A. Veenadevi et al /J. Pharm. Sci. & Res. Vol. 13(5), 2021, 247-253

ISSN:0975-1459
Journal of Pharmaceutical Sciences and Research
www.jpsr.pharmainfo.in

Brainy Dynamic Polymers – A Conceptual Overview

A. Veenadevi, Ch. V. Prasada Rao, K. Pallavi*, P. Srinivasa Babu
Vignan Pharmacy College, Vadlamudi, Guntur, AP, India

Abstract:

Smart polymers are the area of interest for researchers working in the area of formulation development. Despite their countless applications in the fields of biomedical, electrical, sensor-related, and environmental applications, these polymers are yet to be explored further in pharmaceutical development. Extensive research focusses on the development of intelligent and responsive dosage forms using smart polymers. This review highlights various smart polymers which include chameleonic polymers (polymers that change color with various influencing factors like light, temperature, electricity, mechanical force or pressure, etc.) and stimuli-responsive polymers (Polymers which alter their structure, orientation, swelling/shrinking nature, etc.). Besides, this review facilitates useful perception and deeply-rooted investigation on examples and applications of various chromogenic and stimuli-responsive polymers.

Key words: Chameleonic, color-changing materials, intelligent, stimuli responsive polymers, smart polymers.

1. INTRODUCTION:

Material that changes color systematically named as "chromogenics" later employing chameleonic since they changed the color reversibly attributable to changes in environmental circumstances such as temperature, brightness. Theoretically principle involved color altering occurs due to alteration in the symmetry of electrons initiated by the stimulus like cleavage of chemical bonds or deviations occur inside the molecule with consequent modification of optical things such as reflectance, absorption, emission, or transmission. [1]

Stimuli-responsive polymers experience dramatic & abrupt physical & chemical changes in retort to external stimuli. They are known as "smart", "intelligent" or "Environmentally sensitive polymers". [2] Classically "response" of a polymer in solution may modify the individual chain dimensions, secondary structure, solubility & degree of intermolecular relationship & in some cases reaction intensely modifies the polymer structure by bond breakage in the polymer backbone or cross-linking groups. [3] A smart response to external or internal stimuli allows enhanced confined effect in the preferred biological compartment & controlled release of payload at the position of the pathological events & also speedily addressing / imaging of pathological events [4]. Smart polymers are biocompatible, strong, robust, flexible, and easy to sharpen & color. Stimuli responsive changes in shape, surface potentials, dissolvability, & arrangement of bewildering molecular self-assembly & a sol-gel transition & others. [5] They change their microstructure from collapsed to extend when activated by environmental stimuli & reversibly reappearance to their initial state when stimuli are removed. [6] They have endowed a few novel application in the conveyance of the therapeutics, cell culture, tissue engineering, sensor or actuator frameworks, bioseparations, thermoresponsive surfaces, protein purification, reversible bio-catalyst, textile engineering, glucose sensors, gene therapy, protein folding, biomimetic actuators, & bioconjugates.[7,8] The current review focus on a detailed note of color changing and stimuli responsive polymers.

2. CLASSIFICATION OF VARIOUS COLOUR CHANGING MATERIALS:

2.1 Photochromic material:

Photochromic materials change color when the strength of received light changes & reversibly transform between two forms showing different optical spectra by the absorption of electromagnetic radiation. An apparent and revocable color change is a precondition for classes to be called photochromic. [9] Many photochromic materials change color upon exposure to radiation and then return to their original color subsequent removal of radiation is known as T-type photochromism. Although returns to the original state through radiation with the light of different wavelength ranges which driven photochemically & assistance to show P-type photochromism. [10]

2.2 Thermochromic materials:

Thermochromic material that responds to the phenomenon of temperature-dependent color changes due to environmental temperature changes. [11] Smart material whose color varied as a result of phase transition caused by temperature changes. [12] Reversible and irreversible thermochromic effects are known for single organic or inorganic compounds as well as some smart materials is based on the principle of chromogenic effects due to the combination of materials that do not exhibit thermochromism on their own.

2.3 Electrochromic material:

Electrochromic material changes color due to the application of an electric field or voltage. The phenomenon of electrochromism based on the transition metal oxides which conduct both electricity & ions. Among all metal oxide, tungsten oxide is the most widely studied electrochromic material & others include molybdenum, titanium, niobium oxides shows less effective optically.

