SMART POLYMERS: A SMART APPROACH FOR DRUG DELIVERY SYSTEMS

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Abstract

Smart polymers are the macromolecules which show specific physiochemical change due to small changes in their environment such as pH, temp., ionic factors, light, magnetic field etc. These polymers have ability for sensation in even small changes i.e. stimulus in their nearby environment and give response to it and get their original state or form when stimulus is removed. This article includes various types of smart polymers based on various stimuli like pH, temp., enzymes, electric field, mechanical stress, electromagnetic radiation etc. to which it responds. These smart polymers also have advantages in comparison with conventional polymers such as ease of manufacturing, ease of administration; biodegradability and also ability to alter the release pattern of incorporated agents from the formulations. There are different organs, cellular compartments and tissues which may have large differences in pH. Here pH can be act as a stimulus. Stimuli responsive smart polymer are natural as well as synthetic.

Keywords: Smart polymers, pH responsive polymers, temp. responsive polymers, PNIIAM, Glucose responsive polymers.

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INTRODUCTION

Polymers are macromolecules and smart polymers are the macromolecules which show sensation for even the small change in their nearby environment. These changes can be physical, chemical or biochemical. Physical changes include change in temp., ionic strength, electromagnetic radiation or change in highly structured protein due to denaturation, aggregation, precipitation etc. Chemical changes include reactions such as oxidation, deamidation, hydrolysis, racemisation which gives instability to drug. Also change in pH, ionic strength, chemical agents etc. Biochemical changes include changes in biochemical agents like enzymes. Smart polymers have unique feature is that can show sensation to even small change in environment like above by changing structure or nature or form and also can be reversed to their original structure or nature or form after removal of stimuli. Hence these smart polymers have wide range of applicability like it can be used in Controlled drug delivery systems. It can also be used in tissue engineering, also in gene therapies. It can also be used in biomedical technologies. For protein purification also smart polymers can be used.

<table>
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<th>Types of stimuli</th>
<th>Responsive polymeric materials</th>
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<tr>
<td>Temperature</td>
<td>Poloxamers, Chitosan, Xyloglucan, Cellulose, Poly(n-alkyl acrylamide)s.</td>
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<tr>
<td>pH</td>
<td>Eudragit S 100, Eudragit L 100, Dendrimers, Poly(propyl acrylamide), Poly(ethacrylic acid), Polysilamine.</td>
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<td>Light</td>
<td>Modified poly(aryl amide)s.</td>
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<td>Electric potential</td>
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<td>Ultrasound</td>
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<td>UV Radiation</td>
<td>Azobenzene, polyacrylamides-triphenylmethane leuco derivatives.</td>
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<tr>
<td>IR Radiation</td>
<td>Poly (N-Vinyl carbazole) composite.</td>
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</table>

Types of smart polymers

Temperature responsive smart polymers (Thermosensitive Polymers)

Temperature responsive smart polymers show change in their solubility due to even small change in temp. Hence also called as thermosensitive polymers. Normal human body temp.is about 37°C and it can be elevated in conditions like fever or presence of pyrogens. During such conditions Drugs can be delivered in site specific manner by incorporating them in such thermosensitive polymers [1].

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Mechanism of drug release from thermosensitive polymers

These thermosensitive polymers have hydrophobic groups like methyl, ethyl, propyl etc. Hence these have two characteristic properties like LCST (Lower Critical Solution Temperature) and UCST (Upper Critical Solution Temperature). Some uncharged polymers can be soluble in water due to hydrogen bonding with water molecules. This hydrogen bonding efficiency decreases with increase in temp. Hence as the temperature increases above LCST hydrogen bonding disrupts and polymeric monophasic system become hydrophobic i.e. insoluble in water and shows phase separation. Hence LCST also called as Cloud point. But below LCST hydrogen bonding efficiency remains more and hence monophasic polymeric system becomes hydrophilic i.e. polymers remains soluble in water. Such away depending upon critical solution temperatures polymers exists in two forms as either solution or gel. Because below LCST or cloud point polymers shows hydrophilic property due to more hydrogen bonding efficiency and hence remain in solution form with water as a solvent. But above UCST hydrogen bonding efficiency decreases and hence water get swell out from polymers and polymer shows hydrophobic property. Due to this it shrinks and converts in to Gel form. Such away near body temperature (32°C) polymers undergoes Sol-Gel transformations [2].

Good example of thermosensitive polymer is poly(N-isoacrylamide)s or (PNIIAM)

PNIIAM

One of the specific feature of this polymer is that it have Critical Solution Temperature point near normal body temp. i.e. 37°C. This makes it an excellent carrier for drug delivery. Below about 27°C it shows clear solution but above 27°C solution becomes cloudy and upon further heating solution get transformed in to gel. At the temp. about 45°C gel shrinking takes place and it is occurred due to expelling of water from gel i.e. also called as synaeresis [2].

Advantages of Drug delivery system using Thermosensitive polymers

It can be used for site specific drug delivery system.

Both Lipophilic as well as Hydrophillic drugs can be delivered by incorporating them in thermosensitive polymers.

Also can be used for sustained drug delivery system.

