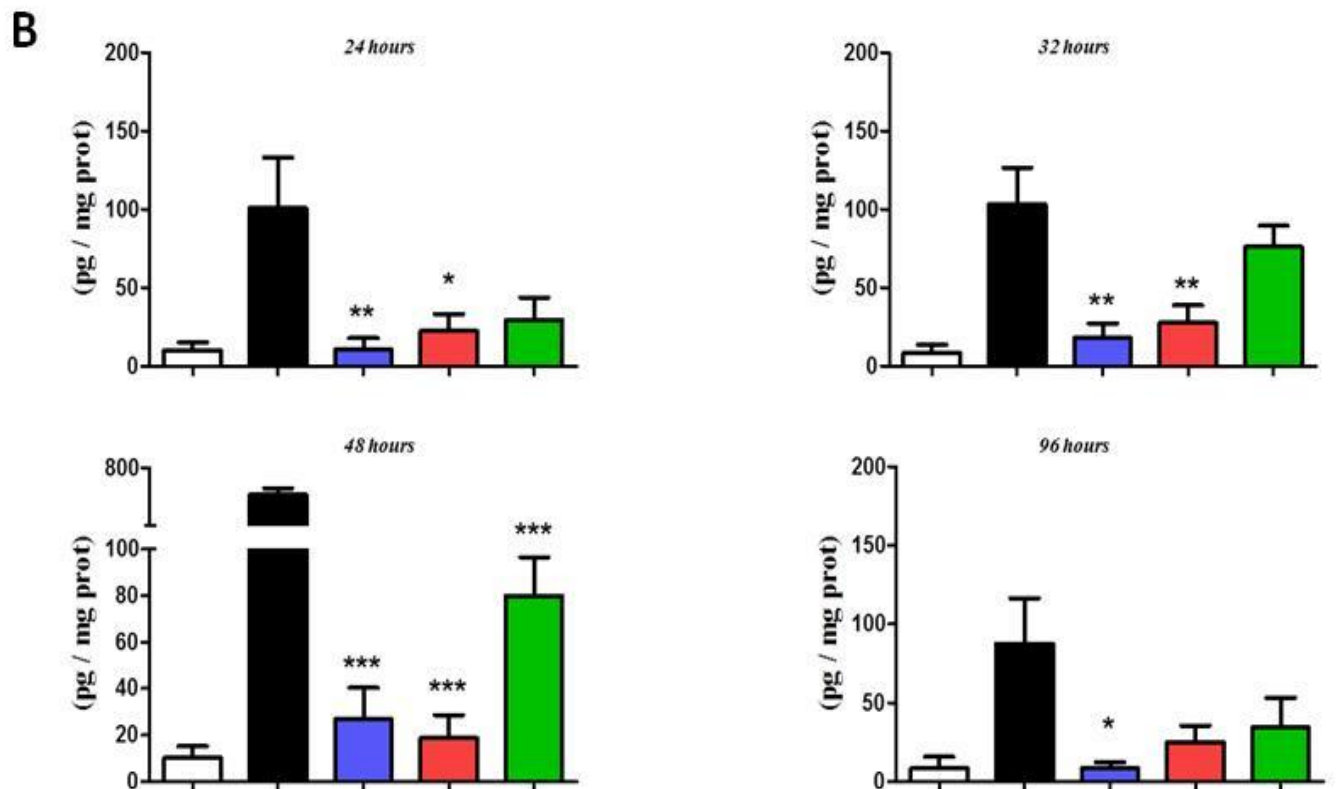


Figure 7: A and B. IL-6 (A) and IL-1b (B) production in naive animals (white column), after UVB irradiation (black column), treated with sodium alginate nanofibers (blue column), sodium alginate nanofibers and lavender oil (red column), and Tegaderm (green column).



Cellulose Acetate Nanofibres encapsulating essential oils with antimicrobial activity

Preventing infections is one of the main focuses of wound care. The colonisation of wounds by microorganisms can in fact have negative consequences on the healing process, delaying it.

