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The Drug Delivery System based Interpenetrating Polymer Network (IPN)

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1. Abstract

Innovations in polymer grafting have been crucial to the development of modern IPN architectures. Controlled drug delivery at the site of interest necessitates the use of microparticle-based interpenetrating IPN devices. Microparticles made from IPN have attracted attention in the medication delivery and biological domains due to their enhanced characteristics. The use of IPN-based microparticles as a drug carrier for the delivery of pharmaceuticals to various bio-targets has been reported in a number of recent studies. A variety of stimuli-responsive delivery systems were also created to shield the medicine from the body's natural elements. The use of IPN microparticles in the medical field is expanding. It has been used effectively to replace damaged tissues. Ophthalmic implants, heart valve regeneration, blood vessel regeneration, and tissue engineering have all been cited as significant areas of use for IPN microparticles.

Key words: IPN, Semi-IPN, Drug carrier.

2. Introduction

The IPNs could be categorised as a type of polymer blend. Polymer blends can be broken down into two groups: mechanical blends, in which no chemical connections are formed between the two polymers, and graft copolymers, in which primary bonds are formed between the polymeric components. The cross-linking extent between the individual components of a graft copolymer determines the subclass into which it falls. IPNs, are the name given to the materials formed when two polymers are cross-linked.(1,2)

"A polymer consisting of two or more networks which are at least partially interlaced on a molecular scale but not covalently bonded to each other and cannot be separated unless chemical bonds are broken," is how the IUPAC defines an IPN. (3)

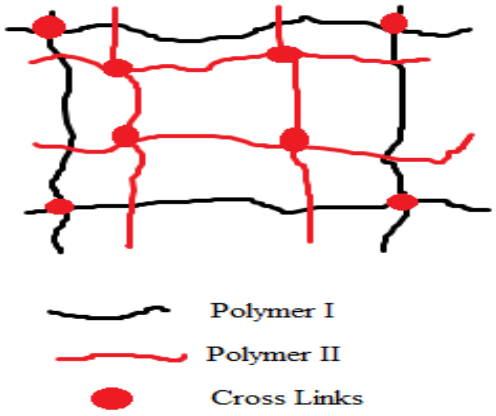

Figure:- 1 Structure of IPN

2.1 Historical overview

Using natural rubber and phenol-formaldehyde resins crosslinked with sulphur, Aylsworth patented the first synthetic IPN. His patent describes the technique of creating an "improved rubber" material. However, the idea of IPN systems was rediscovered several times.(4) The production of large blocks or sheets of a thermoplastic material suitable for optical usage, formed of cross-linked polystyrene or polymethyl methacrylate that had been swelled in a solution of the same monomer, was described by Staudinger and Hutchinson in 1951. In 1955, Solt went off on his own and polymerized a pair of networks, one containing anionic groups and the other cationic. So, it's time to get a fresh batch of ion exchange resin.(1) In 1960, Millar developed the term "IPN" after he created the first IPN, which consisted of two networks of the same chemical makeup. Later, Frisch and Sperling independently constructed IPN made of two distinct polymers. The nature of the constituent materials allowed Frisch's resultant material to be classified as an interpenetrating elastomer network. In 1969, Sperling and Friedman used

ultraviolet (UV) polymerization to create an IPN from polystyrene and poly(ethyl acrylate).(5)

2.2 Classification

There are two basic categories by which IPNs can be categorised. The first categorization considers the nature of the chemical bonds among building blocks of the polymers of the resultant IPN.(1,4,6) Therefore, it is feasible to differentiate based on chemical bonding:

- Covalent semi-IPN: A single polymeric network is generated by the cross-linked polymer systems.
- Noncovalent semi-IPN: The cross-linking occurs in only a single polymer component.
- Noncovalent full-IPN: Both polymers undergo cross-linking independently.
- Synthetic method forms the basis of a second classification.