Limitations: (Specifically of PNIIAM)

Show cytotoxicity due to presence of quaternary ammonium group in it’s structure. It is non biodegradable. It have ability to activate platelets when come in contact with body fluid.
Disadvantages of Drug delivery system using Thermosensitive polymers

- High burst drug release.
- Low mechanical strength of the gel leading to potential dose dumping.
- Lack of biocompatibility of polymeric system.
- Lowering of pH of system due to acidic degradation.

pH sensitive smart polymers

These are the polymers which shows sensation for the change in pH and used for the delivery of various therapeutic agents.

Mechanism of drug release from pH sensitive polymers

These are the polymers having either acidic or basic group upon them and are capable of accepting or donating protons according to the change in pH of external stimuli. Polymers with large number of ionisable groups are called as polyelectrolytes. These are classified in to two groups : weak polyacids and weak polybases.

Most of the pH sensitive anionic smart polymers are based on Polyacrylic acid (PAA) i.e carbopol, Poly methacrylic acid (PMAA). Some are in market like Eudragit L, Eudragit S. There are also some natural pH sensitive polymers like albumin, chitosan, gelatin etc. [3.4].

Good example of natural pH sensitive polymer is chitosan.

Chitosan

It can be used for oral or mucosal application due to its mucoadhesive property. It is one of the good alternative for pharmaceutical implants due to its porosity and ability for controlled drug delivery. It can also be used to carry negatively charged DNA which can easily bind to positively charged amino group of chitosan. One of the example of drug delivery is anticancer drug Paclitaxel. Incorporation of this drug in Chitosan/glycerophosphate gives slow and controlled delivery of this drug and inhibits growing cancer cells.

3. Field responsive smart polymers

These are polymers which gives response to light, electric, sonic or electromagnetic radiation [5].

Light sensitive smart polymers

These can be classified as UV sensitive and visible light sensitive polymers. This is based upon the wavelength of light which triggers phase separation.

UV sensitive polymers: Bis(4-dimethyl amino phenylmethyl leucocyanide), other leuco derivative polymers.
Visible light sensitive polymers: Hydrogel prepared using chromophore like trisodium salt of copper chromophyllin.

**Electric sensitive smart polymers**

These type of polymers have ability of changing their physical properties when change in electric current. Electroresponsive polymers have ability to transform electrical energy in to mechanical energy. Hence can be used on wide scale for developing controlled drug delivery systems.

**Mechanism of action of drug release from electrosensitive polymers**

Generation of electric current during this system causes change in pH. This change in pH causes breaking of hydrogen bondings between long polymeric chains. This disruption of polymeric chains results in release of drug which is get incorporated inside the electrosensitive polymers. Such away we can design controlled drug delivery by controlling the release of drug from such electrosensitive polymers.

Natural polymers like chitosan, alginate can be used to prepare electrosensitive polymers. Also synthetic polymers like methacrylic acid, vinyl acrylic acid, acrylonitrile, vinyl alcohol etc can be used for the preparation of electrosensitive polymers [5].

**Bioresponsive polymers**

**Glucose responsive polymers**

These are also called as sugar sensitive polymers. These have also ability to sense normal endogenous secretion of insulin and help to minimise the diabetic complexes. Such away these polymers play two vital roles at a time as i. Sensing insulin secretion ii. Sensing glucose presence.

**Mechanism of action of Glucose responsive polymers**

Ability of glucose responsiveness is depend upon the response of polymers to the byproducts obtained after the enzymatic oxidation of glucose. Enzymatic oxidation of Glucose is done by enzyme Glucose oxidase that gives the byproducts as Gluconic acid and H₂O₂. Ex. If glucose level increases then it’s oxidation gives more byproducts which will be detected by responsive polymers and will fascillitate release of insulin [6].

**Limitation**

- Short response time
- Non biocompatibility.

**Enzyme responsive polymers**

Enzyme always plays very important role in various cell regulation and development processes. Many times enzyme activities occurred at specific cell site and hence at that site enzyme get
occurred in high concentration. So, by this way we can develop targeted drug delivery systems using enzymes as carriers for drugs. Also, enzymes play a vital role in the field of diagnostics. Such away by using all such enzyme activities we can develop effective therapies which will be based upon the concept of enzyme sensitive polymers [7].

**Applications of smart stimuli responsive polymers** [8,9,10,11]

- For cell culture
- In protein purification
- As a gene carrier
- In textile engineering
- In tissue engineering
- For recovery of oil.
- As a therapeutic agent also etc.

**FUTURE PROSPECTS**

Such away current article shows various roles of smart polymers and also indicates that smart polymers can be used for the advancement of various novel drug delivery systems. Because these polymers plays vital role for both therapeutic necessity as well as effective drug delivery. Also by using such smart polymers we can effectively develop controlled, site specific as well as targeted drug delivery system. Each type of smart polymers shows specific advantages which can be used for effective drug delivery. For example incorporation of both hydrophilic as well as hydrophobic drugs. Also, there are also limitations for some polymers like slow response times. But there are wide opportunities for the development and modification in the smart polymer based drug delivery systems which can show wide applicabilities also.

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