2.4 Mechanochromic/ Piezochromic material:

Mechanochromic polymers are macromolecular materials that change color in response to mechanical stimulus i.e. stress is applied which may be compression, tensile, or shear forces. The Pressure-induced color changes are summarized as piezochromism. Change in the absorption spectrum of the mechanochromic material that changes color but thought to be the alteration of the emission or the reflection properties is also included due to broad range. [13]

2.5 Solvatochromic material:

Solvatochromism is a classically chemical substance that is sensitive to the given solvent. Hydrochromic materials

change color to interaction with water or in the existence of humidity. The substance that contains chromophore groups sensitive to the polarity of the solvent as a purpose of the constant electric field and also to control the spectroscopic properties of a substance. The polarity of a solvent is determined by its solvation performance & depends upon intermolecular forces between the solvent & solute. Solvotochromic evaluation method based on the solvent polarity on the electronic excitation energy of dyes used to evaluate various solvents. [14]

2.6 **Chemochromic material:**

Chemochromic material responds to the exposure of diverse chemicals with a change in color or transmission or reflection of a compound due to chemical reaction takes place within the material. Halochromic materials are also deliberate to be a subgroup that changes color as a reaction to the pH change environment. Ionochromic is also a similar word demonstrating the existence of ions in the medium can changes color. Chemochromic materials are mostly used in the field of hydrogen gas leakage detection & NASA developed a chemochromic detector for sensing hydrogen gas.

2.7 **Biochromic material**:

Biochromic material was established to distinguish and report the occurrence of pathogens with color shift.

Classification, examples & application of various color changing materials were described in table no: 1

Table: 1 colour changing material classification examples & their applications [15-18]

Color exhibiting material	Classification of materials	Examples	Application
Photochromic material	T-type photochromic colorants Inorganic Organic Inorganic–Organic	Spiropyrans Spirooxazines Naphthopyrans Diarylethene Azobenzene	Plastic lenses Textile industry Cosmetic products Packaging industries Bio Sensor
Thermochromic material	**Inorganic material:** Inorganic Metal-Organic **Organic Materials:** Conjugated polymer Leuco Dyes Diffractive Arrays Liquid Crystals	$Ag_2[HgI4]$ $[NH_2(C_2H_5)_2]2CuCl_4$ PDA(Poly(di acetylene) Triphenylmethane lactone and fluoran PNIPAM(poly (N-isopropyl acrylamide) Cholesteric liquid crystalline	Textile industry Anti-counterfeiting field Temperature indicator Daily supplies field Preparation of inks, paints, thermal paper & polymer composites.
Electrochromic material	Inorganic Organic	Tungsten trioxide Poly(ethylenedioxy thiophene) (PEDOT) poly (thiophene)	Night vision safety for cars in the Automobile industry. Smart windows are more used in low-energy buildings. Used for dye-sensitized solar cells. Nano Chromatics ink system.
Mechanochromic material/ piezo chromic material	Compression, Tensile / shear forces Pressure-induced (piezochromism)	**Conjugation length:** poly(thiophene) poly(diacetylene) **Aggregate/ disaggregate:** Pyrene Vinylanthracene (benzoxazolyl) Stilbene	Development of pressure-tunable chromogenic materials & monitoring polymer deformation. Manufacturing security marks on banknotes. Materials that react to strain and stress are more likely & sensor material.
Chemochromic material	--------	Tungsten oxide reacts with hydrogen showing color changes.	Sensing hydrogen gas leakage Litmus paper preparation Pregnancy test HCG traces detection. Fruit ripening
Solvatochromic material	Negative Solvatochromic (hypsochromic shift/blue shift) Positive solvatochromic (bathochromic shift/red shift)	4-(4ˈ-hydroxystyryl)-N-methlpyridinium iodide which is red in 1-propanol, orange in methanol & yellow in water. 4, 4ˈ-bis (dimethylamino) fuchsone, which is orange in toluene, red in acetone.	Optical sensor application & molecular switches. Carbon nanotubes are identified for the detection of the optical sensors.
Biochromic material	-------	Graphene oxide Gold nanoparticles	Biochromic materials include colorimetric detection of pathogens against food poisoning or bioterrorism.

3 CLASSIFICATION OF SMART POLYMERS:

Stimuli-responsive polymers are the type of smart materials that reveal evident changes in their features as a response to their contact with some environmental stimuli variations. [19-20] Stimuli are commonly classified into three categories: physical, chemical, or biological. The stimuli-responsive polymer classification described in figure no.1 & 2.

3.1 **Physical stimuli:**

Physical stimuli may include the following are a response to light, temperature, ultrasound, magnetic, mechanical, electrical are usually modify chain dynamics, i.e. the energy level of the polymer/solvent system.

