PHOTOSENSITIVE HYDROGELS FOR ADVANCED DRUG DELIVERY

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ABSTRACT

Interest in bioresponsive polymers is gaining momentum in the field of controlled drug delivery. This polymers which regulates transport of ions or molecules, change in chemical signals like optical, thermal which help for fruitful application. These polymers play important role wide applications such as drug delivery, tissue engineering and optical systems and other biomedical fields. Polymers are very useful with respect to reversible reactions sol-gel transition or vice versa and also molecular interactions that translate into macroscopic response to physiological conditions. Recent advances and challenges in the developments towards application of stimuli responsive polymers drug delivery systems. Particularly light is interesting property of hydrogel for controlling the drug release for longer duration and with ease of application. Hence we reviewed on recent development and discussion on light responsive polymeric drug delivery systems.

INTRODUCTION

Modern drug delivery system has been made possible advance drug delivery due to advance polymers. As polymers with intricate properties became available, development of critical formulation and their application became grooming. For conventional drug delivery, the plasma concentration of a drug is directly proportional to the administration dose. The only advantage of conventional drug delivery is low cost and to alleviate the shortcoming of conventional formulation controlled drug delivery invented. Which help in prolong plasma drug concentration within a therapeutic window.[1] A review of Gil and Hudson focused on the classification and physical form of stimuli-responsive polymers and their bioconjugates, as well as recent approaches of molecular design which are extremely necessary to develop more desirable and functional stimuli responsive polymers.[2] Many investigations have focused on the synthesis and characterization of bioengineering functional (co)polymers with physical, chemical, and electrical stimuli properties which can respond to different environmental conditions (light, temperature, pH, ionic strength, electric field, shear stress, etc.)[3] These stimuli-responsive polymers undergo a reversible change in response to external stimuli such

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as temperature, pH, ion, light, etc. The change in polymer physical properties through small external changes in temperature, light, ion or pH can be used to controlled drug delivery. A visible light sensitive smart polymer that forms aqueous two phase systems are potentially used in industrial bioseparation techniques. Many of the problems of two phase systems like; they cannot be recycled, result in increasingly expensive bioproducts, purification processes, and environmental pollution have been overcome by the use of light sensitive smart polymers. These systems are biocompatible, biodegradable, polymerizable, and at least partially water soluble macromers.[4, 5] In this review author would like to focus on aged and modern technique which can be apart for current drug delivery development.

LIGHT ACTIVE POLYMERS
Light responsive polymers may be UV or visible light sensitive. However, visible light responsive polymers and hydrogels are safer, inexpensive, readily available, clean and easily manipulated. Bis (4-dimethylamino) phenylmethyl leucocyanide, a leuco derivative molecule, was introduced into a polymers network to produce a UV light responsive hydrogels. Triphenylmethane leuco derivatives are normally neutral but dissociate triphenylmethyl cations. At a mixed temperature, the hydrogels discontinuously swell in response to UV irradiation but shrink when the UV light is removed. The swelling is due to an increase in osmotic pressure within the gel due to the appearance of cyanide ions formed by UV irradiation. [6, 7] A light sensitive chroophore e.g. trisodium salt of copper chlorophyllin to poly (N-isopropylacrylamide) hydrogels, visible light responsive hydrogels can be prepared quoted by Suzuki R. [8] An ionizable group of polyacrylic acid, the light responsive hydrogels can be rendered pH sensitive as well and may be activated by visible light and may be deactivated by increasing in pH. [6] Triphenylmethane leuco derivatives dissociate into ion pairs upon exposure to UV light. The back reaction by recombination the ion pair occurs thermally in the dark. The reversible photo induce ionic dissociation of trienphylmethane leuco derivative are incorporated in hydrogels, the reversible variation of electrostatic repulsion between photogenerated charges will give rise to the photo induced expansion and shrinkage of the hydrogels. [9] Light active azobenzene moieties can also be incorporated into hydrogels to prepare light active hydrogels. [10] Another strategy of preparing light responsive hydrogels is by incorporating spiropyran or its derivatives into hydrogels network. [11] The molecular structural change form and open form upon light trigger is studied by sumaru. [12] Spiropyran bearing a carboxylic acid group to the amide bond of PNIPAAm-allylamine copolymer microgels to prepare light active hydrogels. [13]

Synthesis of Photo responsive Polymer:
Two photo responsive polymers with hydroxyl termini, DMAAm and DMAA, were synthesized by free-radical copolymerization of DMA with AZAAM or AZAA in dimethyl formamide at 60°C for 20 h, using 2-mercaptoethanol as a
chain transfer agent and 2,2'-azobisbutyronitrile as an initiator (monomer concentration _ 2 mol_liter).

