Research Paper

Liposomal Drug Delivery of Metronidazole for the Local Treatment of Vaginitis

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ABSTRACT: The present investigation was aimed to formulate liposomes containing metronidazole for local therapy of vaginitis, capable to efficiently deliver entrapped drug during an extended period of time. Liposomes were prepared by simple thin film hydration technique using soya lecithin and cholesterol. Some preliminary trials and 3² factorial design were conducted to optimize the formulation. The drug to Soya lecithin to cholesterol ratio and volume of hydration media were chosen as independent variables. The percentage drug entrapment, particle size and drug release at 12 h were chosen as dependent variables. To achieve application viscosity and further improve the stability of liposomes, the prepared liposomes were incorporated in the bioadhesive carbopol 934P gel (1%), and the system were evaluated for the in vitro drug release and drug stability in phosphate-buffer pH 4.5 and simulated vaginal fluid (VFS) at 37±1°C. Stability study for liposome suspension and liposomal gel were carried out. All the performed experiments confirm the applicability of liposomes as a novel drug carrier system for the local treatment of bacterial vaginosis.

KEYWORDS: Metronidazole, liposome, mucoadhesive gel, vaginal fluid stimulant, thin film hydration.

Introduction

Metronidazole is classified therapeutically as an antibacterial and antiprotozoal agent, (Jack D. Sobel et al., 2006) indicated for the treatment of bacterial vaginosis (BV) (Jack D. Sobel et al., 2006, Hillier SL. et al., 1993). For the treatment of vaginitis, local administration of metronidazole has been favoured due to numerous side effects, toxicity, and teratogenic potential of the systemically applied drugs (Hope MJ. et al., 1993). Metronidazole vaginal gel is the intravaginal dosage form of the synthetic antibacterial agent, metronidazole USP at a concentration of 0.75% (Grewal MS. 1966). The limitation of local administration of metronidazole in vaginal therapy is the relatively short residence time of the drug at the site of application. To achieve desirable therapeutic effect, vaginal delivery systems for antimicrobial agents need to reside at the sites of infection for a prolonged period (Kukner S. et al., 1996, Fischbach F. et al., 1993). Hence, there is a need to develop effective drug delivery systems that should prolong the contact of the drug with vaginal mucosal surface and enable sustained release of incorporated drug. Liposomes have been widely used as drug carriers in topical treatments of diseases, especially in dermatology. They are capable of incorporating a variety of hydrophilic and hydrophobic drugs, to enhance the accumulation of drug at the administration site and to reduce side effects and incompatibilities (Hope MJ et al., 1993).

Since liposomes can provide sustained and/or controlled release of entrapped drug, they are considered for vaginal application, too (Jain SK. et al., 1997).

However, the major limitation of using liposomes topically and vaginally is the liquid nature of preparation. That can be overcome by their incorporation in an adequate vehicle where original structure of vesicles is preserved (Skalko N. et al., 1998). It has already been shown that liposomes are fairly compatible with gels made from polymers derived from cross linked poly (acrylic acid), such as Carpool® resins (Pavli Z. et al., 1999). Moreover, some Carpool® has proved excellent bioadhesive properties on the mucosal surface that would increase residence time in the vaginal cavity and at the same time increase absorption of the drug (Dittgen M. et al., 1997). Therefore, it seemed logical to choose gels prepared from Carbopol 934P as a vehicle for the incorporation of liposomes destined for vaginal delivery. A previous study has suggested application of liposomes containing antimicrobial drugs for the local therapy of vaginitis (Pavelic Z. et al., 1999), continuing that research, here, we report on the design and in vitro evaluation of a bioadhesive liposomal gel of metronidazole.

Materials and Methods

Metronidazole IP was received as a gift sample from Newcare Pharma Ltd., Mahesana, soya lecithin, cholesterol