CODEN [USA]: IAJPBB ISSN: 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES

http://doi.org/10.5281/zenodo.3263794

Available online at: http://www.iajps.com *Review Article*

INTERPENETRATING POLYMER NETWORK: A NOVEL BIOMATERIAL AND CARRIER SYSTEMS IN DRUG DELIVERY

[1]DAS R. S., [2]BARHATE A. N.

[1]SVPM'S College of Pharmacy, Malegaon (BK), Baramati. 413102, Email- rachanadas46@gmail.com

Article Received: April 2019 **Accepted:** May 2019 **Published:** June 2019

Abstract:

Interpenetrating polymer network (IPN) is a polymer comprising two or more networks each in a network form. It is known as one of the very useful novel biomaterial containing two polymers, each in network form. It offers biocompatibility and safety as it imparts stability to the drug in the formulation and improves solubility of hydrophobic drugs. The importance of biocompatible and biodegradable polymers is widely increasing in pharmaceutical applications because of their ability to form cross linked three-dimensional network hydrogels that tend to swell in water or biological fluids. These systems thus can be used as a potential candidate to deliver bioactive molecules in controlled release system. The blends obtained from natural and synthetic polymers alone are not always able to meet the complex demand of biomaterials. Natural polymers have the advantage of nontoxicity, low cost, biodegradability, biocompatibility and safety. But their mechanical properties are very poor. In contrast Synthetic polymers have broad range of mechanical properties. IPN can produce synergistic effect by sharing the properties of both natural as well as synthetic polymers.

Key Words: *Interpenetrating polymer network (IPN), cross-linked polymers, natural polymer, synthetic polymers, controlled release system*

Corresponding author:

DAS R. S,

SVPM'S College of Pharmacy, Malegaon (BK), Baramati. 413102, Email- rachanadas46@gmail.com.

QR code

Please cite this article in press DAS R. S et al., ***Interpenetrating Polymer Network: A Novel Biomaterial and Carrier Systems in Drug Delivery.,*** *Indo Am. J. P. Sci, 2019; 06(06).*

INTRODUCTION:

Interpenetrating polymer network (IPN) was first invented by Aylsworth in 1914 and the term IPN was firstly coined by Miller in 1960s, a Scientific study about polystyrene network [1]. Usually biocompatible and biodegradable polymers have been used as potential carriers for formulation of controlled drug delivery system (CRDDS). The natural as well as synthetic polymers (homopolymers) alone are not always able to fulfill the complex demands of the delivery systems in terms of properties and performances; development of IPN provides a better approach. The major merits of natural polymers are valuable in pharmaceutical industry due to their non-toxicity, low cost, biodegradability, biocompatibility and safety, the success of synthetic polymers based on their broad range of mechanical properties, but some of their physical attributes are often poor. The combination of physiochemical attributes of different polymers have been of great interest for the CRDDS because the combination provides a convenient route for the modification of properties to meet specific needs for the delivery system. From these methods, considerable interest has been given to the development of IPN based drug delivery systems.

There are mainly 3 conditions of polymer which are necessary in the composition of IPN. These conditions are as follows [2]

1) At least two polymers must be synthesized and crosslinked in the presence of the other.
2) Both polymers have similar kinetics.
3) Polymers are not dramatically phase separated.

Interpenetrating polymer network are combination of two or more network polymers, synthesized in juxtaposition. When two or more polymers are mixed, the resulting composition can be called a multi component polymer material. There are several ways to mix two kinds of polymer molecules (Figure 1). Simple mixing, results in a polymer blend. If the chains are bonded together, graft or block copolymers result: Bonding between some portion of the backbone of polymer I and the end of polymer II, the result is called a graft copolymer and chains bonded their ends, so result in block copolymers.

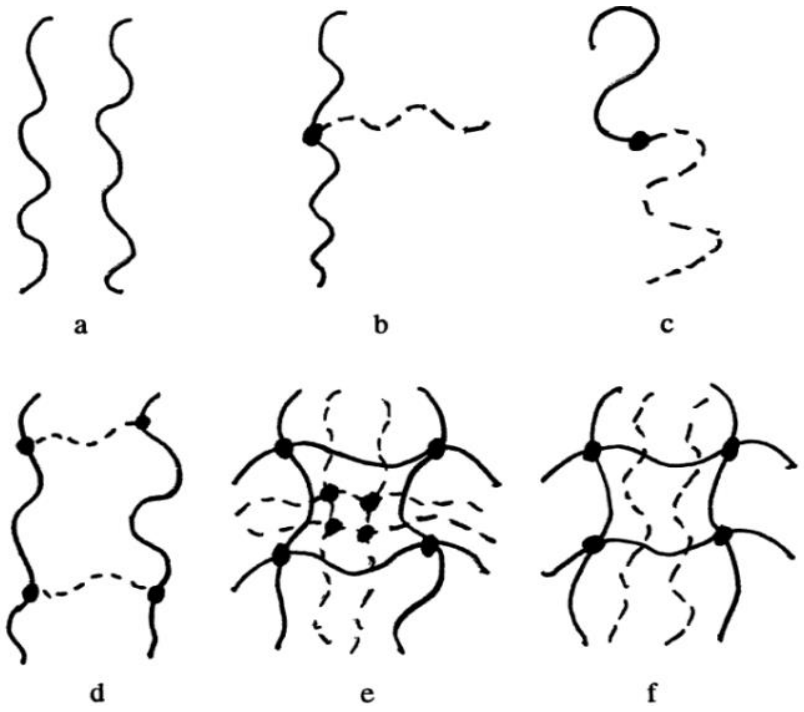

Figure 1: Six basic combinations of two polymers.
a, Polymer blend; b, graft copolymer; c, block copolymer;
d, AB-graft copolymer; e, IPN; f, SIPN.

