Research Paper

Design and Evaluation of Rectal Suppositories of Carvedilol

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ABSTRACT: Carvedilol (non-cardio selective β-blocker) is an antihypertensive used in management of hypertension, angina pectoris and heart failure. But its oral bioavailability is about 25-35% only due to significant degree of first pass metabolism. It has gastrointestinal side effects such as diarrhea, gastric pain and irritation. Hence, rectal suppositories of carvedilol were developed by using different water-soluble polymeric bases like gelatin and agar-agar using propylene glycol as plasticizer. The gelatin suppositories were disintegrating/dissolving type while gelatin–agar based suppositories were non-disintegrating/non-melting. All the formulations were evaluated for various physical parameters like weight variation, drug content uniformity, liquefaction time, micro-melting range, in vitro dissolution, short-term stability and drug-excipient interaction (FTIR). The mechanism of drug release was diffusion controlled and follows first order kinetics in majority of cases. The results suggested that when gelatin is replaced up to 25% w/w with agar, liquefaction time and drug release were not appreciably affected; higher proportions of agar exhibited incomplete and slow release. Stability studies conducted at 25±3º C and 60±5% relative humidity for three months indicated that the formulations were stable in the drug-content and in vitro drug release rate (p<0.05).

KEYWORDS: Carvedilol; rectal suppository; melting/ non-melting; gelatin; agar-agar

Introduction

For a long period of time, the rectal route was used only for the administration of local anaesthetics, anti-haemorrhoidal, vermifugal and laxative agents. Now the majority of natural and synthetic drugs are also formulated in the form of suppositories to produce a systemic effect (Hermann TW, 1995). Rectal route of administration is specifically useful for infants and children who have difficulty in swallowing oral medicine. Blood draining the lower part of the rectum largely bypasses the liver so that drugs showing a high first-pass metabolism when given orally are more effectively absorbed when administered rectally (Svein Oie et al., 1996). Further advantages include: (a) improved enzymatic drug stability, (b) higher drug load, (c) constant and static environment, (d) improved patient compliance, particularly for children and elderly people with swallowing difficulty, (e) avoidance of overdosing (Rytting JH et al., 2002). Drugs are introduced into the rectum either as solid (suppositories) or as liquid (enemas) for local and systemic action (Rawlins EA, 2002). The suppository may be useful long-term treatment of chronic diseases like essential hypertension, angina pectoris and heart failure. But its oral bioavailability is about 25-35% only due to its significant first pass metabolism. The drug carvedilol (CDL) has gastrointestinal side effects such as diarrhea, gastrointestinal pain and gastric irritation (Sweetman SC 2002). Hence, rectal suppositories of carvedilol were developed by using different water-soluble polymeric bases like gelatin and agar-agar with a view to improve the bioavailability and patient compliance and reduce the dose related side effects of the drug. Lipophilic drugs such as CDL are usually incorporated into water-soluble bases while hydrophilic drugs are formulated into the fatty base (Rytting JH et al., 2002).