Essential oils are used as natural antimicrobial agents for cellulose-based fibrous dressings. IIT has developed the production of composite electrospun fibres that effectively encapsulate three different types of essential oils (cinnamon, lemongrass and peppermint, Figure 8). The fibrous scaffolds are able to inhibit the growth of *Escherichia coli*, even when small amounts of essential oils were used. At the same time, they are not cytotoxic, as proved by biocompatibility assays on skin cell models. The created dressings are promising as advanced biomedical devices for topical treatments in skin inflammation, burns and wound healing.

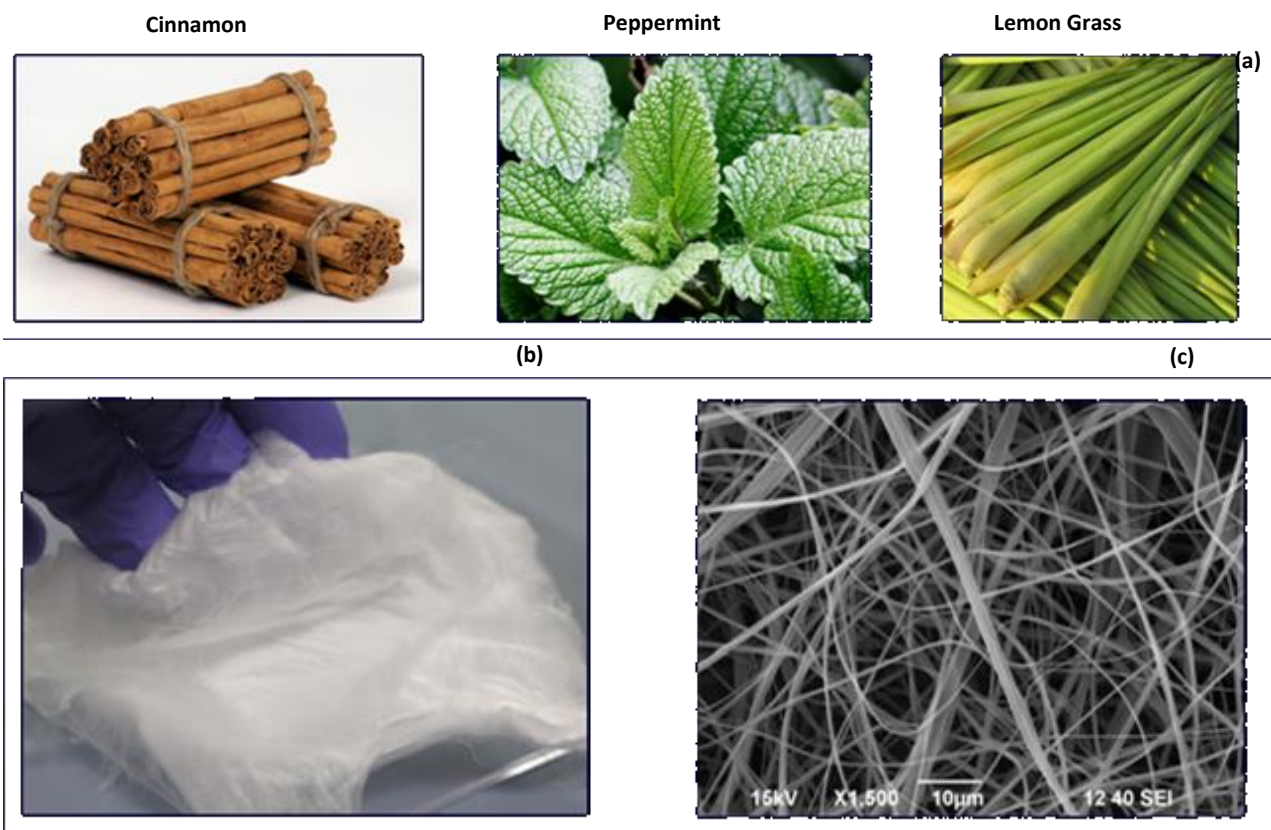


Figure 8. (a) Photograph of the plants used for the extraction of the essential oils. (b) Photograph of the produced electrospun mat and (c) corresponding SEM image.