• Sequential IPN: The name "sequential" is used to describe these networks, which relates to the sequential character of the process of polymerization. Sequential IPN involves first cross-linking polymer (I), and then swelling the resulting network with the monomer of polymer (II). After the cross-linker has been introduced, polymer (II) has the potential to undergo polymerization and/or cross-linking immediately afterward. These methods of synthesis are simple; all that is required is for the monomer (II) and the co-reactants to appropriately expand within the polymer network (I). Elastomers are utilised quite frequently in network I due to the network's reliance on their bendability.

• Simultaneous IPN: An IPN is created in a single step when monomers I and II are mixed with activators and crosslinkers of their respective types. The only other requirement for this synthetic method is that the two polymerization pathways do not cross. Due to the high compatibility of the starting monomeric mixture, simultaneous IPNs result in more intermixing in the final network than sequential ones.

• Latex IPN: Synthetic latex IPNs were initially developed by Frisch et al. in 1969. These IPNs systems are also known as interpenetrating elastomeric networks due to the elastomeric nature of both the latex components. In order to produce a latex particle with two networks, it is usual routine to polymerize a second monomer alongside the cross-linking agent and activator present in the seed latex of the first cross-linked monomer. They often show a “core” and “shell” structure.

• Thermoplastic IPN: There is a presence of physical cross-linking between the polymers in thermoplastic IPNs. Thermoplastic IPNs can undergo one of three distinct physical cross-linking processes. When an ionomer is formed, cross-links are produced because ionic groups are present along the polymer chain. In partially crystalline polymers, physical cross-links are

produced by crystalline regions. In block copolymers with an ABA structure, the end blocks form a discrete phase, and the cross-links are produced by glassy domains. These materials, by virtue of their composition, flow at high temperatures but, because to the existence of cross-links, display IPN behaviour at the use temperature.

• Gradient IPN: There are compositional differences between macroscopic regions of a gradient IPN. A fast polymerization can generate them by enlarging the first polymer network within the second monomer network before equilibrium is reached. The resulting IPN displays a concentration gradient of the second monomer across the first polymer.

IPN can also be categorised into a third group according to the topological configurations of the polymer chains.

2.3 Properties

There are notable differences between graft copolymers, block copolymers, and blends, and IPN and semi-IPN networks. Heterogeneous networks emerge as a consequences of phase separation. This is mostly attributable to the fact that the components making up IPNs networks have such distinctive chemical structures. However, because to the system's high viscosity and the entanglements between chains, separation is a very sluggish process. The creation of an IPN may occur via one of two possible methods of phase separation:

• The second phase nucleates within the first phase matrix, where it grows into spherical structures. As they expand, the diameter of these spheres increases.

• This method of phasing is by far the most used. Here, the second phase forms a network of interconnected cylinders inside the first phase's matrix. The amplitude of the waves causes the expansion of these cylinders. Coarsening and coalescence may have dramatic effects in the future. However, cross-links, which maintain relatively modest domain sizes, may hamper these alterations. The structure of IPN networks changed as a result of phase separation. When gelation precedes phase separation, as in the example of sequential IPN, the resulting network has a more condensed phase domain. The domain sizes of the various phases tend to be bigger, however, if phase separation occurs prior to gelation. Furthermore, phase separation also influenced IPN's glass transition temperature. IPN systems' Tg values may be a reflection of the Tg values of their constituent polymeric materials, with or without an inward shift. The glass transition temperature (Tg) of an IPNs network, on the other hand, may be either broad or acute, depending on the composition of the network. Sperling and others have found that the Tg shifts or merges inward due to the presence of cross-links, which is usually taken as an increase in

miscibility between the two polymers.(1,5) A single transition temperature, however, is not sufficient proof of network compatibility in IPNs. Even in phase-separated IPNs, one glass transition point might be visible if one of the phases is localised to relatively small domains. The greater extent of phase separation in semi-IPNs systems compared to full IPNs typically results in a lower transition temperature. Several benefits can be seen in IPN despite the presence of phase separation. Among these benefits is an increase in mechanical properties over those of the individual polymers that make up the IPN. It follows that in IPN networks, all of the parts work together to great advantage. Networks with the correct mechanical properties can be obtained on this basis by selecting the beginning IPN materials carefully. IPN systems also have the added benefits of being resistant to heat and chemicals. In addition, IPNs expand without dissolving in solvents and can reduce creep and flow compared to other polymeric blends

3. Characterization

Physical (including mechanical, morphological, and spectroscopic) and thermal characteristics are the most common ways to classify IPNs.