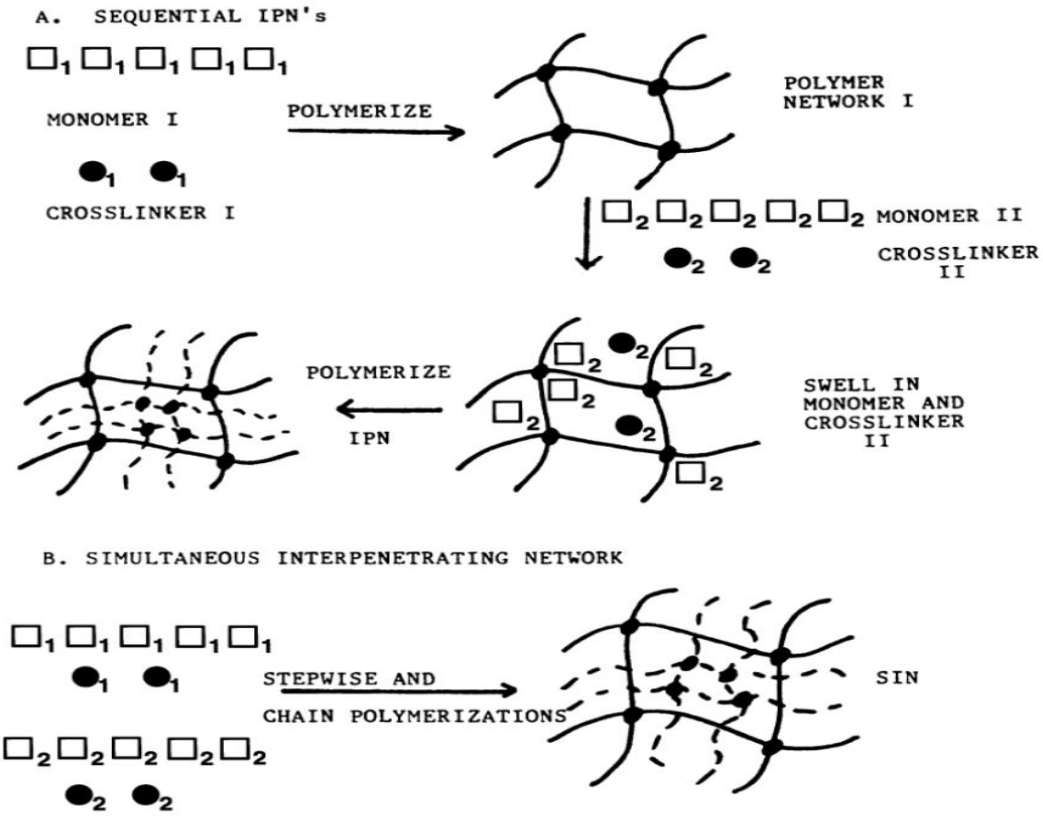

Figure 2: Basic synthesis methods for IPNs.
A, Sequential IPNs; B, simultaneous interpenetrating polymer networks.

Types of IPN:
IPNs are of following types[3]:

- **Sequential IPN**. Polymer network I is made. Monomer II plus cross-linker and activator are swollen into network I and polymerized in situ (Figure 2A). The sequential IPNs include many possible materials where the synthesis of one network follows the another.
- **Simultaneous interpenetrating network (SIN).** The monomers or prepolymers plus cross-linkers and activators of both networks are mixed. The reactions are carried out simultaneously, but by noninterfering reactions. An example involves chain and step polymerization kinetics (Figure 2B).
- **Latex IPN**. The IPNs are made in the form of latexes, more often with a core and shell structure. A variation is to mix two different latexes and then form a film, which cross-links both polymers. This variation is sometimes called an interpenetrating elastomer network (IEN).
- branched are semi-IPN (SIPN).
- **Gradient IPN**. Gradient IPNs are materials in which the overall composition or cross-link density of the material varies from location to location on the macroscopic level. For example a film can be made with network I predominantly on surface, network II on the other surface, and a gradient in composition throughout the interior.
- **Thermoplastic IPN**. Thermoplastic IPN materials are hybrid between polymer blends and IPN s that involve physical cross links rather than chemical cross-links. Thus, these materials flow at elevated temperatures, similar to the thermoplastic elastomers, and at use temperature, they are cross-linked and behave like IPNs. Types of cross-links include block copolymer morphologies, ionic groups, and semicrystallinity.
- **Semi-IPN**. Compositions in which one or more polymers are cross-linked and one or more polymer linear or

Based on Arrangement Pattern, IPNs are of following types:

Novel IPN: Polymer containing two or more pol ymer networks which are at least partially interlocked on molecular scale but not coval ently bonded to each other and separated due to chemical bonds are broken.