MARKET ANALYSIS

Based on the technology described in WO 2013/140362A1, IIT internal documentation on the technology and related literature publications by the inventors and competitors, two major markets have been identified, namely the **Wound Dressing** market, and the **Surgical Suture** market. These markets have been analysed for their current dimension and future trends through a web search-based retrieval of specific information.

Wound Management Market

From the report: *“Wound Management, Worldwide Market and Forecast to 2021: Established and Emerging Products, Technologies and Markets in the Americas, Europe, Asia-Pacific and Rest of World”* (report n. 249 published in 2013 by Medmarket Diligence, LLC), the world market for wound dressing encompasses twelve product segments:

- ✚ Traditional Adhesive Dressings,
- ✚ Traditional Gauze Dressings,
- ✚ Non-Adherent Dressings,
- ✚ Film Dressings,
- ✚ Foam Dressings,
- ✚ Hydrogel Dressings,
- ✚ Hydrocolloid Dressings,
- ✚ Alginate Dressings,
- ✚ Antimicrobial Dressings,
- ✚ Negative Pressure Wound Therapy Devices,
- ✚ Bioengineered Skin and Skin Substitutes,
- ✚ Wound Care Growth Factors.

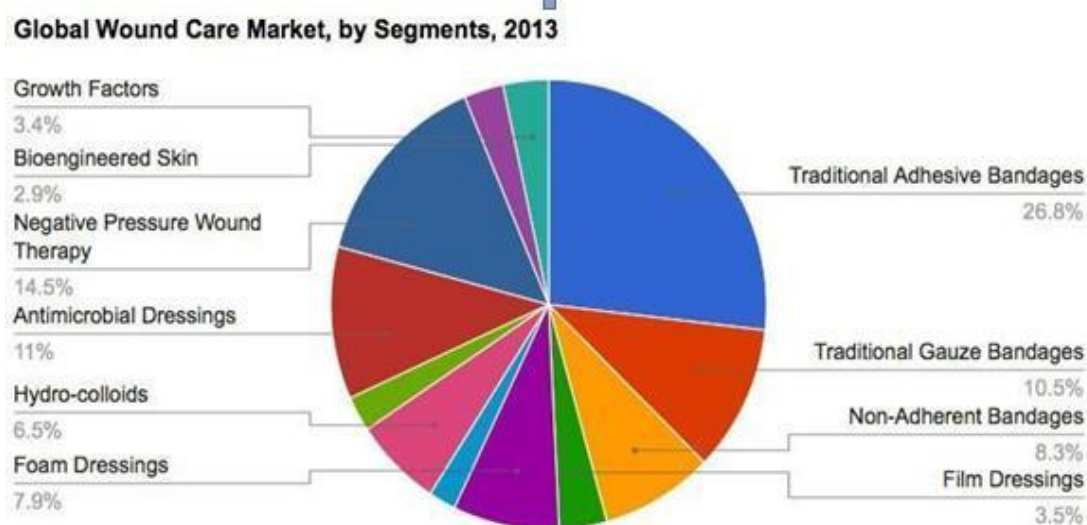
The report examines North and South America, the European Union, Asia-Pacific and Rest of World, and looks at markets and growth rates by product and country for the years 2012-2021. The world market in 2021 for the total wound management market represented by the segments listed above is projected to be worth over USD 22.0 billion, from the about USD 12.0 billion in 2013, with segments growing at widely variable rates, with lowest sales growth in traditional gauze bandages and the highest sales growth in biological growth factors.



There are some market restraints, primarily the high cost of the new technologies. Not all country healthcare budgets can afford advanced wound care products, even if they are proven to decrease healing times and hospital costs over the longer period. The development of substitute products threatens existing product categories, while a lack of sufficient clinical and economic evidence backing new technology hinders growth and acceptance of some of the more advanced wound management technologies.

In addition, improved wound prevention and a lack of regulation on tissue engineering in the EU are also expected to hold back the development of new technologies. In addition to market restraints, there are a number of drivers that are expected to shape this market in the years to come. One of the primary drivers is the aging of the global population. Chronic diseases, such as circulatory conditions, anemia and autoimmune diseases influence the healing process as a result of their influence on a number of body functions. Illnesses that cause the most significant problems include diabetes, chronic obstructive pulmonary disease (COPD), arteriosclerosis, peripheral vascular disease (PVD), heart disease, and any conditions leading to hypotension, hypovolemia, edema, and anemia.

