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Polymer-granulated Excipients as Matrix Material for the Controlled Delivery of Nifedipine and Its Solid Dispersion Systems

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Key Words
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ABSTRACT

Background. The use of ethylcellulose as the granulating material might introduce a more-hydrophobic nature to excipients by partial coating or fitting into the interstitial structure of the granules. As a result, their sustained/controlled-release properties both *in vitro* and *in vivo* are suitable as a matrix type of controlled-release dosage form.

Aims. To study the influence of different drug solubility characteristics on the release properties of this matrix system.

Methods. Polymer-granulated excipients of lactose or dicalcium phosphate with ethylcellulose were prepared, and their suitabilities for use as a matrix material to produce a controlled-release dosage form by direct compression with the poorly soluble drug nifedipine were examined. The physical characteristics of both polymer-granulated excipients and their resulting matrix tablets mixed with nifedipine alone or with its 3 solid dispersion forms were evaluated.

Results. We found that it was necessary to add HPMC to improve the cohesion of polymer-granulated excipients as previously reported. Results further demonstrated that the higher the amount of ethylcellulose (as Surelease) used, the better the performance was for sustained release. Solid dispersion systems of nifedipine also enhanced the drug release rate. But the sustainability deteriorated as a result of destruction of the integrity of the matrix tablets due to dissolution of a larger quantity of nifedipine when a more-soluble form of nifedipine was used. The hydrophobic nature of ethylcellulose made it possible to hinder the release of nifedipine from all these matrix formulations. Additional HPMC in the matrix granules similarly influenced the physical properties of lactose and dicalcium phosphate matrix granules and tablets, but there was a conflicting influence on the dissolution of nifedipine from matrix tablets using both granules irregardless of which form of nifedipine was used. The higher solubility and hydrophilic nature of lactose increased the dissolution of nifedipine from matrix tablets based on lactose compared to that of matrix tablets based on dicalcium phosphate.

Conclusions. With these types of matrix materials, a controlled-release dosage form of nifedipine can be prepared by direct compression. However, the water-soluble polymers (PVP and HPMC) used to improve the solubility of nifedipine in water further interactively affected the dissolution rate of nifedipine from these matrix tablets. The in vitro sustainability of nifedipine was also dependent on the solubility and weight fraction of the total tablet weight, which are important for maintaining the integrity of the matrix tablets during dissolution.

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