Bioactive wound dressings

Description

Bioactive wound dressings

Cellulose: One of the advantages of cellulose in wound dressings is its ability to absorb water and therefore, exudate while providing a moist environment at the wound site (Basu et al. 2017). There are some commercially available cellulose-based dressings, such as Dermafill®, Nanoderm® and Vermac®. Bacterial cellulose, in particular, is used in wound dressings and is considered a suitable material for wound dressings because of its high purity and favourable characteristics of non-toxicity, mechanical stability and high moisture content (Sulaeva et al. 2015). Bacterial cellulose dressings ensure thermal and gaseous exchanges while exhibiting permeability to microorganisms. Real-time monitoring of the wound was allowed when transparent bacterial cellulose dressings were produced (Springer et al. 2019). The issue of using bacterial cellulose lies in the high production costs and difficulty of mass production, although becoming less difficult considering the recent developments. On the other hand, large quantities of cellulose nanofibrils and to a lesser extent of cellulose nanocrystals can be produced.
Wound dressings materials from CNFs and CNCs (nanocellulose only or in composites) were also studied. Faster recovery of surgical wounds was observed with CNF dressings in Sun et al. (2017) study. Oxidized-cellulose exhibit good hemostatic properties (Lewis et al. 2013; Vosmanska et al. 2014). Song et al. observed enhanced wound healing for wounds dressed with tunicate CNCs-alginate or tunicate CNCs-selenium membranes (Song et al. 2017). Bacakova et al. reviewed the applications of nanocellulose in tissue engineering and wound healing (Bacakova et al. 2019). Because cellulose does not exhibit antimicrobial activity, it has been functionalized to produce wound dressings with antimicrobial activity (Wiegand et al. 2015b; Napavichayanun et al. 2015). Bioactive wound dressings from biopolymers and more specifically from cellulose are discussed in the following section.

Bioactive wound dressings
As discussed previously, in case of wound infection, the healing step does not happen, and the wound becomes chronic. A non-healing wound presents risks of spread infection and sepsis. Antimicrobial agents dispensed at the site of infection would prevent microbial growth and allow for the healing process to progress. As previously discussed, a wide range of antimicrobial agents is available. To select a suitable agent, several parameters such as the emergence of antibiotic resistance, cytotoxicity, antimicrobial efficiency, ease of delivery etc. should be taken into account.
The development of bioactive wound dressings is beneficial for infection control to prevent delayed healing. In the case of wound care, antimicrobial activity is one of the main properties required. The delivery, on the site of a wound, of active substances susceptible to promote healing are also looked for. Additional features such as hemostatic properties, fibroblasts proliferation enhancement or growth factors would encourage wound closure.

Biopolymers materials with bioactivity . Biopolymers have been functionalized to exhibit antimicrobial activity. Dressings of collagen, gelatin, chitosan etc. have been incorporated with various

