Mucoadhesive Tablets for the Vaginal Delivery of Progesterone: In Vitro Evaluation and Pharmacokinetics/Pharmacodynamics in Female Rabbits


Abstract:

OBJECTIVE: To develop mucoadhesive tablets for the vaginal delivery of progesterone (P4) to overcome its low oral bioavailability resulting from drug hydrophobicity and extensive hepatic metabolism. METHODS: The tablets were prepared using mixtures of P4/Pluronic® F-127 solid dispersion and different mucoadhesive polymers. The tablets physical properties, swelling index, mucoadhesion and drug release kinetics were evaluated. P4 pharmacokinetic and pharmacodynamic properties were evaluated in female rabbits and compared with vaginal micronized P4 tablets and intramuscular (IM) P4 injection, respectively. RESULTS: The tablets had satisfactory physical properties and their swelling, in vitro mucoadhesion force and ex vivo mucoadhesion time were dependent on tablet composition. Highest swelling index and mucoadhesion time were detected for tablets containing 20% chitosan-10% alginate mixture. Most tablets exhibited burst release (∼25%) during the first 2 h but sustained the drug release for ∼48 h. In vivo study showed that chitosan-alginate mucoadhesive tablets had ∼2-fold higher P4 mean residence time (MRT) in the blood and 5-fold higher bioavailability compared with oral P4. Further, same tablets showed 2-fold higher myometrium thickness in rabbit uterus compared with IM P4 injection. CONCLUSION: These results confirm the potential of these mucoadhesive vaginal tablets to enhance P4 efficacy and avoid the side effects associated with IM injection.

Keywords:

Progesterone; absorption; bioavailability; chitosan; mucoadhesion; vaginal

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