3.2 **Chemical stimuli:**

Chemical stimuli may include the following reaction to Solvent, ionic strength, electrochemical, pH are usually modified molecular interactions, whether between polymer and solvent molecule or between polymer chains.

3.3 **Biological stimuli**:

Biological stimuli may include the following are react to enzymes, receptors relate to the actual functioning of molecules: enzymatic reactions, receptor recognition of molecules.

Besides, there are dual stimuli-responsive polymers that instantaneously respond to more than one stimuli.

Classification of stimuli responsive polymers based on the various stimuli: [21]

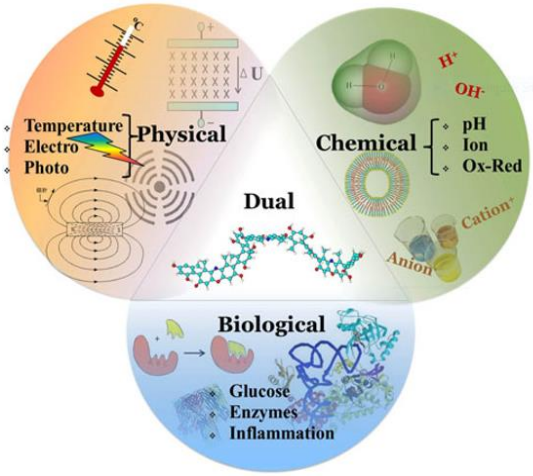

Figure: 1 Classification of stimuli responsive polymer based on the stimuli.

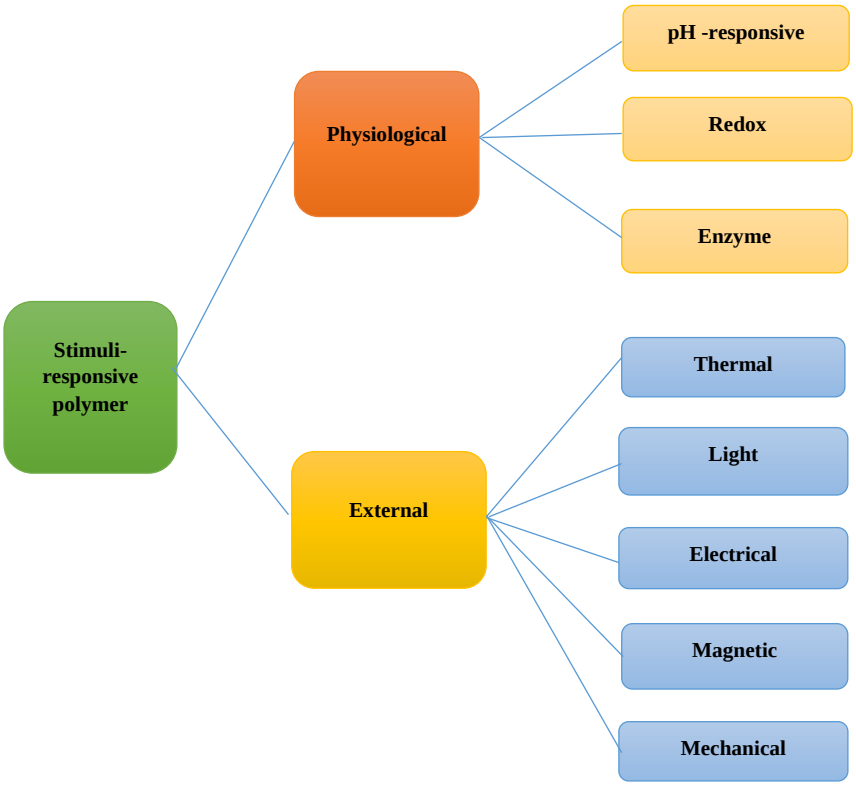

Figure no: 2 Classification of stimuli-triggered polymers.

3.1 **Physically dependent stimuli:**

3.1.1 **Thermo-responsive polymers:**

These smart polymers are delicate to the temperature and modification of their microstructural structures in retort to change in temperature. [22] Thermo-responsive polymers existing in their arrangement a very delicate balance among the hydrophobic and the hydrophilic groups and a minor change in the temperature can generate new alterations.[23] Established on their reaction to change in temperature, these polymers are characterized in two classes; first, polymers that develop insoluble beyond a critical temperature called the lower critical solution temperature (LCST), and second, polymers that precipitate and capability phase change beneath a critical temperature called as the upper critical solution temperature (UCST). [24] Above the critical solution temperature (LCST), the interface strengths (hydrogen bonds) among the water molecules and the polymer become opposed, it dehydrates and the prevalence of the hydrophobic interaction occurs, causing the polymer swelling. [25] Normally, these copolymers are categorized by hydrophobic and hydrophilic interactions between the polymeric chains and the aqueous media shortly change within a small temperature array & bring the interruption of intra- and intermolecular electrostatic and hydrophobic interactions and consequences in chain folding or growth. Though, in the case of polymers with an LCST, the solubility declines as temperature rises, and consequently hydrogels made of these polymers shrink as the temperature rises above the LCST. This type of swelling performance is identified as opposite temperature dependence and follows due to prevailing hydrophobic interactions. The polymeric solution that seems as monobasic below a precise temperature & biphasic above it mostly controlled LCST & this phenomenon most commonly understood in water-soluble polymers which incline to phase separate from the solution upon heating.