Sequential IPN: In sequential IPN the second po lymeric component network is polymerized follo wing the completion of polymerization of the first component network.

Simultaneous IPN: Simultaneous IPN is prepared by a process in which both component networks are polymerized one after another, the IPN may be referred to as a simultane ous IPN.

Semi IPN: If only one component of the assemb ly is cross linked leaving the other in a linear fo rm, the system is termed as semi-IPN

Advantages of IPN

There are the following inherent advantages due to which IPN system gained huge popularity for the advancement of polymers. They are as follows-

1. IPN system increases the mechanical strength, phase stability and biological acceptability of the final product.
2. IPN are causes the synergistic effect from the component polymer.
3. Phase separation between the component polymers is not possibleDue to the infinite zero-viscosity of the gel.
4. Thermodynamic incompatibility can be made to overcome as the reacting ingredients are blended thoroughly at the time of synthesis, Due to permanent interlocking of the network segment.
5. By using IPN ,controlled release system drug delivery are prepared for Colonic Delivery.
6. IPN used to in field of tissue engineering. [4,5]

Disadvantages of IPN

1. The main disadvantage of IPN is that, sometimes the polymers interpenetrate to such an extent and the drug released from the matrix becomes difficult.
2. The problem with the non-covalent system is that it can also be a problem with the covalent system due to the lack of an effective interface. [6,7]

Ideal characteristics of IPN

There are the following ideal characteristics of IPN -- There are the following ideal characteristics of IPN which are as follows-

1. In ideal IPN suppresses creep and flow.
2. IPN can swell but does not dissolve in solvent.
3. IPN has high tensile strength.
4. Most ideal IPNs are heterogeneous systems which contain one rubbery phase and one glassy phase to produce a synergistic effect yielding.
5. When the blends are subjected to stress, they keep the phases separated together.
6. IPN mainly forms insoluble network.
7. IPN systems having number and types of cross-links.
8. IPN contains adhesive property. [8,9]

Properties of IPN

- A gel composed of two interpenetrating networks by cross linking a polymer (or polyelectrolyte) into a pre-existing highly cross linked network of a polymer (or polyelectrolyte) of a different kind have increased elastic and mechanical properties which was measured by the stress–strain behavior and comparing their elastic moduli and breaking points.
- According to US Patent data the calculated true stress per unit solid and strain shows that PGA/PAA IPNs are much stronger than either the unite polymer networks or copolymers. The effect of IPN formation on tensile strength is nonlinear, as the maximum strength is many times higher than that of PEGPAA copolymer. The elastic moduli and tensile strength can be modified by changing the molecular weight.
- Oxygen permeability- IPN hydro gels composed of PEG as the first network and a second network of poly acrylic acid had oxygen permeability of 95.9±28.5 Barriers.
- Shape memory-Materials are said to show shape memory effect if they can be deformed and fixed into a temporary shape and reform their original permanent shape only on the exposure of external stimuli, like heat, light etc [10]
- Equilibrium water content- IPN can swell in solvent without dissolving. The water content of hydro gels was evaluated in terms of the swollen weight to dry weight ratio. The dry hydro gel was weighed and then immersed in water as well as phosphate buffered saline. At regular intervals the swollen gel was lifted, patted dried and weighed until the equilibrium was attained. The percentage of equilibrium water content(WC) was

calculated from the swollen and dry weight of hydro gel:

$$WC = (Ws-Wd)/Es \times 100$$

Where, Ws and Wd are weight of swollen and dry hydro gels respectively

Methods of Preparation of IPNs

1. Casting Evaporation.

Castings Evaporation method has been used widely to form cross-linked polymer network. In this method each polymer constituent is heated until it is dissolved and then added to cross-linker solution [11]. In case of sequential process, solution of polymer I is added to the cross-linker solution followed by addition of polymer II solution. In both cases the solution is heated and mixed and then casted and dried. IPN gels can be prepared by this technique.

.

