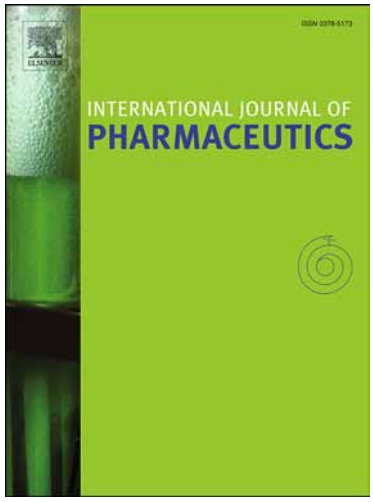

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Electrospun fixed dose formulations of amlodipine besylate and valsartan

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Abstract

Increasing numbers of elderly people require multi-drug therapies. One route to improve adherence rates is to prepare fixed dose combinations (FDCs), in which multiple active ingredients are loaded into a single formulation. Here, we report the use of electrospinning to prepare fast-dissolving oral FDCs containing amlodipine besylate and valsartan, two drugs prescribed as FDCs for the treatment of hypertension. Electrospun fibers were prepared loaded with one or both drugs, using polyvinylpyrrolidone as the polymer matrix. The fibers were cylindrical in morphology and comprise amorphous solid dispersions except with the highest loadings of amlodipine besylate. HPLC demonstrated drug entrapment efficiencies of between 90 and 99% of the theoretical dose. The mats have folding endurances and thicknesses suitable for use as oral films. The amlodipine besylate-loaded systems are fast-dissolving, with 100% release obtained within 120 s. In contrast, valsartan release from its single-drug formulations took longer, ranging from 360 s to 24 min. With the FDC formulations, rapid release within 360 s was achieved when the loading was 5% w/w of each drug, but again the release time increased with drug loading. Electrospun fibers therefore have significant promise as FDCs, but the target drug and its loading need to be carefully considered.

Keywords: Fixed dose combinations, electrospinning, polyvinylpyrrolidone, amlodipine besylate, valsartan, fast dissolving films.

1. Introduction

In the UK, older people make up 20% of the population and consume almost 50% of prescription drugs (Gorard, 2006). The majority of people aged 65 and older are diagnosed with multiple diseases that require management with several active ingredients simultaneously, often to the extent of polypharmacy, which is loosely defined as synchronous use of two to five or more medicines (Fulton and Allen, 2005). The adherence of patients to their drug regimen is crucial for successful therapeutic outcomes (Jimmy and Jose, 2011), and patients involved in polypharmacy are likely to find it challenging to take all their medicines at the appropriate times. This can profoundly affect the patient's quality of life, and also adds extra economic costs for healthcare providers (Hughes, 2004). Therefore, it is the task of formulators to prepare medicines to minimize the burden on patients and maximize the likelihood of a dosage regimen being accurately followed.