3.1 Morphological characterization

Synthetic approach, compatibility of individual IPN components, network cross-link densities, interfacial tension, and network formation rates all have significant impacts on the resulting system shape. Transmission electron microscopy on thin slices that have been stained and ultramicrotomed reveals several morphological features of IPNs. Osmium tetroxide is used in conventional staining because it reacts with reactive groups in polymers, such as the double bonds in diene type polymers. However, when dealing with saturated or nonreactive polymers, transmission electron microscopy is of no use. These methods allow one to ascertain the micro- and nanoscale structure, the degree of mixing, and the location of phase domains. The IPN's structure can be fully and clearly explained in this manner. The shape of IPNs can also be determined by employing different methods. Experiments using X-rays, atomic force microscopy, confocal laser scanning microscopy, energy-dispersive X-ray analysis, and atomic force microscopy are all examples.(7,8)

3.2 Thermal characterization

Infrared thermography, differential thermal analysis and thermogravimetric analysis, are the most used thermal characterization methods for IPNs. DSC analysis on IPN networks can reveal one or two Tg values, as previously described. Two Tgs may or may not be different from the Tgs of the individual polymeric components. Researchers have observed that Tg indicates the onset of mobility in polymer chains. Due to the polymerepolymer delay in chain mobility, higher

temperatures would be required if interactions between polymer chains were strong. A value of 2 Tg is indicative of the occurrence of two phases in both IPN and semi-IPN networks. Thus, these thermal analyses can be used to learn about the degree of interpenetration between the network's components and to spot micro- or macrophase separation in IPN. TGA study helps us learn how well IPN networks withstand heat. Mass loss or gain as an effect of temperature or time has traditionally been reported using TGA analyses, which include subjecting a sample to a controlled temperature regimen in a controlled atmosphere. Most studies have found that IPN have greater heat stability than its homopolymers.(9)

3.3 Mechanical characterization

Young's modulus, hardness, tensile strength, and elongation at break, are some common mechanical parameters used to describe IPN. Characterization of IPN or semi-IPN materials often involves mechanical testing such compression, tearing, extensiometry, tensile, and rheology. Rheological information can be used to learn more about the networks' structures, identify the conditions necessary for their development, analyse the consequences of alterations to chemical factors, and assess the networks' utility. The gel point of an IPN can be calculated using rheological experiments, which can shed light on its kinetic properties. The polymerization conditions can be improved with the help of the kinetic results. Furthermore, cross-linking the activation energy can be computed by determining the gel points at various temperatures. Several mechanical parameters, such as elongation at rupture, yield strength, and Young's modulus, can be measured by subjecting a sample to a tensile test. The fracture toughness of IPNs systems is an additional desirable quality that could be put to use in tailored tissues or drug delivery systems. Tear tests are a reliable way to ascertain this quality. Mechanical properties and swelling of IPNs can be adjusted by associating a stiffer hydrogel with a more swellable, less swellable, softer hydrogel, as IPNs often display mechanical features intermediate of the distinct polymeric components. When compared to their individual components, IPNs often exhibit greater toughness. Furthermore, dynamic mechanical spectroscopy is the most effective technique for studying the viscoelastic characteristics of polymeric materials.(10)

3.4 Spectroscopic characterization

Multiple spectroscopy analyses, such as NMR, infrared, and ESR, are used to get the spectroscopic characterization. The degree of polymer interpenetration in IPN at the nanoscale is estimated using nuclear magnetic resonance spectroscopy. In addition, this method has the potential to reveal IPNs' microstructure, miscibility, and morphology. When IPNs contain

functional groups that are difficult to observe visually, IR and Fourier-transform infrared (FTIR) spectroscopy can be employed to get insight into how the reaction proceeds to completion. Finally, ESR studies shed light on the variability and structure of IPN down to the sub-5 nm range.(6,11)