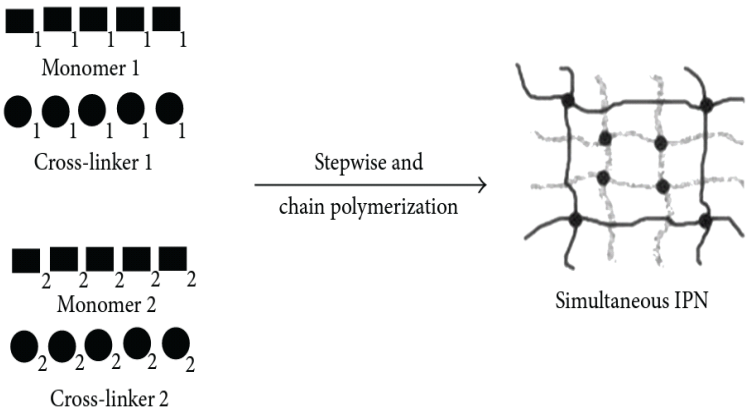

Figure 3: Sequential steps involved in IPN formation

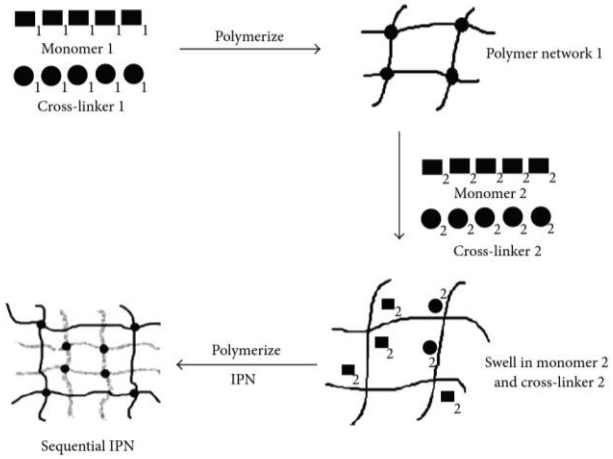

Figure 4: Formation of simultaneous IPN

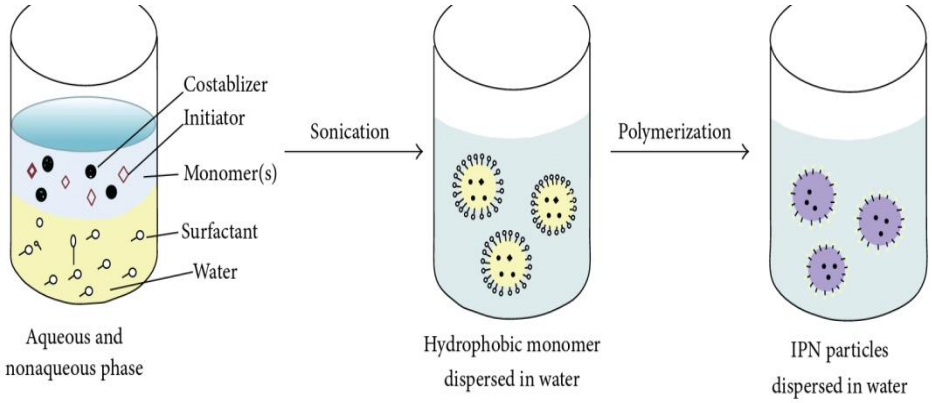

Figure 5: Synthesis of IPN particles by miniemulsion polymerization

2. Emulsification Cross-Linking.

This method is based on phase separation. Generally single emulsion cross-linking technique is based on w/o emulsion but recently w/w emulsion method has also been developed to form IPN[12]. The advances of w/w emulsion method is that there is no use of organic solvents which might leave toxic residue that is not compatible with IPN biomaterials. In w/o emulsification method, the water soluble materials are dissolved in aqueous phase at specific temperature to form homogenous solution by continuous stirring. This aqueous phase is added to oil phase to prepare w/o emulsion with continuous emulsificationbut in w/o/w emulsion technique an aqueous solution of water soluble polymers is emulsified as a dispersed phase in an aqueous solution of another polymer that acts as continuous phase. Then the dispersed polymer phase is cross-linked to form IPN network. [13]

3. Miniemulsion/Inverse Miniemulsion Technique.

This technique allows one to create small stable droplets in a continuous phase by the application of high shear stress [14]. The idea of miniemulsion polymerization is to initiate the polymer in each of the small stabilized droplets. To prevent the degradation of miniemulsion through coalescence, a surfactant and a costablizer are added that are soluble in dispersed phase but insoluble in continuous phase. This process of IPN formation can be divided into three steps. Initially, constituent polymers are obtained by sonication using specific initiator. In the second step, one of the constituent polymers is polymerized and cross-linked using a cross-linking agent. As a result a semi-IPN is formed till the second stage. In the last step, a full IPN is formed polymerizing and cross-linking the second constituent polymer by the addition of second cross-linker. Figure 5 represents the formation of IPN particles by the process of direct (oil in water) miniemulsion polymerization

4. In case of inverse miniemulsion (water in oil).

Hydrophilic monomers can be easily polymerized. In this case the monomer solution is miniemulsified in a continuous hydrophobic phase. The polymerization process can be initiated either from the continuous phase or from the singlet. Koul et al. Created ovell IPN nanogels composed of poly(acrylic acid) and gelatin by inverse miniemulsion technique. The Acrylic acid monomer stabilized around the gelatin macromolecules in each droplet was polymerized using ammonium persulfate and tetramethyl ethylene diamine and cross-linked with N, N-methylene bisacrylamide (BIS) to create semi-interpenetrating polymer Network nanogels, which were sequentially cross-linked using glutaraldehyde to form IPNs [15]

Evaluation of Morphology of IPNs

The domain size of sequential IPNs is controlled by several features like, the interfacial tension coefficient between the two polymers, γ, the volume fraction of polymers 1 and 2, v1 and v2, respectively, effective network concentration of the two polymers ν1 and ν2 respectively, and the gas constant times the absolute temperature, RT. Both assumed spheres of polymer 2 dispersed in polymer 1, although the spinodal decomposition model and much electron micros-copy suggests that interconnected cylinders may be more

$$D_2 = \frac{4\gamma}{RT(Av_1 + Bv_2)}$$

where

$$A = \frac{1}{2v_2}(3v_1^{1/3} - 3v_1^{4/3} - v_1 \ln v_1)$$

and

$$B = \frac{1}{2}(\ln v_2 - 3v_2^{2/3} + 3)$$

prevalent. The Yeo et al., equation is used to evaluate morphology of IPNs.