3.1.2 **Electro-Responsive Polymers:**

Transport systems manipulating this external stimulus are prepared from polyelectrolytes, which are polymers that comprise a relatively high concentration of ionizable groups besides the backbone chain. This property concentrates these polymers pH-responsive as well as electro-responsive. [26] Beneath the influence of an electric field, electro-responsive hydrogels commonly shrink or swell and this property has permitted its use in drug delivery systems. Characteristic electrically responsive polymers are conducting polymers, for example, polythiophene (PT) or sulfonated-polystyrene (PSS), which can display swelling, shrinking, or bending in retort to an external field. Here different properties upon electrochemical stimulation: (a) an influx of counterions and solvent molecules causes a rise in osmotic pressure in the polymer, consequential volumetric expansion, (b) control of the charging/adsorption of polyelectrolyte on to oppositely charged porous materials, (c) formation and swelling of redox-active polyelectrolyte multilayers. Established an indirect electric-responsive system involving a complex of poly (methacrylic acid) and poly (ethyloxazoline) designed via hydrogen bonding between the carboxylic group and the oxazoline group, respectively.

3.1.3 **Photo-Responsive Polymers:**

Light-responsive polymers experience a phase alteration in retort to exposure to light. Photoresponsive polymers possess light sensitive chromophore moiety on exposure to external stimuli upon light absorption & the chromophoric moiety break down from polymeric chains and further degraded into smaller molecular fragments. Azobenzene takes the Trans form under ambient circumstances & isomerizes from Trans to cis below photoirradiation with UV light and from cis to Trans below photoirradiation with visible light or at higher temperatures. Azobenzene can turn as a mesogen in the Trans form since of its rigid-rod arrangement, although it cannot in the cis form. [27] Limitations of light-sensitive polymers comprise unpredictable response due to the leaching of noncovalently bound chromophore through swelling or shrinkage of the structure and the slow response of hydrogel toward the stimulus.

3.1.4 **Pressure-responsive polymers:**

The theory that hydrogels may experience pressure-induced volume phase transition originated from thermodynamic calculations created uncharged hydrogel theory & according to this theory, hydrogels are collapsed at low pressure would enlarge at higher pressure. Pressure-controlled adhesion among flat, stiff substances and an elastomeric surface with sharp pyramidal structures were obtainable. [28] The degree of swelling of poly (N-isopropylacrylamide) hydrogels increased below hydrostatic pressure when the temperature is near to its LCST.

3.1.5 **Magnetic –responsive polymers:**

Magnetic field-responsive polymers are considered as a system of hydrogels to have swelling, shrinking, or twisting performance in retort to an external field & their properties of such polymers have been applied for many biological applications such as drug delivery systems, artificial muscle, or biomimetic actuators. [29] Magnetic field-sensitive gels were acquired by integrating colloidal magnetic particles into cross-linked PNIPAM-co-poly (vinylalcohol) hydrogels. [30] Oscillating magnetic usage in drug delivery from the polymer matrix can be characterized through properties of carrier particles, field strength & geometry, drug binding capacity, and some physiological factors like the depth to target, rate of blood flow & vascular supply, and body weight. The gel beads designed straight chain-like arrangements in uniform magnetic fields, while they aggregated in nonhomogeneous fields & rapid, controllable shape alterations of gels are estimated towards imitator of muscular contraction.

