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Thermo-sensitive hydrogelsas carrier-systems for insect-based proteins in chronic wound management

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The aim of this study was the development ofa thermo-sensitive hydrogel containing insect-based enzymes for treatment of chronic wound infections. The designed formulation based ongelling agentPoloxamer (a triblock copolymer with central polyoxy-propylene and two lateral polyoxy-ethylenes). For an ideal application, the wound-dressingshould be liquid at ambient temperature and form a gel instantly at skin temperature in order to achieve sustained release of the drug. The gelling temperature represents the point of sol-gel transition and is reflected by the inflection point of viscous and elastic modulus (G´´ and G´). The influence of several concentrations of different additives such as additional thickeners, moisturizing factors or preservatives on viscoelastic properties of the hydrogel were investigated by oscillatory measurements.The results indicated that generallywith an increasing concentration of additives, the viscosity of the system and the gelling temperaturewereinfluenced.Based on experimental data two possible final-formulations were designed. The first one contained 16% (w/w) Poloxamer407, 3% (w/w) glycerin, 0.2% (w/w) potassium sorbate, 0.1% (w/w) citric acid in water and a second formulationcontained additionally 15% (w/w) Poloxamer 188.

Recently, chronic wound infections are a major challenge in health care. The insect-based enzyme IMPI (Inducible Metalloprotease Inhibitor) represents an innovative promising drug candidate in that field. It inhibits M4 Metalloproteases, which arebuilt by several bacteria and are responsible for necrosis.

The API (active pharmaceutical ingredient), IMPI was produced as GST fusion protein by fermentation of E.coli and entrapped within these cold hydrogelsin concentrations between 0.2 and 0.3 mg/ml.It could be demonstrated that IMPI as API,similar tothe additives, influenced the rheological characteristics of the hydrogel.An increaseof viscosity and adecrease of gelling temperature were observed. The effect might be caused by hydrolayer of protein, which decreased the amount of free water molecules. However, the formulation fulfills the requirements and is approved by stability testing.

The quantitative analysis of proteinsin the formulation was performed by analytic methods likeHPLC, Bradford- and GST-Assay. HPLC analytics revealed a high limit of quantification. The

other methods exhibited immense standard deviation and are partially influenced by hydrogel compounds. Qualified detection of bioactivity of the enzyme was reached with casein fluorescence quenching assay. The results showed thatthe activity of IMPI in hydrogel after preparation was comparable to its activity in water solution. Furthermore, the bioactivity was not altered during storage.

It could be concluded, that the prepared thermo-sensitive hydrogelsare suitable formulations for treatment of chronic wound infection with IMPI. In further studies the time-release profile of IMPI from the hydrogel will be further elucidated.