For lightly crosslinked systems of 50/50 com-position, the value of D_2 is of the order of several hundred Angstroms. Even though spheres rather than cylinders were specified in the derivation, the numerical result is surprisingly accurate. [16]

Factors That Affect IPN Morphology

Most IPN materials that have been studied show phase separation.

- The phase however varies in amount, size, shape, and sharpness of their interfaces and degree of continuity. These aspects together constitute the morphology of IPN which includes chemical compatibility of the polymers, interfacial tension, cross-linking densities of the networks, polymerization methods, and IPN composition.
- Monomers or prepolymers must be in solution or swollen networks during synthesis, hence Compatibility between polymers is necessary for IPNs Phase separation generally ensues in the course of polymerization, but the resulting phase domain size is smaller for higher compatibility systems [17].
- In IPN, Increase in cross-linking density of polymer network I, decreases the domain size of polymer II. This isbecause the tighter initial network must restrict the size of the regions in which polymer II can phase separate. Different Polymer composition also plays an important role in IPN morphology. The IPN composition determines the relative amounts of the two phases present after polymerization. Increase in the amount of polymer II generally leads to increase in domain size, but effect depends upon method of polymerization. [18]
- Ratio of viscosity between dispersed phase and matrix also plays an important role in affecting the morphology of IPN. If the minor component of the blend has lower viscosity than a major component, that component will be homogenously mixed. On the other hand the minor component will be coarsely dispersed if it has higher viscosity than the major component.

IPN Based Drug Delivery Systems

The major challenge is development of suitable carrier systems for delivery of active pharmaceuticals. New technological advances have brought many novel drug delivery systems. A variety of drug delivery approaches have been investigated for the controlled release of drugs and their targeting to selective sites including hydrogel, microspheres, nanoparticles, tablet, capsule, and films. The current based drug delivery systems are designed to deliver drugs at a particular rate with minimum fluctuation for a desired period of time.

1) Sheet

IPN Sheets are, hydrogels, which are formed with a three-dimensional (e.g., chemically or physically cross-linked) network of hydrophilic polymer chains, swell, but do not dissolve in an aqueous environment. A novel method of producing IPN based drug delivery system is sheeting and type of shape memory polyurethane (SMPU) with high mechanical properties and biodegradability was constructed by using a lactone copolymer (poly(ε-caprolactone-co-γ-butyrolactone), PCLBL), a diol- or triol-based chain extender (1,5-pentanediol, glycerol and 2-amino-2-hydroxymethyl-1,3-propanediol) and a disocyanate cross-linker (1,6-hexamethylene disocyanate) [19]

Novel protein/synthetic polymer hybrid interpenetrating polymer networks (IPNs) of poly(N-isopropylacrylamide) (PNIPAAm) with Bombyx mori silk fibroin (SF) has been, created by Gil *et al*., used for the dermal drug delivery. [20]

Chitosan is a natural polymer, now a days widely used for formation of the grafted, semi- and full-IPNs coatings from PU with natural products, such as depolymerized chitosan, nitrocellulose, nitrolignin, and elaeostearin, have been satisfactorily synthesized, exhibiting excellent mechanical properties and biodegradability. [21]

2) Films

IPN films can be used as piezodialysis membranes. These membranes are not mosaic membranes. Semi-

IPN ofpoly(vinyl alcohol) (PVA)/polyacrylamide can bestrengthen with various doses of nanocellulose. The different composite films are characterized with respect to their mechanical, thermal, morphological and barrier properties. [22]

3) Sponges

IPN sponges have the ability to easily absorb large quantities of tissue exudates, smooth adherence to the wet wound bed with preservation of low moist climate as well as its shielding from mechanical harm and secondary bacterial infection. The cutaneous tissue contains cellular protein and polysaccharide components which together maintain the functionality of the tissue. Generally silk fibroin (SF) and konjacglucomannan (KGM) are physically crosslinked to form biocompatible protein/polysaccharide sponges with adjustable mechanical properties for wound dressing application. The pore structure of sponges can be adjusted by changing blend ratio of SF/KGM, forming homogeneous interconnected pore structure.Therefore, due to the strong water-absorption capacity, moist environment, similar compressive modulus with skin tissue and excellent biocompatibility, the composite sponges have potential application in wound dressings. [23]

4) Capsules

Supracolloidal interpenetrating polymer network reinforced capsules are (Bon*et al.*)prepared byusing micron-sized colloidosomes of poly(methyl methacrylate-co-divinylbenzene) microgels as reaction vessels. An IPN polymer as scaffold can be generated via radical polymerization of the interior phase to produce hollow supracolloidal structures with raspberry coreshell morphology. Their flexibility is tailored by variation of the monomer feed composition. [24]

5) Hydrogels

Hydrogels have been widely used as a drug carrier due to its ease in manufacturing and self-application. Semi-IPN hydrogels with improved mechanical properties and sensitivity toward pH changes wereprepared using chitosan reinforced with cellulose nanocrystals by Sampath*et al.* Glutaraldehyde is used as a crosslinker because of its high reactivity toward the amine groups of chitosan which is advantage for IPN. Antibiotics loaded interpenetrating network hydrogel based on poly (acrylic acid) and gelatin for treatment of experimental osteomyelitis are prepared. [25]

