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RESEARCH PROGRESS ON INSULIN DRESSINGS TO PROMOTE WOUND HEALING

Aneta Ostróżka-Cieślik, Marcin Przybyła, Barbara Dolińska

Department of Pharmaceutical Technology, Faculty of Pharmaceutical Sciences in Sosnowiec, Medical University of Silesia, Kasztanowa 3, 41-200 Sosnowiec, Poland

1.Introduction

Insulin is a hormone whose efficacy in wound healing was recognised in the late 1920s. Research in subsequent years has confirmed its significant contribution to reducing inflammation, regulating oxidative processes, fibroblast proliferation, and enhanced collagen deposition and vascularization in a variety of experimental wound models. Intensive research is currently underway to develop materials that will provide effective stabilisation of insulin and allow its controlled diffusion rate. The aim of this review was to bring together research on the development of innovative wound care strategies based on insulin-enriched bioactive dressings.

2. Materials and Methods

An analysis of the literature contained in bibliographic databases (Embase, Medline, PubMed, Cochrane Library) and published up to 30 June 2023 was performed. Keywords used were: dressing, polymers, insulin, stability, topical, local treatment, sustained release, diabetic ulcers, wound healing, and chronic wounds. The literature was analysed, which met the established conditions of the review. 12 publications met the search criteria.

3. Results and Discussion

To date, there have been many promising studies on the development of insulin dressings. The results of the included basic and preclinical studies confirm that engineered polymeric matrices/scaffolds with insulin show high efficacy and good tolerability in topical wound treatment. This type of dressing, which belongs to the latest generation of dressing materials, can be used in the provision of hard-to-heal wounds such as diabetic foot and burns.

4. Conclusion

Polymeric matrices/scaffolds are a promising direction for insulin carrier development.

Table 1
Strategies used to incorporate the insulin into the polymeric matrices/scaffolds.

Author, year of publication	Carrier insulin	Effects of the insulin preparation
Hrynyk et al. 2012 [1]	Insulin-loaded poly(d,l-lactide-co-glycolide) (PLGA) microparticles into alginate sponge dressing (ASD)	• effective long-term delivery platform for bioactive insulin • bioactivity of released insulin maintained for at 10 days
Nanda et al. 2014 [2]	Insulin-releasing PLGA (poly lactic-co-glycolic acid) microbeads incorporated into collagen scaffold	• release profile of insulin exhibited initial burst and then sustained slow rise • high viability of the cells cultured in the porous scaffold • intense cell proliferation during the culture period
Li et al. 2017 [3]	Insulin-encapsulated silk fibroin (SF) microparticles	• dressing accelerated chronic wound closure rate, • enhanced collagen deposition and vascularization
Ehterami et al. 2018 [4]	Insulin delivering chitosan (Cs) nanoparticles were coated onto the electrospun poly (ε-caprolactone) (PCL)/Collagen (COLL)	• the incorporation of insulin containing Cs particles enhanced the PCL/COLL hydrophilicity, water-uptake, and blood compatibility • dressing could reach to nearly full wound closure compared with the sterile gauze which exhibited nearly 45% of wound size reduction
Lee et al. 2020 [5]	Nanofibrous insulin/PLGA (poly-D-L-lactide-glycolide)	• reduced the amount of type I collagen in vitro • increased the transforming growth factor-beta content in vivo • promoted the healing of diabetic wounds • prolong the release of insulin and promote diabetic wound healing
Yang et al. 2020 [6]	Insulin-loaded silk fibroin microparticles	• promoting reepithelialization, angiogenesis, and extracellular matrix, especially collagen deposition
Rajalekshmy et al. 2021 [7]	Alginate-g-poly (methacrylic acid) cross-linked xerogel (AGM2S)	• >70% of loaded insulin was released in two days, which modulated the healing response
Gao et al. 2022 [8]	Nanofibrous mats made of PLLA (poly (L-lactic acid) coated with cross-linked multilayer made of mCH (maleilated chitosan) and tHA (thiolated hyaluronan) uploaded with insulin	• promoted adhesion and growth of MSCs (mesenchymal stem cells) but also wound healing
Chen et al. 2022 [9]	Insulin was loaded in the three-dimensional network structure of ICOQF (quaternized chitosan (QCS) and the aldehyde groups on F108-CHO micelles)	• antioxidant (by scavenging ROS and activating the expression of HO-1) • antibacterial (by causing the rupture of bacterial cell membranes, mitochondrial dysfunction, and inhibiting ATP synthesis) • anti-inflammatory (by inhibiting the proliferation of activated macrophages and promoting the polarization of M1 phenotype to M2 phenotype).
Raei et al. 2022 [10]	Polivinyl pyrolidone (PVP)/Polylactic acid (PLA) nanofibers containing insulin, nitroglycerin and titanium dioxide nanotubes	• external layers made of polylactic acid (PLA) significantly increased the release time of insulin • addition of titanium dioxide nanotubes makes the dressing resistant to both Gram-negative and Gram-positive bacteria
Walther et al. 2023 [11]	Electrospun core–shell fibers of a combination of polycaprolactone and polyethylene oxide	• increased in wound healing biomarkers • increased migration speed of primary human dermal fibroblasts and keratinocytes
Lee et al. 2023 [12]	Nanofibrous insulin/vildagliptin/PLGA (poly lactic-co-glycolic acid) core-shell scaffold	• high hydrophilicity resulting in increased vildagliptin and insulin release • the addition of vildagliptin caused significantly faster wound healing • increased EPCs (endothelial progenitor cells) migration

5. References

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6. Acknowledgements

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