INTRODUCTION

Various technologies have been investigated for achieving different aims of modified release like sustained, delayed, pulsatile, targeted or programmed release. Regardless of the delivery type, the main mechanisms associated with drug release in these systems include diffusion, swelling, erosion, ion exchange or osmotic effect (Theeuwes, 1975).

Orally administered drugs often suffer from poor pharmacokinetics. The absorption may be slow or too fast while the dosage form travels through the gastrointestinal tract. Rate-controlled release systems allow maintaining the drug concentration within the body at an optimum level. This minimizes the risk of disadvantageous side effects, poor therapeutic activity, or even adverse effects. Therefore a lot of effort is dedicated to the development of controlled drug delivery systems for orally administered drugs. Hydrophilic matrix systems have been the most popular because of the simplicity of formulation, ease of manufacturing, low cost, FDA acceptance, and applicability to drugs with wide range of solubilities (Sako et al., 2002). Drug release from these systems is the consequence of controlled matrix hydration, followed by gel formation, altered textural/rheological behavior, matrix erosion eventually leading to drug dissolution and/or diffusion. The significance of these processes depend on type of polymer, its concentration, drug solubility and changes in matrix characteristics as the process of drug release proceeds (Fassihi et al., 2006). Polyvinyl pyrrolidone sustained release grade kollidon SR, hydroxypropyl methylcellulose and polyethylene oxide, which are available in a range of molecular weight (MW)/viscosity grades are the most commonly used polymers in hydrophilic matrix formulations, owing to their swellability in water, availability, US FDA acceptance, and unique swelling/erosion characteristics. Over the years, a multitude of different technological approaches addressing this goal have been developed. However,
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only few of them succeeded in becoming cutting edge technologies for application to versatile therapeutic applications. A very successful approach for rate controlled drug delivery is represented by osmotic micropumps. This might be related to the ion driven water imbibation concept applying one of the most fundamental principles of biology, osmosis, in a technical device.

Osmotically controlled oral drug delivery systems (OCODDS) utilize osmotic pressure as the energy source for the controlled delivery of drugs. Drug release from these systems is independent of pH and hydrodynamic conditions of the gastro-intestinal tract (GIT) to a large extent, and release characteristics can be easily adjusted by optimizing the parameters of the delivery system (Theeuwees, 1975; Verma et al., 2002; Verma and Garg, 2004). These include intended core matrix design and hydrophobic coating over the compressed tablets. Osmotic drug-delivery systems utilize osmotic pressure as the driving force for releasing the drugs from the dosage form. The local pH, presence of food and other physiological factors may affect drug release from conventional CR systems (matrices and reservoirs), whereas drug release from peroral osmotic systems is independent of these factors to a large extent. In recent years hot melt extrusion (HME) process has gained a lot of attention in the pharmaceutical industry as it is a continuous, scalable process in a closed unit with high throughput rate and easily controllable process parameters. The extrusion process offers several advantages over conventional pharmaceutical processing techniques, which include uniform mixing (suitable for potent drugs), fewer processing steps, continuous processing and short processing time, lifecycle management/Intellectual property positioning/design around strategy, solubility enhancement (BCS class II and IV drugs), taste masking and modulating drug release (McGinity and KOleng, 2004; Jones, 2008; Grunhagen and Muller, 1995, Singhal et al., 2011).

This approach has been utilized in the delivery of poorly water-soluble, class II drugs mainly for enhancing their dissolution rate. In addition to solubility enhancement, the technology/process can be applied for other applications including sustained release, wet granulation, melt granulation etc. Extrusion is the process of converting a raw material into a product of uniform shape and density by forcing it through a die under pressure. An advantage of preparing granules by the HME technique is better
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consolidation of the dry powders due to melting of the polymer(s) at the desired temperature. In addition, this process does not involve the use of water or solvents for formation of granules. The molten mixture forms uniform granules as the blend is passed through a twin-screw system, avoiding variation due to different levels of human skill. In wet and dry granulation methods, granules are not very well consolidated and are non-uniform because the process is completely dependent on the skill of worker. An oral osmotic drug-delivery system resembles a film-coated tablet. A typical elementary osmotic drug delivery system consists of an osmotically active core composed mainly of drug substance surrounded by a semipermeable membrane through which a single opening is drilled using a high-energy laser beam. The membrane is permeable to water but not to the drug or to other molecules present in gastric or intestinal fluid. When the tablet comes into contact with the aqueous medium, water permeates slowly into the system due to osmosis and dissolves the drug contained in the core tablet, thus producing its saturated solution (Verma et al., 2002). This saturated solution of drug is then pushed out through the laser-drilled hole owing to the osmotic pressure generated inside the tablet due to the solubility of the osmogens.

Glipizide, an oral hypoglycemic agent, is one of the most commonly prescribed drug for the treatment of patients with type II diabetes mellitus (Brogden et al., 1979). It is practically water-insoluble, but the absolute bioavailability is close to 100%. Thus, it belongs to class II of Biopharmaceutic Classification System (http://166.78.14.201/tsrllnc.com, 2013). It has a relatively short elimination half-life (2–4 h), thereby requiring twice daily dosing in large number of patients (Berelowitz et al., 1994 and Foster et al., 2000), which often leads to fluctuating blood glucose levels and often decreases the compliance of multidose therapy. Originally available in 1984, it is marketed by Pfizer under the brand name Glucotrol in the USA, where Pfizer sells Glucotrol in doses of 5 and 10 milligrams and Glucotrol XL (an extended release form of glipizide) in doses of 2.5, 5, and 10 milligrams. Other companies also market glipizide, most commonly extended release tablets of 5 and 10 milligrams.

Glucotrol XL of Pfizer has been designed by employing push-pull type bilayer osmotic drug delivery system technology and is required to release glipizide at 1,2,4,8 and 16 hrs (not less than 80% in 16 hrs) as per office of generic drugs (OGD) media. US
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Patent 5591454 (Kuczynski et al., 1997) suggests bilayer (bilaminate) push-pull type osmotic drug delivery system of glipizide. Marketed products of glipizide in India are available as monolayer matrix designed tablets.

The present study is aimed at designing, administrating and optimizing controlled release of glipizide from an oral osmotic drug delivery system. The marketed controlled release tablets of glipizide (Glucotrol XL) were proposed to be used for comparing the release profile with the developed formulation.