6) Microspheres

One of the successful use of interpenetrating network is for the controlled release of drugs. Salidroside, a functional food agent, was incorporated into novel IPN microspheres (Chem*et al.*,)prepared by chitosan (CS) and methylcellulose (MC) for controlled release and stabilization. [26]

Interpenetrating polymeric network (IPN) microsphere was(Soni*et al.*) prepared byusing glutaraldehyde assisted water-in-oil emulsion crosslinking method for controlled delivery of pirfenidone for the treatment of Idiopathic Pulmonary Fibrosis (IPF) and the natural biopolymer pullulan is harnessed in combination with synthetic polymer PVA for drug delivery applications.[27]

7) Nanoparticles

Current state of art is witnessing a revolution of nanoparticles in new techniques for drug delivery systems. These techniques are capable of controlling the rate of drug delivery, sustaining the duration of therapeutic activity or targeting the drug to specific site of tissue. Novel methods such as quasi-interpenetrating network/gold nanoparticles composite matrices were studied on DNA sequencing performances by capillary electrophoresis technique.

Laponites were capable of self-driven within the gel structure of the silated hydroxypropylmethyl cellulose hydrogel. Laponites were mixed with Si-HPMC to prepare composite hydrogels leading to the development of a hybrid interpenetrating network, and to increases the mechanical properties of the hydrogel. [28]

Novel biomedical applications of the interpenetrating polymer network-based drug delivery system

IPN based formulations can be used as a cancer therapy, infectious diseases, cardiac diseases containing drug delivery and protein delivery, repair and regeneration of organs.

1) Protein delivery and tissue engineering:

The IPN hydrogel supports effective cell adhesion, proliferation, long-term survival, and migration. While alginate is known to be inefficient in promoting cell adhesion, sericin is naturally cell adhesive. New IPNs are biocompatible, biodegradable, and tough elastomeric hydrogels provide a platform for studying stem cell behaviors such as proliferation and differentiation under mechanical stimulation and may broaden the applications of hydrogels in the fields of tissue engineering and regenerative medicine. [29]

2) Repair and regeneration of living organs:
Double network (DN) hydrogels, are produced by two unique similar or identical contrasting networks with designed network entanglement burst into the field of materials science. The admixing polymers are kind of promising soft and tough hydrogels The DN hydrogels is characterized by extraordinary mechanical properties providing efficient biocompatible and high strength for holding considerable promise in tissue engineering. [30]

FibriDerm are the Fibrin based gel structure are Interpenetrated Fibrin Scaffolds for the Construction of Human Skin Equivalents for Full Thickness Burns are prepared by scientist in 2018 obtained through enzymatic hydrolysis of fibrinogen, is associated with a synthetic polymeric network, synthesized by photochemistry. These materials are self-supported and not retractable, properties which open new fields of application for these biomaterials as mechanical support for cellular growth, and particularly relevant for tissue regeneration. [31]

3) Infectious Diseases
The localized treatment of infections can be scientifically improved by site-specific antibiotic drug delivery systems, as due to the failure of conventional treatment pH-sensitive polymers have been frequently used to develop the controlled release formulations using the IPN technique. IPN hydrogels prepared by the cross-linking process showed greater swelling, mucoadhesion, and drug release at lower pH values and maintained antibiotic concentration for prolonged periods of time. [32]

4) Wound healing management:
The hydrogel system has new possibilities in drug delivery and healing management. In a study with the use of natural polymer cellulose pulp, a SIPN hydrogel cell/ PEG/poly (sodium alginate) are formed by free radical polymerization when the cellulose pulp dissolved in PEG/NAOH solvent system, which is polymerized in the presence of monomer acrylic acid with N,N'-methylene bisacrylamide as a cross-linker. [33]

5) Tissue scaffolds:
Since Pelrine et al. reported giant electrically induced strain from dielectric elastomers, also known as electroelastomers, it has become obvious that prestrain significantly enhances performance by increasing the dielectric breakdown strength and particularly with acrylic elastomers. [34]

PVA/GE hydrogels based on the IPN structure and prepared by the enzymatic and cyclic freeze–thawing method have shown promise as tissue scaffolds. The IPN PVA/GE hydrogels showed excellent physical and mechanical properties, which met ideal medical applications. Because of the swelling property of hydrogels, they exhibited high capability in absorbing fluids and thus can be used for exudative wounds. Thus, the gels with a cross-linked network structure were stable enough, suggesting that developer scaffolds might be used in tissue engineering. [35]

Ha Soon Monk et al., reported that High performance IPNs based on VHB acrylic elastomers, poly(HDDA), and poly(TMPTMA) have been prepared for dielectric elastomer artificial muscles. [36]

6) Medical implant:
Fiber-reinforced composites (FRCs) are a group of nonmetallic biomaterials that are growing in popularity in several dental applications such as removable dentures, minimally invasive fixed dental prostheses, periodontal splints, root canal posts, and orthodontic retainers. [37,38]

Researchers have focused attention on the development of methods for repairing an orthopedic joint, including replacing cartilage with water-swellable IPN or SIPN having a hydrophobic thermoset or thermoplastic polymer and an ionic polymer and engaging the IPN or SIPN with a bone surface defining the joint. [39]

