Chapter 44
Smart Hydrogels for Pharmaceutical Applications

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ABSTRACT

The latest development in the field of smart hydrogels application as drugs carriers is shown in this chapter. Hydrogels are three-dimensional polymer network consisting of at least one hydrophilic monomer. They are insoluble in water, but in the excess presence of water or physiological fluids, swell to the equilibrium state. The amount of absorbed water depends on the chemical composition and the crosslinking degree of 3D hydrogel network and reaches over 1000% of the xerogel weight. Stimuli-responsive hydrogels exhibit significant change of their properties (swelling, color, transparency, conductivity, shape) due to small changes in the external environment conditions (pH, ionic strength, temperature, light wavelength, magnetic or electric fields, ultrasound, or a combination thereof). This smart hydrogels, with different physical and chemical properties, chemical structure and technology of obtaining, show great potential for application in the pharmaceutical industry. The application of smart hydrogels is very promising and at the beginning of the development and exploitation.

INTRODUCTION

A short overview of the development and current state-of-art relating to the implementation of "smart" gels as carriers of pharmaceuticals in systems for modified/controlled drug release is presented in this chapter. In today's rapid technology expansion, there is an ever-growing trend for a new generation of "smart" materials. They have the advantage of being less limited by design constraints. One such category of these intelligent materials is "smart" or stimuli-responsive polymers. Researches in this chapter were focused on:

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- Different ways of synthesis and characterization of stimuli-responsive hydrogels,
- Analysis by the type of stimuli they respond to, and
- Implementation of systems for the controlled delivery of drugs (chemically controlled systems, diffusion controlled systems, systems controlled by the swelling and systems for modulated release) (Milić & Petrović, 2003).

Smart hydrogels with different physical and chemical properties, chemical structure and obtainable technology show great potential for application in the pharmaceutical industry. The aim of this chapter is to provide the latest trend and idea for further research opportunities in the field of smart hydrogels application as drugs carriers. Also, it could be the basis for the synthesis of new smart materials and for their new applications.

Background

Hydrogels are three-dimensional polymer network consisting of at least one hydrophilic monomer. They are insoluble in the water, but in the excess presence of water or physiological fluids, swell to the equilibrium state. Koetting et al. (2015) cited that hydrogels are three dimensional network structures consisting of polymeric chains, joined by tie points or joints and swell in water up to thermodynamic equilibrium. There are some variations of this basic definition. Hydrogel is defined as a solid, crosslinked three-dimensional network which swells in water, and the hydrophilic macromolecules contain 20-95% of water, according to Grant & Hackh's Chemical Dictionary (1987). According to IUPAC recommendations, *hydrogel* is defined as a gel in which the swelling agent is water (Slomkowski et al., 2011). The network component of a hydrogel is usually a polymer network, while a hydrogel in which the network component is a colloidal network may be referred to as an *aquagel*. Polymer network without water is *xerogel*. *Gel* is defined as non-fluid colloidal network or polymer network that is expanded throughout its whole volume by a fluid (Jones et al., 2009). Gels also may be defined as a substantially diluted crosslinked system, which exhibits no flow when in the steady-state (Ferry, 1980). It is consequential to understand difference between the term *gel* and *hydrogel*. Their polymeric network may be similar in chemical composition, but different in physical features. When *gel* is swollen to equilibrium, the further addition of fluid polymer network should be diluted. But, *hydrogel* may absorb large amounts of fluid, increasing the volume to the equilibrium state, while still maintaining a three-dimensional structure and shape (Gupta et al., 2002).

Network structure of the hydrophilic polymer chains absorbs and holds water within the pores. The pores in hydrogels were created during swelling of the polymer network when water molecules penetrate the network and volume of the system increases. The pores are usually not present in the dry network before swelling. The only exception is when the pores are formed intentionally during synthesis of the dry network. The amount of water that the hydrogel may receive depends on the chemical composition and the crosslinking degree of three-dimensional hydrogel network and reaches over 1000% of the weight in the xerogel state (Hoffman, 2002; Pal et al., 2009; Jagur-Grodzinski, 2010). Graham (1861) gave a description of the gel: "while the rigidity of the crystal structure is excluded from the outside looks, the softness of gelatin colloids gives fluidity and allows the colloid to become a medium for the diffusion of liquids, like water itself". He was the first to introduce the term hydrogel in 1864. and described special diffusion properties of the gel (Graham, 1864). Jordan-Lloyd (1926) gave a concise and useful