3.1.6 **Mechanical-responsive polymers:**

Wrinkled PDMS sheet with a thickness of 1mm was incorporated into micro pillars & generate wrinkles in the micro pillars through oxygen plasma treatment of the prolonged PDMS (polydimethylsiloxane) sheet and consequent strain release. Active, the dynamic regulator of regular and shear adhesion was accomplished by reasonably strong and shear forces were achieved for a fully strained PDMS sheet, whereas the forces could remain fast condensed to closely zero when the strain was released. Development of vascular endothelial growth factor

(VEGF)-loaded alginate hydrogels with pulsatile release as a retort to altered strain amplitudes of compressive forces and VEGF has released the application of compression while release stopped when the strain was removed. [31]

3.1.7 **Solvent-responsive polymers:**

The heterogeneous binary polymer brushes are sensitive to some solvent molecules like toluene, ethanol, and water. Biocompatible and biodegradable polymer brushes of PEG and polydimethylsiloxane (PDMS) was newly fabricated. At room temperature, these polymers have identical mobile chains since low glass transition temperature (Tg), and their intelligent to instantaneously adjust to their environmental changing conditions & confirmed that PDMS–PEG brushes show low adhesion in both wet and dry conditions. [32]

3.1.8 **Ultrasonically Responsive polymers:**

An innovative approach of manipulating ultrasound in drug delivery by the application of ultrasonic waves directly at the polymers shows a virtual mechanism driven by the cavitation. Generally, ultrasound waves generate both high & low pressure whereas high-pressure waves regulate the intermittent opening of pores in the polymers. Most widely employed polymers are biodegradable polymers or non-biodegradable polymers. [33]

3.2 **Chemically-dependent stimuli:**

3.2.1 **pH-Responsive Polymers:**

pH-responsive polymer shows protonation/ deprotonating procedures by allotting the charge over the ionizable clusters of the molecules, such as carboxyl or amino groups. pH makes a phase transition in pH-responsive polymers identical sharply deviations in the environmental pH consequently prime conformational changes of the soluble polymers and a change in the swelling performance of the hydrogels when ionizable groups are associated with the polymer structure. The swelling of pH-responsive hydrogels is directed by their degree of ionization i.e. protonation or deprotonation. Proteins having a minimal surface charge at their isoelectric point (pI) and display widespread swelling at a pH away from their pI & occur due to the change in the high surface net-charge and improved electrostatic repulsive forces.

3.2.2 **Ion-Responsive Polymers:**

Changes in ionic strength might cause the size of the polymeric micelles changes, polymer solubility, and the fluorescence quenching kinetics of the chromophore bound to electrolytes and show rare rheological behavior consequently attractive Columbic interactions among oppositely charged species. Further, reduce the polymer insoluble in deionized water then soluble in the existence of a critical concentration of electrolytes where attractive charge/charge interactions are shielded & further Increase in the ionic strength causes the polymer chains binding the proteins to lead to precipitated. The high salt concentration reduced the repulsive electrostatic strength of the copolymer, which effects an increase in the hydrophobic interactions and further lead to precipitation. The study of polyelectrolyte-drug complex dispersions showed that the equilibrium of counter ionic condensation is not inclined by the occurrence of nonelectrolytes, although a liberal displaced drug by the addition of neutral salts, such as NaCl causes increasing concentrations can be observed in case of ion-responsive polymer systems. [34]

3.2.3 **Redox-Responsive Polymers:**

Since the synergetic site-specific effect two key stimuli-responsive reasons for exactly controlled release of anticancer drugs showing similar actions of both redox- and pH-responsive polymeric Nanocarriers are widely studied to realize more effective chemotherapy effects. [35] Advantages of redox responsive polymers are good biocompatibility, water dispersibility & design ability, and encapsulation of hydrophobic drugs into copolymers with both hydrophilic & hydrophobic of part for therapeutic drug delivery. [36] Redox reaction modifies the hydrophobic and the hydrophilic belongings of the polymer chains and further consequences in swelling and deswelling of the polymer. Disulfide groups have also been used to bring redox reaction since they are unstable in a reducing environment & cleavage of thiol groups. For example Polymers with disulfide cross-links aminoacid based molecules like cysteine or glutathione which are reductive on exposure with reducing agents.

3.3 **Biologically dependent stimuli:**

3.3.1 **Glucose Responsive Polymers:**

When the concentration of glucose in the blood becomes high due to improper functioning of the pancreas producing the hormone insulin a patient suffering from diabetes mellitus usually requires insulin that has to be administrated via periodic injection. The glucose-responsive hydrogel system can deliver self-regulating insulin release in retort to the concentration of glucose in the blood, which can regulate the concentration of insulin within a normal range. For glucose Enzyme-Responsive Polymers responsive polymers, glucose oxidase (GOx) is conjugated to a smart, pH-sensitive polymer and the GOx which can oxidize glucose to gluconic acid causes a pH change in the environment & subsequently drastic changes in the conformation of a polymer.

