Solubilization and Enhancement of Ex Vivo Vaginal Delivery of Progesterone Using Solid Dispersions, Inclusion Complexes and Micellar Solubilization


Abstract:

BACKGROUND: Progesterone (PG), a natural female sex hormone is used clinically in menopausal hormone replacement therapy and to control reproductive functions. Its very limited aqueous solubility results in reduced oral bioavailability and low patient compliance when administered in high doses. The aim of this study was to enhance PG aqueous solubility and vaginal delivery using solid dispersion, inclusion complex and micellar solubilization techniques. METHODS: PG solid dispersions and inclusion complexes were prepared by solvent evaporation method using different polymers, such as cyclodextrins, polyvinyl pyrrolidone (PVP), poly (ethylene glycol) 6000, Pluronic® F-127 and Pluronic® F-68. PG was also incorporated into polymeric micelles of Pluronic® F-127, Pluronic® F- 68, Brij®35 and Myrj®52. The prepared solid dispersions, inclusion complexes and micelles were characterized using different techniques. Drug permeability across rabbit vaginal mucosa was also studied. RESULTS: Dissolution studies of PG solid dispersions showed that the highest drug dissolution rate was achieved at PG/polymer weight ratio of 5:5. Further, complete drug dissolution was obtained for PG/Pluronic® F-127 solid dispersion after 15 min compared to 42% dissolution for the drug alone. Brij®35 micelles had a drug loading capacity ~15%, which increased the drug aqueous solubility by more than 20 folds. PG permeability coefficients through rabbit vaginal mucosa for PG/Brij®35 micelles and PG/Pluronic® F-127 micelles were ~ two times higher than that of the drug alone. CONCLUSION: These results confirm that Brij®35 and Pluronic® F-127 micelles are promising carriers to overcome PG shortcomings through enhancing its aqueous solubility and vaginal permeability.

Keywords:

Cyclodextrins; inclusion complexes; micellar solubilization; progesterone; solid dispersion; vaginal permeability.

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