

## **Capsules based on pectin, chitosan and hyaluronic acid for the delivery of manuka honey into skin ulcers**

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### **Purpose**

The aim of the present work was the development of capsules based on pectin (PEC), chitosan glutamate low MW (CS) and hyaluronic acid (HA) for the delivery of Manuka honey (MH) components for the treatment of skin lesions. Two different fractions of MH were examined: one (Fr1), rich in methylglyoxal, the other (Fr2), rich in polyphenols.

### **Methods**

Capsules were obtained by dropping a CaCl<sub>2</sub> (0.75% w/w) / CS mixture (500 µl) into an aqueous PEC/HA mixture (50 ml). Particles were filtered, freeze-dried and subsequently characterized for size, hydration and mechanical properties.

The optimization of the formulation was supported by a DoE approach (Statgraphics 5.0, Statistical Graphics Corporation, Rockville, MD, USA). In a screening phase, the following factors were investigated at two levels: CS (0.5% - 1% w/w), PEC (0.5% - 1% w/w) and HA (0.3% - 0.5% w/w). For the optimization phase a "central composite design" was used. The response variables considered were: particle size, buffer (PBS) absorption and mechanical resistance.

*In vitro* cell proliferation properties of MH fractions were investigated on human fibroblasts. Capsules were loaded with the MH fraction having the highest cell proliferation properties and characterized for loading capacity by a HPLC assay. Cell proliferation induced by unloaded and loaded particles was also evaluated.

### **Results**

MH Fr1 was able to improve cell proliferation in comparison with Fr2. Capsules showed a Fr1 loading capacity close to the theoretical one. The loading of Fr1 did not modify the technological properties of capsules and produced an increase in cell proliferation with respect to the unloaded ones.

### **Conclusions**

Capsules developed were able to absorb wound exudate and to load and release MH Fr1. The results obtained from *in vitro* proliferation test indicate that capsules loaded with MH Fr1 constitute a promising formulation for the treatment of skin ulcers.