While chronic diseases are more frequent in the elderly, wound healing will be delayed in any patient with underlying illness. Whereas most wounds heal without any problems, chronic wounds may take months or years to fully close, or may never close. Chronic wounds adversely affect the individual's quality of life, and are a leading cause of burgeoning healthcare costs. Type-2 diabetes represents 85-95% of all diabetes in developed countries, and accounts for an even higher percentage in developing countries. There were 26 million diabetic patients in the US in 2012 and 285 million patients globally. Of these patients, approximately 15% will develop a diabetic foot ulcer and 50% of these will become infected, representing an estimated 2 million patients. Diabetic foot infections are currently treated with systemic antibiotics, but the estimated failure rate of antibiotics for diabetic foot ulcers exceeds 22%. A patient with diabetes is at significant risk of damage to tissues caused by impaired homeostasis due to the disease process. For example, there is a tendency for such tissues to develop blockages in smaller blood vessels, which reduces the ability of these vessels to provide sufficient oxygen to tissues already under stress due to compromised nutrient supply and the diabetic condition. These patients then develop arterial ulcers. They may also have a tendency to suffer from venous ulcers, due to the underlying poor condition of cells as a result of the diabetes. The diabetic foot is the most common cause of non-traumatic lower extremity amputations in the US and Europe: there is an average of 82,000 amputations per year in the US, costing an estimated USD 1.6 billion annually. The estimated cost of foot ulcer care in the US ranges from USD 4,595 per ulcer episode to more than USD 28,000 and the total annual cost of foot ulcer care in the US has been estimated to be as high as USD 5 billion.

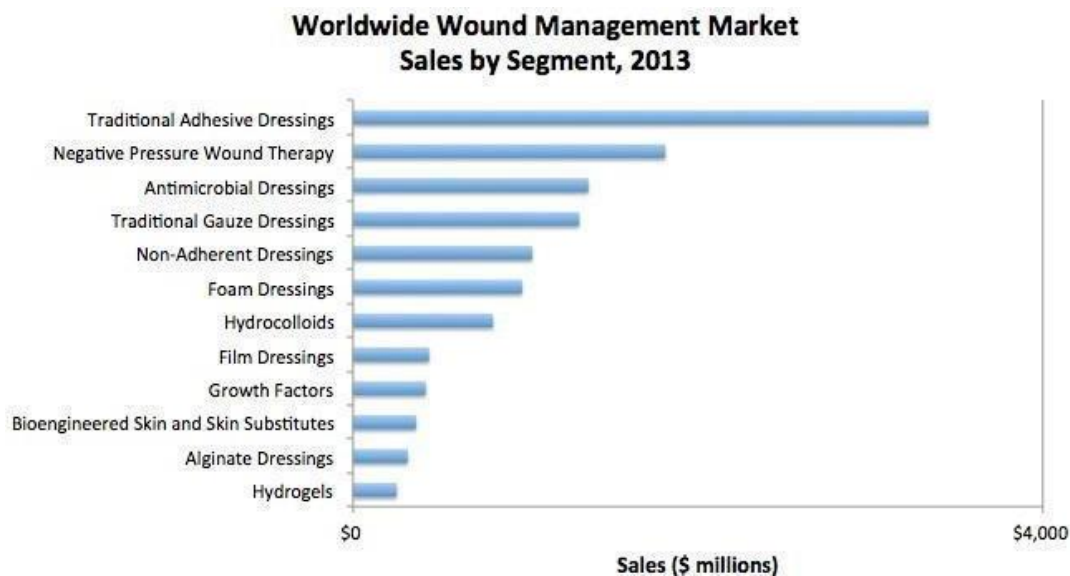


The Figure above illustrates global wound care market share by segment in 2013.

