Formulation and In vitro Release Characterization of Metoprolol Succinate Extended Release Tablets

T. Sakthikumar, N.N. Rajendran and R. Natarajan
Department of Pharmaceutics, Swamy Vivekananda College of Pharmacy, Elayampalayam, Tiruchengodu, Namakkal – 637205, India
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ABSTRACT
The present study was aimed to develop an extended release tablet of metoprolol Succinate for the treatment of hypertension. Four extended release formulations F1-F4 were developed using varying proportions of hydroxylpropylmethylcellulose K100M, sodium carboxy methyl cellulose and Eudragit L30D55 by wet granulation. Five extended release formulations F5-F9 containing HPMC K100M and HPMC 5 cps in varying concentration were developed by direct compression. The physicochemical and in vitro release characteristics of all the formulations were investigated and compared. Two formulations, F7 and F8 have shown not more than 25% drug release in 1st h, 20%-40% drug release at 4th hour, 40%-60% drug release at 8th hour and not less than 80% at 20th hour and the release pattern conform with USP specification for 24 hours extended release formulation. It can be conclusively stated that optimum concentration of HPMC K100M (58%-65%) by direct compression method can yield an extended release of metoprolol succinate for 24 hours.

KEYWORDS: Metoprolol succinate; HPMC; CMC Na, Eudragit L30 D55; extended release

Introduction
Conventional oral drug delivery systems are slowly fading away in the market owing to disadvantages. These delivery systems produce fluctuation of drug plasma level that either exist at safe therapeutic level or quickly falls below the minimum effective level. This effect is usually totally dependent on the particular agent’s biological half life, frequency of administration and release rate. It is recognized that many patients can benefit from drugs intended for chronic administration by maintaining the plasma level within a safe effective range (Barhate et al., 2010). Extended oral drug delivery systems are highly recognized today for their benefits, improving the disadvantages of conventional drug delivery systems.

To be a successful, extended-release products the drug must be released from the dosage from at a predetermined rate in gastrointestinal fluids, maintain sufficient gastrointestinal residence time and be absorbed at a rate that will replace the amount of drug being metabolized and excreted. Extended drug delivery systems are used in the treatment of chronic rather than the acute condition, and they process a good margin of safety (Allen et al., 2009).

Metoprolol succinate is a cardio selective β-blocker used in the treatment of hypertension, angina pectoris and heart failure. It is available commercially in 25 mg, 50 mg strength as immediate release tablets. Its half life is about 3-7 hours. Its bioavailability is 50% following oral administration. It has been reported that conventional dosage forms increase the plasma concentration of metoprolol above that achieving the maximum β1 blockage (>300 nM). A therapeutic level of β blockage is achieved when plasma concentration is in the range of 80-300 nM. Higher concentration produces more β2 blockage but little additional β1 blockage. Lower concentration may result suboptimal β1 blockage. To meet the need for effective and well tolerated β1 blockage an extended release formulation of metoprolol succinate is beneficial to meet the objective of providing once daily dosing that maintains therapeutic plasma concentration and avoids the extreme peaks and troughs characteristics of metoprolol immediate release formulation (John et al., 2003).

Hydrophilic polymer matrix systems are widely used in oral controlled drug delivery because they make it easier to achieve a desirable drug-release profile; they are cost-effective and they have broad US Food and Drug Administration acceptance (Hamid et al., 2006). Among the hydrophilic polymers, cellulose derivatives such as methyl cellulose, hydroxy propyl methyl cellulose, and sodium carboxy methyl cellulose are generally considered to be stable and safe as release retardant excipients in the development of oral extended release dosage forms. HPMC is widely used in oral and topical formulations. In oral product, HPMC is primarily used as a tablet binder, in film-coating, and as an extended-release tablet matrix.