antimicrobial agents, from metal nanoparticles to synthetic antibiotics and natural molecules. Silver nanoparticles have been extensively studied for its antibacterial, antifungal and antiviral properties and have also found diverse applications in the form of wound dressings or coatings for medical devices (Rai et al. 2009). Kumar et al. reviewed the use of these nanoparticles loaded in biopolymers materials, and they have been shown to promote healing and effectively control the growth of microorganisms (Kumar et al. 2018). The main drawback of their extensive use is due to the nanotoxicity that causes health problems and ecological concern (Prabhu and Poulose 2012).
Examples of the incorporation of synthetic molecules and more specifically antibiotics are found. Chitosan-PEG-PVP blend was coated on the surface of cotton gauze and impregnated with tetracycline hydrochloride. The dressings exhibited antimicrobial activity against *S. aureus* and *E. coli*. The healing improvement was observed in rats wounds, and reduced scaring was reported (Anjum et al. 2016). Chitosan was functionalized in chitosan-sulfonamides derivatives to exhibit antimicrobial activity as well as re-epithelization enhancement (Dragostin et al. 2016). Besides, their biocompatibility, biodegradability, swelling capacities were characterized and show non-toxicity *in vitro* and improved swelling. Improved healing rates were observed *in vivo.*
Naturally occurring molecules have also been introduced into bio-based materials. Dried chitosan microsphere with melatonin where produced by spray-drying by Romic et al. (2016). In contact with exudate moisture, the powder forms a hydrogel that offers protection and a suitable environment for healing. The dressing exhibited antibacterial activity against methicillin-resistant *S. aureus* strains (MRSA). Electrospun cellulose acetate-PVP containing curcumin were designed to produce antimicrobial materials (Tsekova et al. 2017). Depending on the composition of the polymer matrix preparation process, various curcumin release profiles were observed. The incorporation of a water-soluble polymer resulted in hydrophilization of the mat and more rapid release of curcumin from the cellulose acetate mat. Antibacterial activity was assessed, and one formulation exhibited a log 5 reduction of bacteria after 4 hours. A review on electrospun fibres mat for wound dressing application summarizes the various incorporation of antimicrobial and therapeutic agents during the electrospinning process (Pilehvar-Soltanahmadi et al. 2018).
Essential oils molecules with antimicrobial activity have also been studied for the design of bioactive wound dressings. Cross-linked gelatin films were impregnated with thymol for potential wound dressing applications. The antioxidant properties were assessed and antibacterial activity against *B. subtilis*, *P. aeruginosa, E. coli* and *S. aureus* was observed (Kavoosi et al. 2013). Thymol was incorporated into collagen films in a simple evaporation procedure (Michalska-Sionkowska et al. 2017). Direct contact and drug diffusion antibacterial effects were observed. Additionally, thymol prevented biofilm formation. Pérez-Recalde et al. classified essential oil molecule activity used in wound healing (Pérez-Recalde et al. 2018). They reviewed the incorporation of essential oils in biopolymer matrices and their potential use for wound dressings. An increased interest since 2010 was observed and the potential use of essential oil in biopolymer dressings is promising especially in the treatment of chronic wounds.

Nanocellulose materials with antimicrobial activity . More specifically, nanocellulose materials from CNCs, CNFs and bacterial cellulose have been used as dressing scaffolds for wound healing, with added antimicrobial properties.
Antimicrobial wound dressings composed of bacterial cellulose hydrogel impregnated with silver sulfadiazine (SSD) were produced. Activity against *P. aeruginosa, E. coli* and *S. aureus* was reported. The use of bacterial cellulose hydrogel counteracts the drawbacks in the use of SSD in topical applications by limiting inflammation and absorbing exudate (Luan et al. 2012). Copper and calcium cross-linked bacterial cellulose hydrogels exhibited bacteriostatic activity by retarding the growth of *S. epidermidis* and *P. aeruginosa* as well as inhibition of the bacterial biofilm formation (Basu et al.

2018). Films of CNCs were incorporated with silver nanoparticles (Singla et al. 2017). *In vivo* studies demonstrated enhanced healing resulting from the decreased inflammatory response and increased fibroblast production. The antibacterial activity was established from in vitro experiments and prevented wound infection.
Water-insoluble drugs were incorporated into CNF films using filtration by Kolakovic et al. (Kolakovic et al. 2012b). Indomethacin, itraconazole, and beclomethasone dipropionate remained in the filtration mass. Drug loading of 40 % of the total amount used was achieved, while 60 % were lost in the process and sustained drug release was observed.
Antimicrobial molecules have also been covalently grafted to provide long-term contact activity. Antibacterial enzymes, lysozyme and nisin were attached on CNCs with amorphous hairy regions and functionalized with aldehyde groups (Tavakolian et al. 2018). Antimicrobial activity against Gram-positive bacteria was observed. A phenanthridinium silane with antibacterial activity was grafted on CNFs. The antibacterial activity of the resulting films was either bactericidal or bacteriostatic against *E. coli* and *S. aureus*. Previously, an aminopropyl trimethoxysilane was grafted onto CNFs films and resulted in antibacterial activity against B. subtilis, S. aureus and E. coli (Saini et al. 2016).

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