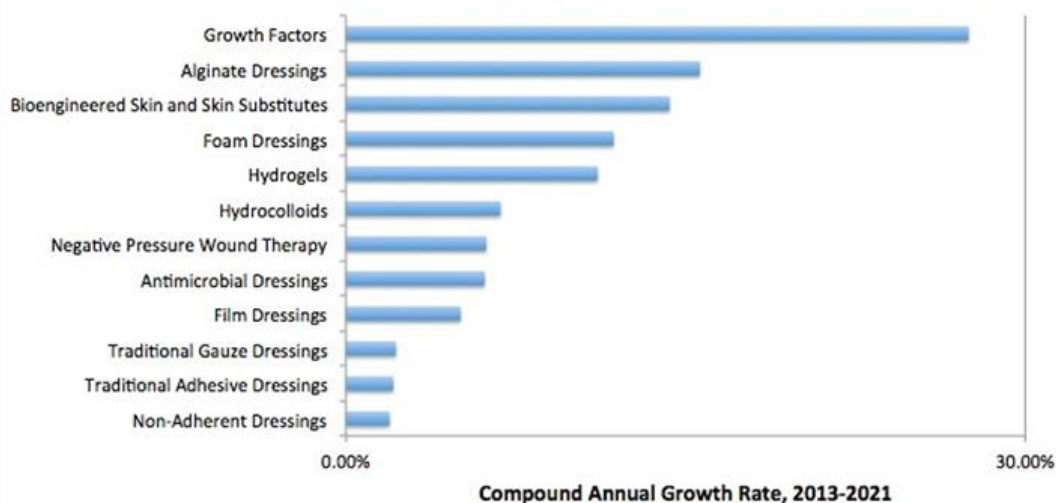
Pressure (decubitus) ulcers are another form of the most common types of chronic wounds. The treatment of pressure ulcers places a major burden on healthcare systems worldwide, with an emerging additional cost of litigation increasing in importance over recent years. Healthcare practitioners need to be aware of both the direct and indirect costs and consider how the implementation of prevention protocols may offer cost savings in the longer term. The cost of a dressing for example as a prevention tool is minimal in comparison to the costs of treating an established pressure ulcer.

The cost of treating chronic wounds is one element driving the development and utilization of advanced wound care technologies. Other drivers are the aging of the population, and the obesity epidemic, which is expected to produce a wave of diabetics in the years to come. The global wound care market is expected to always be represented by sizeable share of basic products in wound dressings and bandages, which for the majority of wound types have clearly proven to be cost effective in producing acceptable time-to-healing and other clinical outcomes. However, advanced wound products to address complex wound types - many of which may simply evolve from otherwise simple wounds that have been neglected - are increasingly demonstrating their potential for accelerating the pace and therefore reducing the cost of wound healing. The result is that well established wound care products that have largely tapped most of their potential patient populations have relative flat growth in sizable current sales. Emerging technologies, on the other hand, are in various stages of being developed and introduced, so they have considerable potential yet to be realized.

The following graphs below represent the current (2013) market size of major wound sales by segments, and the compound sales growth over the 2013-2021 forecast period, respectively (Source: MedMarket Diligence, LLC; Report #S249)



Worldwide Wound Management Market Sales Growth by Segment 2013-2021



Factors other than cost-consciousness are driving the advanced wound care market. Patients' desire for less scarring, as well as an increased awareness of infection issues, drive the development of advanced dressings and biomaterials that reduce bacteria and heal wounds faster. An aging world population and lifestyle changes that contribute to disease frequency also factor into the market's continued growth. Still, there are some market restraints, primarily the high cost of new technologies. Development of substitute products threatens existing product categories, while a lack of sufficient clinical and economic evidence backing new technology hinders growth and acceptance of some more advanced wound management technologies.

Surgical Suture Market

Surgical sutures are medical devices used to repair damaged tissue by closing the edges of a wound, holding body tissues together after an injury or surgery. They are a specific segment of the wider market for surgical equipment, that is segmented into:

- Surgical sutures and staples,
- Surgical handled instruments,
- Electrosurgical devices.