3.3.2 **Enzyme-Responsive Polymers:**

Enzyme –responsive polymer has been demoralized recurrently & they have become the most significant in the drug delivery system. Bacteria which are mainly located in the colon produce special enzymes namely reductive enzymes (e.g. azoreductase) or hydrolytic enzymes (e.g. glycosidases) which are capable of degrading the polysaccharides, such as pectin, chitosan, amylase/amylopectin, cyclodextrin and dextrin.

3.3.3 **Inflammation-Responsive Polymers:**

The inflammatory process is started by T- and B-lymphocytes, but amplified and continued by polymorphonuclear (PMN) leukocytes and macrophages further inflammation-responsive systems released the reactive oxygen metabolites nothing but oxygen free radicals or hydroxyl radicals by PMNs and macrophages through the early phase of inflammation at the site.

3.4 **Dual-Stimuli:**

Different functionalities retort to different stimuli are temperature, pH, light, ionic strength, electron transfer (redox), and host-guest interactions. Sometimes the dual- and multi stimuli-responsive polymeric nanoparticles are particles that react to the grouping of two or more signals.

For example: pH/redox, pH/magnetic field, temperature/reduction, pH/temperature, double pH, pH and diols, temperature/enzyme, and temperature/magnetic field. Some are triple responses Temperature/pH/magnetic, temperature/pH/redox, pH/redox/magnetic, temperature/redox/guest molecules, and temperature/pH/guest molecules are multi stimuli which are recently created a new era for the development of stimuli-responsive polymers.

The dual-stimuli responsive approach is ideally suited for the combination of diagnostics and therapy because some functionalities can provide on-site feedback and diagnostics purposes of using these special types of stimuli polymers while others might initiate curing and therapy. Types of stimuli-responsive polymers classification based on the external stimuli with examples and their application are given in table no -2

Table: 2 Summarize on the stimuli responsive polymers examples & its application [37-39]

Type of stimulus-response	**Stimulus- responsive polymers examples**	**Application**
Physically dependent stimuli		
Temperature- responsive polymer	**Synthetic:** PNiPAAm [poly(N-vinylcaprolactam)] PNVC [poly(N-isopropylacrylamide] PLLA/PEG/PLLA [poly (L-lactic acid)-poly(ethylene glycol)-poly(L-lactic acid)] PEO-PPO-PEO [poly (ethylene oxide)-poly(propylene oxide)-poly (ethylene oxide)] **Natural:** Polysaccharides & proteins	Water-soluble polymer sensor, Tissue adhesion prevention material. Thermosensitive hydrogel at any temperature Potential anti-cancer drug carrier. Ability to transport both hydrophilic &lipophilic drugs
Electro- responsive polymer	**Synthetic:** PT [polythiophene] PSS[sulphonated-polystyrene] Polyaniline Polypyrrole Ethylene vinyl acetate Polyethylene **Natural:** Chitosan Alginate Hyaluronic acid	Drug release & cancer chemotherapy Drug carrier.
Photo- responsive polymer	Azobenzene or spiropyran containing PAA [poly(acrylic acid)] PHPMAm[poly(N-(2-hydroxypropyl)methacrylamide)] PNIPAM [poly(N-isopropylacrylamide)]	Photochromic polymer sensor Photodegradation material.
Chemically-dependent stimuli		
pH – responsive polymer	Chitosan Albumin Gelatin PAA/Chitosan IPN [poly(acrylic acid) (PAAc)/chitosan (inter penetrating network)] P(MAA-g-EG) [poly(methacrylic acid-g-ethylene glycol)] PEI [poly(ethylene imine)] PDAAEMA [poly(N,N-diakylamino ethylmethacrylates)] PL [poly(lysine)]	Drug release Enzyme immobilization Immunoassay Wound dressing material & drug release. Controlled insulin delivery pH-sensitive controlled release system. Vector for gene delivery.
Ion- responsive polymers Redox- responsive polymers	Polyanhydrides PLGA [poly(lactic/glycolic acid)] PbAEs [poly(b-amino esters)] Poly(NiPAAm-co-Ru(bpy)3) DEAAm[N,N-diethylacrylamide] DMAEMA [2-(dimethhylamino)ethyl methacrylate]	Potential oral drug delivery system Controlled drug delivery system Efficient carrier for cytotoxic agents Artificial muscles.
Biologically dependent stimuli		
Glucose-responsive polymers	GOx [glucose oxidase] conjugated chitosan GOx encapsulated within PEG-PSS-PEG [(poly(ethylene glycol))-(poly(propylene sulfide))-PEG	Self –regulated insulin delivery
Enzyme- responsive polymer	DEXS / Chitosan Azoaromatic crosslinked hydrogel	Local & sustained drug release Specific delivery of peptide & proteins
Inflammation-responsive polymers	Glycidylether crosslinked HA(hyaluronic acid)	Implantable drug delivery
Dual-stimuli	PLL block PEG-PLL [(L-lactic acid)-poly(ethylene glycol)-poly(L-lactic acid)	Enhanced gene expression