7) Cancer therapy:
IPN nanoparticles as a novel temperature-responsive agent can be used in formulating an intelligent therapeutic system capable of loading and releasing the therapeutic agent in response to controlled temperature fluctuations. More, specifically PEGylation is advantageous for the polymeric material in the case of treatment of neoplasms due to the inherent nature cancerous tissues to have leaky vasculature. 'Stealth' nanoparticles or long circulating PEGylated nanoparticles accumulate in tumors. Thus, surface PEG chains could be functional with antibodies, peptides, or other ligands to achieve active targeting of integrins, growth factors, and receptors that are up regulated in tumors. Thus, IPN-based nanoshells can be used for the leaky vasculature of cancer. [40]

CONCLUSION:

IPN has numerous advantages as a biomaterial and is widely used as carrier systems for the delivery of drugs, proteins and gene. The study of IPN for

drug delivery systems and tissue engineering may lead to a better understanding of critical diseases. The concepts of high swelling capacity, specificity and sensitivity play a crutial role in targeting delivery of drugs. By understanding the nature of drug delivery systems and their durability in the body, which can interact with the systems, can be identified.

Its major advantages include its high mechanical strength, phase stability and biological acceptability. It can be used to provide prolonged drug delivery to eradicate critical diseases like AIDS, cancer and cardiac diseases as well as inflammatory diseases like rheumatoid arthritis and osteoarthritis. The use of these systems in chemotherapy, protein delivery, and tissue regeneration requires further research and may prove to be of strategic importance in the future. Thus it is concluded that IPN systems can be used as a carrier system providing better treatment options, eradicating various pathological diseases, and can serve as a better candidate for the treatment of various diseases.

REFERENCES:

1. Lohani A, Singh G, Bhattacharya SS, Verma A. Interpenetrating polymer networks as innovative drug delivery systems. J Drug Deliver, 2014; 1-11.
2. Margaret MT, Brahmaiah B, Krishna PV, Revathi B, Nama S. Interpenetrating polymer network (IPN) microparticles an advancement in novel drug delivery system: a review. Int J Pharm Res Bio Sci 2013; 2(3): 215-24.
3. Sperling, L. H. Interpenetrating Polymer Networks and Related Materials; Plenum: New York, 1981.
4. Wu X, He G, Gu S, Hu Z, Yao P. Novel interpenetrating polymer network sulfonated poly (phthalazinone ether sulfoneketone)/polyacrylic acid proton exchange membranes for fuel cell. J MembrSci, 2007; 295: 80-7.
5. Sperling LH. Interpenetrating polymer network and related materials. New York: Plenum Press, 1981; 1: 265.
6. Shidhaye S, Surve C, Dhone A, Budhkar T. Interpenetrating polymer network: An overview. Int J Res Rev Pharmacy ApplSci; 2(4): 637-50.
7. McNaught D, Wilkinson A. IUPAC compendium of chemical terminology (the "Gold Book"). Oxford: Blackwell Scientific Publications, 2007; 2(2): 1815.
8. Singh P, Kumar SKS, Keerthi TS, Mani TT, Getyala A. Interpenetrating polymer network (IPN) microparticles and advancement in novel drug delivery system: a review. Pharm Sci Monitor, 2012; 3(1): 1826-37.
9. Thakur A, Monga S, Wanchoo R.K. Sorption and drug release studies from semi-ipn of chitosan and xantham gum. Chem Bio-chem Engin Quarter, 2014; 28(1): 105-15.
10. DebdattaRatna, J. Karger-Kocsis Shape memory polymer system of semi –interpenetrating network structure composed of crosslinked poly(methyl methacrylate) and poly(ethylene oxide), Polymer, 2011;52:1063-1070.
11. Kosmala J. D,Henthorn D. B, andBrannon-Peppas L, "Preparation of interpenetrating networks of gelatin and dextran as degradable biomaterials," Biomaterials,2000; 21(20):2019-2023.
12. Bhattacharya S. S, Shukla S, Banerjee S, Chowdhury P, Chakrabortyc P, and Ghosh A, "Tailored IPN hydrogel bead of sodium carboxymethyl cellulose and sodium carboxymethyl xanthan gum for controlled delivery of diclofenac sodium," Polymer-Plastics Technology and Engineering,2013;52:795-805.
13. Banerjee S,Chaurasia G,Pal D,Ghosh A. K,Ghosh A,and Kaity S, "Investigation on crosslinking density for development of novel interpenetrating polymer network (IPN) based formulation," Journal of Scientific and Industrial Research,2006;69(10): 777–784.
14. Landfester K, "Synthesis of colloidal particles in miniemulsions," Annual ReviewofMaterialsResearch,2006;36:231–279.
15. Koul V, Mohamed R, Kuckling D, Adler H. J. P, and Choudhary V, "Interpenetrating polymer network(IPN)nanogels based on gelatin and poly(acrylic acid) by inverse miniemulsion technique: synthesis and characterization," Colloids and Surfaces B,2011;83(2):204–213.
16. Sperling L H, Hu R,INTERPENETRATING POLYMER NETWORKS, Polymer Blends Handbook, Kluwer Academic Publishers,2003;417-447.
17. Lipatov Y. S. andAlekseeva T. T,"Phase-separated interpenetrating polymer networks," Advances in Polymer Science,2007;208(1): 1–227.
18. Ignat L. and Stanciu A, "Advanced polymers: interpenetrating polymer networks," in Handbook of Polymer Blends and Composites, A. K. Kulshreshtha and C. Vasile, Eds., Rapra Technology, 2003;3: 275-280.
19. Dueramae I, et al.,Biodegradable shape memory polymers functionalized with anti-biofouling interpenetrating polymer networks,. Mater. Chem. B, 2016;4: 5394-5404.

