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Polyacrylates and Chitosan Derivatives are Safe Penetration Enhancers for Hydrophilic Drugs

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With the advent of new methods in biotechnology peptide and proteins of human origin became available for the treatment of chronic diseases. However, until now the only successful therapeutic application is by injection. Alternative and more patient friendly application routes as the nasal, pulmonary, buccal and the peroral routes are currently investigated with much efforts in both industry and academia. Because peptides and proteins are hydrophilic macromolecules, they are not absorbed by the nasal, buccal, and peroral tissues. In order to facilitate absorption suitable penetration enhancers have to be developed which only allow for paracellular absorption and are non-toxic.

Weakly crosslinked polyacrylates as e.g. Polycarbophil™ and Carbomers™ (which are FDA approved) have been found to fulfill these requirements. By Ca^{2+} complexation they are able to trigger the reversible opening of the tight-junction between the cells and to allow the paracellular transport of peptides (1,2). Additionally they locally de-activate the most important enzymes of the gastrointestinal tract.

Chitosan and chitosan derivatives as trimethyl chitosan (TMC) have been shown to have similar properties to reversibly open the tight junctions. This mechanism is thought to occur by ionic charge transfer between the positive charge of chitosan molecule and the negative charges (sulfate and sialine groups) of the glycocalix (3).

In contrast to most of the absorption enhancers used so far, polyacrylates and chitosan derivatives do not interact with the phospholipid bilayer of the cell membranes and hence show no toxic effects to the cells of the absorbing membranes.

References

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