CONCLUSION:

Chromogenic materials have opened new scientific trajectories for the development of microclimatic and interior comfort of buildings, which resolve energy savings with increased thermal and luminous performance. The flexibility and unfamiliar possible of stimuli-responsive polymers make this category of pharmaceutical excipients a cluster of materials with a great potential for discovering in the fields of chemistry, biology, pharmacy, and medicine, having as its main objective the design of innovative solutions and therapeutic approaches for optimizing the effectiveness and adherence to therapy. The various responsive polymer is based on the dramatic alteration of its structure or on a change in its properties, such as charge, solubility, or polarity & also an alteration in the polymer structure takes place when the polymer is degraded by breaking chemical bonds in the backbone or at specific positions where cross-linking moieties are inserted in its structure. The change in properties is accomplished by presenting functional groups that induce changes in chain dimension, secondary structure, or assembly architecture.

REFERENCES:

1. Marinella Ferrara & Murat Bengisu. *Intelligent design with chromogenic materials*. Journal of the International Color Association. 2014, *13*, 54-66.
2. Raju Francis., Geethy P., Gopalan., Anjaly Sivadas., and Nidhin Joy. *Properties of stimuli- responsive polymers.* Biomedical Applications of Polymeric Materials and Composites. First edition. 2016, *3*, 187-231.
3. Etienne Cabane., Xiaoyan Zhang., Karolina Langowska., Cornelia G., Palivan., Wolfgang Meier. *Stimuli- responsive polymers & their application in Nanomedicine.* Biointerphases. 2012, *7*, 1-27.
4. Priya Bawa, Viness Pillay, Yahya E Choonara and Lisa C du Toit. *Stimuli –responsive polymers and their applications in drug delivery*. Biomed. Mater. 2009, *4*, 1-15.
5. Apoorva Mahajan., Geeta Aggarwal. *Smart polymers: innovations in novel drug delivery*. Int.j.Drug Dev. & Res. 2011, *3*, 16-30.
6. Priya Patel., Vaishali Koyani. *Smart polymers: innovative drug delivery system.* 2014, *3*, 508-527.
7. Rushi Ghizal Gazala Roohi Fatima., Seema Srivastava. *Smart polymers and their application.* 2014, *2*, 104-115.
8. Carolina de las Heras Alarcon., Sivanand Pennadam., and Cameron Alexander. *Stimuli responsive polymer for biomedical application.* Chem. Soc. Rev. 2005, *34*, 276–28.
9. Detlef lo tzsch., volker eberhardt Christian rabe. *Chromogenic Materials Ullmann's Encyclopedia of industrial chemistry.* 2016, *2000*, 1-26.
10. Chowdhury M. A., Joshi M., and Butola B. S. *Photochromic and Thermochromic Colorants in Textile Applications*. Journal of Engineered Fibers and Fabrics. 2014, *9*,107-123.
11. Arno Seeboth., Detlef Lotzsch., Ralf Ruhmann., & Olaf Muehling. *Thermochromic Polymers -Function by Design.* American chemistry society. 2013, *2*, 1-32.
12. Youliang Cheng., Xiaoqiang Zhang., Changqing Fang., Jing Chen., Zhen Wang. *Discoloration mechanism, structures & recent application of thermochromic materials via different methods: A review* .J.Mater.Sci.Technol. 2018, *34*, 2225-2234.
13. Douglas A., Davis., Andrew Hamilton., Jinglei Yang Lee D., Cremar., Dara Van Gough., Stephanie L., Potisek., etal. *Force-induced activation of covalent bonds in mechanoresponsive polymeric materials.* 2009, *459*, 68-72.
14. Shalini Nigam & Sarah Rutan. *Principle and applications of solvatochromism*. 2001, *55*, 362A-370A.
15. Jesse h. day. *Thermochromism.* 1963, *63*, 65-80.
16. Fu.F., Hu. L., *Temperature sensitive color- changed composites.* Advanced High Strength Natural Fiber Composite in Construction. 2017, *3*, 404- 423.
17. Taufik Abidin., Qiang Zhang., Kun-Li Wang., Der-Jang Liaw. *Recent Advances in electrochromic polymers.* 2015, *55*, 5293-5304.