From a report produced in 2013 by the marketing department at AdvaCare Pharmaceuticals (a company out of the surgical equipment market), that examined opportunities for growth in the global surgical suture market, the surgical equipment industry was worth USD 5.2 billion in 2012 and will reach USD 7.5 billion in 2017 according to some projections (Transparency Market Research). Surgical sutures, which are used in the vast majority of surgeries, currently account for 57% of the surgical equipment market. However, during the forecast period 2013 to 2017, the electrosurgical devices market segment is expected to show highest growth at a compounded annual growth rate (CAGR) of 6.1%, owing to the growing demand for minimally invasive procedures that extensively utilize these devices.

According to a report by GlobalData, in the US, about 80% of surgical and traumatic wounds use some form of wound closure device such as sutures. Substitutes include staples, glues and wound closure strips, however they all lack reliability (sturdiness) and flexibility when compared against sutures.

In Europe, healthcare reforms and budgetary restraints make healthcare providers under pressure to cut costs. As a response, hospitals are cooperating to centralize procurement and save on administration and

purchasing costs. This also gives them more bargaining power over medical equipment suppliers. As a high-volume, commodity product, surgical sutures are vulnerable to downward pressure on prices. The US still accounts for one-third of the global market for surgical sutures. However it is effectively a closed market with one firm, a Johnson & Johnson subsidiary, controlling 80% of the market. This can be attributed to J&J's clout (because of its size and wide product range) over distributors - Group Purchasing Organizations (GPO). These GPOs, a lot of which will have contracts with J&J, have a strong influence on hospital procurement.

In developing countries, market actors are less entrenched and companies face fewer barriers to entry. The number of surgeries performed is growing fast due to improving healthcare facilities (more hospitals and operating facilities), and increased expenditure on healthcare by populations benefiting from rising incomes. In India, China and Brazil, the surgical sutures market is forecast to grow at a CAGR of 4.3%, 4.7% and 3.8% respectively, through to 2018 (GlobalData). Companies focused on supplying developing countries, are well positioned to benefit from this growth. However, developed markets will still see growth due to aging populations. According to the WHO, by 2050 there will be more than 2 billion people aged 60 or over; for the first time in history, people older than 60 will outnumber children younger than 15. Increases in the number of cosmetic (plastic) surgeries and cardiovascular procedures (where there is high blood loss) will also be reasons for a growing market. In both developed and developing countries the number of private clinics is rising. This global trend lends itself to an accompanying rise in cosmetic (plastic) surgery, which will support demand for non-absorbable sutures (absorbable sutures tend to provoke greater immune response and inflammation, causing scarring).

On the other hand, product development, particularly around precisely controlling the absorption or degradation rates of tissue-specific absorbable surgical sutures, will likely to lead to higher demand for sophisticated absorbable sutures. Absorbable sutures are already a growing segment for manufacturers. They are convenient in cases of patients who cannot return for suture removal, or for internal body tissues (the body will naturally degrade and absorb the suture material over time while the wound heals). Today's sutures are the result of a 4000 years innovation process going back to Ancient Egypt where they used linen and animal sinew to close wounds. It was not until the 1860s though, when English physician Joseph Lister discovered disinfecting techniques, that sutures and surgery in general became a lot safer.

Today, sutures be coated with antimicrobial substances to reduce the chances of wound infection, and this is exactly the great advantage of the novel IIT technology, coupled with its capability to be re-absorbed.

A new report by a leading market research firm (Research & Markets, *"Global Surgical Equipment Market 2012-2016"*) indicates that a new surgical technique is fueling global demand for absorbable sutures, and the study says there are a number of companies active in this space already. The study forecasts a strong 6.25% growth rate for public and private firms in this niche market, an outgrowth of the "minimally invasive surgery" procedures that are being developed by doctors to keep hospital stays, and overall medical care costs, down.

Analysts said the increasing demand for minimally invasive surgery has caused medical supply companies to switch to offering absorbable sutures, creating a new technology trend in medicine. According to the report, the demand for minimally invasive surgeries worldwide is expected to continue. Minimally invasive surgeries offer many benefits to patients as well as surgeons, such as faster recovery, fewer chances of post-surgery infections, less pain, reduced visible marks, bleeding control, and enhanced accuracy.

FOR FURTHER READING

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