20. Gil E S, Hudson S M,Effect of Silk Fibroin Interpenetrating Networks on Swelling/Deswelling Kinetics and Rheological Properties of Poly(N-isopropylacrylamide) Hydrogels, Biomacromolecules 2007; 8: 258-264.
21. Liye H , Zang L, Structure and Properties of Semi interpenetrating Polymer Networks Based on Polyurethane and Nitrochitosan, Journal of Applied Polymer Science, 2017; 82: 3109–3117.
22. Reddy T T,TakaharaA,Simultaneous and sequential micro-porous semi-interpenetrating polymer network hydrogel films for drug delivery and wound dressing applications, Polymers 2015; 50(15): 3537-3546.
23. Dengan Y, Li X, et al., Mechanically robust and flexible silk protein/polysaccharide composite sponges for wound dressing, Carbohydrate Polymers, 2019; 216:17-24.
24. Bon S A, Cauvin S, Cover P J, Colloidosomes as micron-sized polymerisation vessels to create supracolloidal interpenetrating polymer network reinforced capsules, Soft Matter, 2007;3:194-199.
25. Sampath T M, Ching Y C, et al., Preparation and characterization of nanocellulose reinforced semi-interpenetrating polymer network of chitosan hydrogel, Cellulose, 2017; 24(5):2215- 2228.
26. Chem Z, et al., Controlled Release of Salidroside Microspheres Prepared Using a Chitosan and Methylcellulose Interpenetrating Polymer Network, International Journal of Food Engineering, 2017;13(10):1556-3758.
27. Soni S R, Ghosh A, Exploring pullulan-poly(vinyl alcohol) interpenetrating network microspheres as controlled release drug delivery device,Carbohydrate Polymers, 2017; 174: 812-822.
28. Boyer C, et al, Laponite nanoparticle-associated silated hydroxypropylmethyl cellulose as an injectable reinforced interpenetrating network hydrogel for cartilage tissue engineering, ActaBiomaterialia, 2018; 65: 112- 122.
29. Jion O, et al., Highly Elastic and Tough Interpenetrating Polymer Network-Structured Hybrid Hydrogels for Cyclic Mechanical Loading-Enhanced Tissue Engineering, Chem. Mater,2017, 29(19); 8425-8432.
30. Gu z, Huang K, Luo Y, et al., Double network hydrogel for tissue engineering, Wiley Interdisciplinary Reviews: Nanomedicine and Nanobiotechnology, 2018, 10(6); 1-15.
31. Gsib O, et al., FibriDerm: Interpenetrated Fibrin Scaffolds for the Construction of Human Skin Equivalents for Full Thickness Burns, Innovation and Research in Biomedical Engineering, 2018, 38 (2); 103-108.
32. MyungD ,Farooqui N , Waters D , Schaber S , Koh W , Carrasco M, et al. Glucose-permeable interpenetrating polymer network hydrogels for corneal implant applications: a pilot study. Curr Eye Res 2008; 33:29–43.
33. Annaka M, IIlmain F, Etsuo K, Toyoichi T. Interpenetrating-polymer network phase-transition gels. 1992; WO 1992013566 A 1.
34. Pelrine , R. , Kornbluh , R. , Pei , Q. and Joseph , G. High-speed electrically actuated elastomers with strain greater than 100% . Science, 2000; 287:836 – 839.
35. Rani M, Agarwal A, Maharana T, Negi TS. A comparative study for interpenetrating polymeric network (IPN) of chitosan-amino acid beads for controlled drug release. AfrJ Pharm Pharmacol, 2010; 4:35–54.
36. Ha S M, et al., INTERPENETRATING POLYMER NETWORKS AS HIGH PERFORMANCE DIELECTRIC ELASTOMERS, Dielectric Elastomers as Electromechanical Transducers, 2008:44- 50.
37. Duncan, J.P., Freilich, M.A., Latvis, C.J.,Fiber-reinforced composite framework for implant supported overdentures. J. Prosthet. Dent,2000; 84 (2): 200–204.
38. Ballo A, NarhiT,Biocompatibility of fiber-reinforced composites for dental applications, Biocompatibility of Dental Biomaterials, 2017: 23-39.
39. Gupta KC, Ravi-Kumar MNV. Semi-interpenetrating polymer network beads of chitosan-glycine for controlled release of chlorpheniramine maleate. JApplPolymSci, 2000; 76:672–683.
40. Mayet N , Kumar P , Choonara YE , Tomar LK , Tyagi C , du Toit LC , Pillay V. Synthesis of a semi-interpenetrating polymer network as a bioactive curcumin fi lm. AAPS Pharm Sci Tech, 2014; 15:1476–1489.