18. Celine Calvino., Laura Neumann., Christoph Weder., Stephen Schrettl. *Approaches to polymeric mechanochromic materials.* Journal of polymer science. 2017, *55*, 640-652.
19. Ibrahim M., El-Sherbiny., Islam A., Khalil and Isra H. Ali. *Updates on stimuli-responsive polymers: synthesis approaches and features.* Science and fundamentals. 2018, *2*, 129 -146.
20. Olivier Bertrand and Jean –Francois Gohy. *Photo responsive polymer: synthesis and applications.* 2013, *1*, 1-23.
21. Devendra G. Kapadnis., Mahendra G.Sonule., Dhiraj B., Dabhade. *Smart polymers: A smart approach for drug delivery system.* 2015, *3*, 411-417.
22. Hugo Almeida., Maria Helena Amaral and Paulo Lobao. *Temperature and pH stimuli-responsive polymers and their applications in controlled and self-regulated drug delivery.* Journal of Applied Pharmaceutical Science. 2012, *2*, 01-10.
23. Bajpai A.K., Shukla S.K., Bhanu S., Kankane S. *Responsive polymers in controlled drug delivery.* Prog. Polym. Sci. 2008, *33*, 1088-1118.
24. Teotia.h.Sami A.K., Kumar A. *Thermo-responsive polymers: structure and design of smart materials.* Switchable and responsive surfaces and materials for biomedical application. 2015, *8*, 3-43.
25. Macewan S.R., Callahan D.J., Chilkoti A. *Stimulus-responsive macromulecules and nanoparticules for cancer drug delivery.* Nanomedicine UK. 2010, *5*, 793-806.
26. Anal A K. *Stimuli-induced pulsatile or triggered release delivery systems for bioactive compounds Recent Patents Endocrine Metab.* Immune Drug Discov. 2007, *1*, 83–90.
27. Akihito Hashidzume & Akira Harada. *Stimuli-Responsive Polymers. Encyclopedia of polymeric nanomaterial.* 2013, *1*, 1-6.
28. Kim, S., Wu, J., Carlson, A., Jin, S.H., Kovalsky, A., Glass, P., Liu, Z., Ahmed, N., Elgan, S.L., Chen, W., Ferreira, P.M., Sitti, M., Huang, Y., and Rogers, J.A. *Microstructured elastomeric surfaces with reversible adhesion and examples of their use in deterministic assembly by transfer printing.* Proc. Natl. Acad. Sci. U.S.A., 2010, *107*, 17095–17100.
29. Shiga, T. *Deformation and viscoelastic behavior of polymer gels in electric fields.* Adv. Polym. Sci. 1997,*134*, 131–163.
30. Zrinyi, M. *Intelligent polymer gels controlled by magnetic fields.* Colloid. Polym. Sci. 2000, 278, 98–103.
31. Lee K., Yoon J., Lee J., Kim S., Jung H., Kim S., Joh J., Lee H., Lee D., Lee S. *Sustained release of vascular endothelial growth factor from calcium-induced alginate hydrogels reinforced by heparin and chitosan.* In: Transplantation proceedings, 2004, *2*, 2464–2465.
32. Sheparovych, R., Motornov, M., and Minko, S. *Adapting low-adhesive thin films from mixed polymer brushes.* Langmuir. 2008, *24*, 13828–13832.
33. Roberta Cassano and Sonia Trombino. *Drug Delivery systems: Smart polymeric Materials.* Advanced polymeric medicine. 2015, 341-370.
34. Monica Cristina Garcia. *Ionic-strength-responsive polymers for drug delivery applications.* Stimuli responsive polymeric Nanocarriers for drug delivery applications. 2019, *5*, 393-409.
35. Peng Liu. *Redox- and pH-responsive polymeric Nanocarriers.* Stimuli responsive polymeric Nanocarriers for drug delivery applications. 2019, *5*, 3-36.
36. Xiaoyong Zhang., Lu Han., Meaning Liu., Ke Wang., Lei Tao., Qing Wan & Yen Wei. *Recent progress and advances in redox- responsive polymers as controlled delivery nanoplatforms.* Mater. Chem. Front. 2017, ***1***, 807-822.
37. Li Jun., Wang Bochu and Wang Yazhou. *Thermo-sensitive polymers for controlled-release Drug Delivery systems.* 2006, *2*, 513-519.
38. Dirk Kuckling & Marek W. urban. *Synthetic and physicochemical aspects of advanced stimuli-responsive polymers.* Hand book of stimuli-responsive materials. 2001, *71*, 239-241.
39. Anand Ganesh V., Avinash Baji., and Seeram Ramakrishnab. *Smart functional polymers – a new route towards creating a sustainable environment.* RSC Adv, 2014, *4*, 53352-53364.