ABSTRACT

The major challenge encountered with the use of thermoplastic polymeric drug delivery devices is that during insertion or removal, they tend to cause injury and inflammatory response due to friction of the device with the biological tissues. The use of biocompatible hydrophilic polymer coatings on the thermoplastic polymeric device can provide a smooth surface to reduce adverse tissue reactions and facilitate implantation at the target site. Hydrophilic polymers are also necessary for most drug delivery systems as the drugs do not adhere to the hydrophobic polymer surface, effectively. Entrap the drugs in polymeric hydrogels to ensure controlled release of sufficient quantity of drug in a beneficial manner, and also provide a platform for appropriate drug elution kinetics. This proposed system can be helpful for many diseases with different types of drug.

Endometriosis is an estrogen-dependent disease characterized by the presence of functional endometrial tissue outside the uterus. The treatment options for endometriosis primarily include analgesics and non-steroidal anti-inflammatory drugs (NSAIDs) and hormonal therapy. A new treatment has recently emerged for the treatment of endometriosis. Aromatase is an enzyme which helps in the conversion of androgen to estrogen. Letrozole, primarily a breast cancer drug, is the most effective non-steroidal, third generation aromatase inhibitors (AIs) which inhibit aromatase in peripheral tissues and is associated with suppression of estrogen. The various side effects, viz., hot flashes, headache, breast tenderness and short half-life (≈ 45 h), associated with this drug motivated us to consider, targeted drug delivery system by providing controlled or sustain release.

In the present research work we have successfully prepared drug release system by cross-linked hydrophilic polymer coating on the modified low density polyethylene (LDPE) surface by direct dip coating or coating via *in-situ* polymerization of monomer. In first phase poly (vinyl alcohol) (PVA) was covalently coated on the maleic anhydride grafted LDPE for PVA/MA–g–LDPE release system. This prepared system showed a constant release of letrozole up to 35 days. In second phase the 2-hydroxyethyl methacrylate (HEMA, monomer) was polymerized onto acrylamide grafted LDPE by *in-situ* co-polymerization for preparation of pHEMA/AAm–g–LDPE release system. From this system aapproximately 95% drug release was observed up to 72 h. Therefore, this release system will be applicable to deliver the drug maximum for 5 to 6 days. Furthermore, to obtain more controlled and extended drug release behavior we have developed the letrozole-loaded microparticles and found more controlled release up to 30 days. These developed letrozole-loaded microparticles were incorporated into pHEMA/AAm–g–LDPE system and their release behaviors were analyzed. It was found that embedded microparticles into coated polymer matrix released drug repectively slow but at constant rate up to 32 days. These finding suggest that the release system hold potential for targeted and controlled release over a long period of time.

Keywords: Hydrophilic LDPE, surface modification, letrozole, endometriosis, thin layer polymer coatings, PLGA, microparticles, controlled drug release system.