The ratios of DMA_AZAAm or AZAA_2-mercaptoethanol_2, 2'-azobisbutyronitrile were varied to change the molecular weights and the photo responsive phase transition temperatures. The products were purified by precipitation in diethyl ether three times and dried in vacuo. The contents of AZAAm or AZAA incorporated in the copolymers were determined by 1H-NMR (Spectrospin and Bruker, dpx200), comparing the ratio of aromatic and aliphatic hydrogens. The number average molecular weights ($M_n$) of the copolymers were determined by gel permeation chromatography, (Waters, Styragel HR3 and HR4) in tetrahydrofuran, using polystyrene standards. The hydroxyl terminus of DMAA or DMAAm was converted to a vinylsulfone (VS) group for conjugation to sulphhydryl group in proteins. DMAA or DMAAm was dissolved in 20 ml of methylenechloride with 0.03 g of potassium tertbutoxide and 100 _l of divinylsulfone (DVS_OH _ 10:1 molar ratio). The solution was stirred for 12 h at room temperature under nitrogen atmosphere. [4]

![Fig. 1. Schematic model for the photo responsive enzyme switch](image)

A light-sensitive polymer was synthesized by using N-isopropylacrylamide, $n$-butyl acrylate, and chlorophyllin sodium copper salt as monomers. The polymer was applied to form aqueous two-phase systems with Dextran20000; the polymer containing chlorophyllin sodium copper salt was sensitive to visible light. The light-sensitive copolymer would precipitate from solution under light irradiation (488 nm) and could be reused. [14, 15]

**Mechanism Action of Light responsive polymers:**
The macromers include at least one water soluble region, at least one region which is biodegradable, and at least two free radical polymerizable regions. Macromers are polymerized by free radical initiators under ultraviolet light, visible light excitation, or thermal energy. The core water soluble region can consist of PEG, poly (vinyl alcohol), PEO-PPO, polysaccharides such
as hyaluronic acid, or proteins such as albumin. The biodegradable regions may be polymers made up from polylactic acid, polyglycolic acid, poly (anhydrides), poly (amino acids) and polylactones. Preferred polymerizable regions include acrylates, diacrylates, methacrylates, or other biologically accepted polymerizable groups. Initiators that can be used for generation of free radicals include ethyl eosin, acetophenone derivatives, or camphorquinone.\[14\]

**Application of photo responsive polymers:**

Responsive polymer systems can be used for a variety of applications, such as switching surfaces and adhesives, protective coatings that adapt to the environment, artificial muscles, sensors and drug delivery. Biochemistry, environmental sciences and biomedical sciences are just a few examples of important areas that will benefit greatly from further development of applications of stimulus-responsive polymeric materials.\[16\]

Delivery systems with a pulsatile or triggered release pattern are receiving increasing interest for the development of various drugs, where conventional systems with a continuous release are not ideal. Biomicroelectronic and microfabricated systems are actively targeted by many researchers and even by companies. A commercially available microchip, ChipRx, which integrates silicon and electroactive polymer technologies for controlled delivery and micromachined particles for a variety of drug delivery applications.\[17\]

**Photo responsive hydrogels**

Photo responsive hydrogels that can show changes upon photo irradiation in their physical and/or chemical properties such as electrical, viscosity, shape, degree of swelling are of interest for various biomedical applications. To contrast photoresponsive systems, the choice of the photoreactive group and the fundamental structure of the gels are crucial. Both physically cross linked and gelators also show a gel to sol transitions because of the discussions of the polymeric structure. Hydrophobic interaction of amphiphilic polymers can also be controlled by adding cyclodextrins, which can form inclusion complex with hydrophobes on the polymers and shield the hydrophobic interaction. If photoresponsive competition guest molecules were added, which can form inclusion complexes with the cyclodextrins only when it is at certain form, hydrophobic interaction among the polymers can be governed by these photoresponsive additives, thus a photo responsive hydrogels systems can be obtained.\[18\]

**CONCLUSION**

In this review we highlighted recent developments of photoresponsive polymeric systems and their applications. The controlled drug delivery through hydrogel with help of photon or light makes these systems beneficial for biomedical applications. Light as a stimulus is exclusively efficient as it is easily available in the environment and does not include the use of secondary sources of energy for its activation. Stimuli responsive polymers are valuable in applications for site and self regulated drug delivery systems like bioresponsive or
environmental responsive, biomedical sciences. Responsive polymeric drug delivery is grooming for development in medical sciences. Looking towards application of environmental sensitive or bio sensitive polymers foresight for drug delivery system is wide and fruitful. Physic-chemical requirements necessary to achieve stimuli-responsiveness in heterogeneous polymer networks as well as discusses recent developments and future trends. While individual structural components of polymeric networks are responsible for localized chain-responsiveness, desirable spatial and energetic network properties are necessary for collective and orchestrated responsiveness to external or internal stimuli [19].

REFERENCE


