Drug layering with the aqueous polymer dispersion Kollicoat® SR 30 D for controlled release pellets

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ABSTRACT SUMMARY
A one step process to produce controlled release pellets by layering the drug with aqueous polymer dispersion Kollicoat® SR was developed. Drug release was highly dependent on the water solubility of the drug, core type and the plasticizer amount.

INTRODUCTION
A typical manufacturing procedure for multiparticulates includes drug layering on a neutral core followed by coating with the release-controlling polymer. Matrix-layered systems potentially have several advantages, such as easy manufacturing, lower costs (one step process) and less risk of dose dumping (if the coating accidentally ruptured or damaged). Their main disadvantage is the fast initial release\(^1\). In this study, matrix layering with aqueous polymer dispersions and the factors affecting the drug release were investigated.

MATERIALS AND METHODS
Drugs with different water solubilities (carbamazepine, 0.2 mg/ml; theophylline, 10 mg/ml; metoprolol tartrate, \(> 1000\) mg/ml) were dissolved or dispersed/dissolved in Kollicoat® SR 30D (poly vinylacetate, BASF SE, Ludwigshafen, Germany) with a solid content of 15 % w/w and plasticized with TEC 5% w/w. The mixture was layered onto sugar or microcrystalline cellulose cores in a fluidized bed coater (Miniglatt, Glatt AG, Binzen, Germany) to achieve 50% w/w weight gain. The drug release was investigated in a USP paddle apparatus II (50 rpm, 37 °C) using 900 ml 0.1 N HCl.

RESULTS AND DISCUSSION
Controlled drug release was achieved with all drugs using different ratios of drug:Kollicoat® SR 30D (Fig. 1). With the poorly soluble drug carbamazepine, the release was already controlled with small amounts of Kollicoat® SR 30D (10-20% w/w) (Fig. 1 A). The more soluble drugs theophylline and metoprolol tartrate required more Kollicoat® SR 30D to control the release. The release profile is characterized by an initial release phase, which represents the release of uncovered/incompletely covered drug at the pellets surface, followed by a typical sigmoidal release phase which tends to be zero order release at higher portions of Kollicoat® SR 30D (Fig. 1 B, C). The high initial release phase (25 %) of metoprolol tartrate can be decreased by applying a top coating of 2 % w/w drug-free Kollicoat® SR 30D (Fig. 1 C).

![Fig. 1: Effect of drug : Kollicoat® SR 30D ratio on the release of A) Carbamazepine B) Theophylline C) Metoprolol tartrate.](image-url)
The release of carbamazepine was independent of the core type (Fig. 2 A). This is probably because at the low amount of Kollicoat® SR, where the drug is dissolution-controlled and not by diffusion through the polymeric film. With more soluble drugs at higher portions of Kollicoat® SR 30D, the drug was released by diffusion through the polymeric matrix and pores. The release profiles therefore changed when osmotically active sugar core vs. osmotically inactive MCC core were used (Fig. 2 B, C).

Layering of theophylline with Kollicoat® SR 30D resulted in slightly faster release when plasticized with TEC 5% w/w (based on polymer weight) because of the pore-forming effect by leaching of the plasticizer (Fig. 3 A). In case of metoprolol tartrate, pellets layered with plasticized Kollicoat® SR 30D released significantly slower than pellets prepared with unplasticized Kollicoat® SR 30D (Fig. 3B). Also a stronger swelling of pellets prepared with plasticized vs. unplasticized Kollicoat® SR 30D was observed (Fig. 4) indicating a more flexible matrix and less cracking.

CONCLUSION
Matrix layering with the aqueous polymer dispersion Kollicoat® SR 30D is an effective tool to produce controlled release pellets. The required ratio of Kollicoat® SR 30D was dependent on the drug solubility, core type and plasticizer.

REFERENCES