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REVIEW OF RESEARCH IN DEVELOPING HYDROGELS WITH INSULIN TO PROMOTE WOUND HEALING

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1.Introduction

Insulin is a peptide hormone that has a number of physiological functions, and in particular, is involved in the regulation of blood glucose levels. The hormone has been found to affect wound healing by reducing inflammation, regulating oxidative reactions, and increasing collagen deposition. Despite the many benefits of insulin, there is still no topical preparation on the skin on the market. The problem is the lack of stability of this peptide in the wound bed. The presence of proteases in the wound environment deactivates the hormone. Research efforts undertaken in recent years to develop a topical form of insulin have focused on designing an effective carrier to improve the stability of the peptide drug. The aim of this study was to review the literature on the development of a hydrogel formulation of insulin to promote wound healing and to identify the benefits of this carrier.

2. Materials and Methods

An analysis of papers published between 2000 and 2022 was carried out. Embase, Medline, PubMed, and Cochrane Library databases were used. Keywords used: hydrogel, polymers, insulin, topical, diabetic ulcers, wound healing, chronic wounds. Conference abstracts and non-English language articles were omitted. 12 publications met the search criteria

3. Results and Discussion

The literature analysis confirmed that topical insulin administration improves wound healing without significantly affecting the occurrence of side effects. Hydrogels may provide a starting point for developing new or improving the efficacy of designed epidermal forms of insulin. The hydrogels used allow efficient delivery of the peptide into the wound environment.

4. Conclusion

Hydrogels are a promising direction for insulin carrier development.

6. Acknowledgements

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Table 1

Strategies used to incorporate the insulin into the hydrogel.

Author, year of publication	Hydrogel carrier/ insulin form	Effects of the insulin preparation
Dhall et al. 2015 [1]	alginate gels; insulin - loaded PLGA microparticles	accelerated healing via a decrease in oxidative stress and tissue damage, early recruitment of neutrophils, management of inflammatory cells, enhanced angiogenesis, and proper collagen deposition and maturation
Cai et al. 2016 [2]	glycerol/PVA hydrogel	addition of glycerol reduced the swelling ratio and hardness of the hydrogel, and enhanced the release of insulin in vitro and in vivo glycerol disrupted the crystallite structure of PVA molecules while forming crosslinked structures between them, thereby promoting insulin release insulin-loaded PVA hydrogel film exhibited a hypoglycemic effect in diabetic rats over 10 days
Besson et al. 2017 [3]	Carbopol 940 gel; insulin complexed with 2-hydroxypropyl-β-cyclodextrin (HPβCD-INS)	Formulations: showed no cytotoxic or irritative effects prolonged the proliferation and migration of keratinocytes increased deposition of type I and III collagen fibers
Abdelkader et al. 2018 [4]	PVA-borate hydrogel; Insulin - loaded PLGA nanoparticles	in non-diabetic rats, there was no significant difference between healing observed in control and wounds treated with free insulin in diabetic rats insulin induced significant improvement in wound healing histological images of diabetic wounds: reduction in the inflammatory process, increased angiogenesis, formation of granulation tissue, completely reconstructed epidermis and collagen deposition.
Dawoud et al. 2019 [5]	chitosan gel; insulin - loaded liposomes	release was sustained up to 24 h release rate of 91.521 μg/cm²/h improvement in the wound healing rate reduction in the erythema of the ulcer and no signs of hypoglycemia
Li et al. 2019 [6]	Keratin - conjugated insulin hydrogel (Ins-K)	promoted wound healing by stimulating cellular migration Ins-K hydrogel shows a stronger hemostatic ability than keratin hydrogel stronger wound healing effect of Ins-K was found in the early regeneration stage more smooth skin tissues at excision section obtained treatment with Ins-K hydrogel
Kaur et al. 2019 [7]	Carbopol 980 gel; insulin - loaded silver nanoparticles (AgNPs)	higher wound healing activity in higher hyperglycemic condition improvement in collagen deposition insulin regulates the early inflammatory phase rapid decrease of pro-inflammatory cytokines and an increase in anti-inflammatory cytokine antibacterial activity
Ribeiro et al. 2020 [8]	chitosan gel; insulin - loaded chitosan nanoparticles	stimulate inflammatory cell and angiogenesis improve wound maturation in diabetic rats
Zhu et al. 2020 [9]	Oxidized hyaluronic acid/succinyl chitosan gel; insulin-loaded micelles	the rate of insulin release depends on the glucose concentration in the wounded tissue high biocompatibility and low cytotoxicity promotion of fibroblast proliferation and tissue internal structure integrity, as well as the deposition of collagen and myofibrils combining insulin with epidermal growth factor resulted in even more effective wound healing
Ostrożka-Cieślik et al. 2021 [10]	Carbopol Ultrez 10, Carbopol Ultrez 30, methyl cellulose, glycerol ointment	insulin release from the formulations occurs in a prolonged manner methyl cellulose-based hydrogel released API reaching 75% after 9 h
Chakraborty et al. 2021 [11]	Aloe vera gel; insulin - loaded nanoemulsion	greater wound contraction (75% in 15 days) improvement in the skin histological architecture gel is nonirritant and is safe for topical use aloe vera with insulin-loaded nanoemulsion showed synergistic effect
Quitério et al. 2021 [12]	Pluronic ® F 127 gel; insulin – loaded PLGA nanoparticles	insulin was completely released from NPs and its structure was preserved in vitro release studies suggested a controlled release profile (5 μg/cm²/8h) improves wound healing without causing side effects

7. References

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