Preparation Process and In Vitro Release Performances of HPMC-coated Systems for Pulsatile Release of Verapamil

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Purpose.

The aim of this work was to evaluate the preparation process and in vitro release performances of HPMC coated systems for pulsatile release, containing verapamil as the active ingredient. Tableted cores of different size, formulated either for an immediate or prolonged drug liberation, were investigated in order to possibly meet diverse needs connected with the chronotherapy of ischemic heart disease, mainly occurring around awakening time.

Methods.

Tablets containing different amounts of verapamil hydrochloride were obtained by rotary press (AM8S, Ronchi, I) and coated with HPMC (Methocel®E50 8% w/v aqueous solutions) in a tangential-spray rotary fluid bed (GPCG 1.1 Glatt®, D) equipped with a Teflon-coated disk. Release tests (n=3) were performed in a three-position USP28 disintegration apparatus (DT3, Sotax, CH; 800 ml distilled water, 37.0±0.5°C). A single test unit was placed in each basket-rack assembly. Fluid samples were withdrawn automatically at fixed time points. Acetaminophen was quantified by spectrophotometer.

Results.

The selected operating conditions allowed a feasible, high-yield process to be performed on the tablets in exam. Moreover, thanks to the relative flexibility of the coating technique, only minor modifications were introduced when coating different size cores. The in vitro release tests carried out on immediate release tablets with increasing coat thickness showed a typical lag phase preceding the prompt release of verapamil. Delayed release performances dependent on the coating level were also exhibited by systems prepared starting from prolonged release cores. From such systems, as pursued, the drug was released slowly over an extended time period. For all system typologies, a linear relationship was found between lag time and the applied amount of coating polymer.

Conclusion.

The results obtained in terms of low-viscosity HPMC-based aqueous spray-coating feasibility and programmable delayed release behavior seem to point out a potential suitability of the system for evening-dosing chronotherapy of ischemic heart disease.