4. Methods of fabrication of IPN

4.1 Method of Irradiation by Microwave

Microwave-assisted crosslinking of natural polymers for the synthesis of IPN is gaining popularity due to the higher quality and improved properties of the IPN it produces, the lower amounts of toxic chemicals needed, the shorter preparation times, and the lower overall production costs. Scientists used microwave irradiation to create IPN synthetically. The polysaccharides/polymer, crosslinker, and initiator dissolved in sterile water will be used in the IPN's preparation. The oxygen that was dissolved was removed from the mixture via nitrogen bubble solution bubbling for 1 hour. The resulting concoction was microwaved at 300 W for 10 minutes. After the reaction had finished, the IPN that had been formed was placed on a Petri plate and allowed to dry at a temperature of 50 degrees Celsius for nine hours.(12)

4.2 Casting evaporation method

The casting evaporation process is a good illustration of a method of preparation that involves successive steps. After heating the polymer to the point where it entirely dissolves, a solution of the cross-linker is then added. In a step-by-step process, polymer-I is the first component to be brought into the crosslinker solution. In both cases, the solutions were first heated, then blended, then cast, and last dried. Casting evaporation is the method that is utilised during the production of IPN gels.(13,14)

4.3 Emulsification cross-linking

Emulsion cross-linking accomplished through phase separation. Although the cross-linking of emulsions without the use of w/w emulsions is the standard, w/w emulsion creation of IPN has garnered more attention from researchers. An o/w emulsion is formed when one polymer-containing aqueous phase is combined with another polymer-containing aqueous phase. The resulting IPN system is the result of cross-linking. This is the most typical approach taken for making IPN.(14)

4.4 Miniemulsion/inverse miniemulsion technique

Miniemulsion polymerization initiates polymerization in small, stable droplets. Miniemulsion degradation caused by coalescence can be avoided if the surfactant is incorporated into a

stabilizer that is easily soluble in the dispersed stage but insoluble in the continuous stage. Polymerization of hydrophilic monomers is at the heart of inverse miniemulsion (w/o). The monomer solution is continuously hydrophobized during miniemulsification. It would be possible to distinguish the polymerization process from the steady phase or the droplet.(15)

4.5 Radiation polymerization method

In this technique, polymerization is achieved via exposure to Gamma radiation. Polymerization occurs in a "one-step" synthesis method when no chemical initiator or cross-linking agent is used. IPN was synthesised by Ahmed M. Elbarbary and Mohamed MohamadyGhobashy by irradiating chitosan and 2-hydroxyethyl methacrylate with -rays; it has been shown to be effective in the adsorption-based separation of Ca(II), Cu(II), and Zn (II) metal ions from aqueous solution.(14)

5. Applications of Microparticles IPN in Drug Delivery

5.1 Anti-carcinogenic Drugs Delivery

To treat metastatic breast and colorectal cancer, the oral chemotherapy drug capecitabine was envoloped in a semi-IPN matrix composed of polyacrylamide, poly(ethylene oxide), and chitosan. For the grafting of polyacrylamide and poly(ethylene oxide), ceric ammonium nitrate was utilized as an initiator for free radical polymerization. To investigate the impact of grafting factors, a matrix of IPNs was created. The results showed that the medication was dispersed amorphously in the polymer matrix. The in vitro drug release test was conducted first in a buffer solution that mimicked the conditions of the stomach for a period of two hours, and then in a buffer solution that mimicked the conditions of the small intestine for the remaining time required for full drug release.(16) The emulsification cross-linking procedure was used by researchers to manufacture 5-fluorouracil-loaded IPN microspheres constructed of pluronic F-127 and chitosan. The cross-linker they used was glutaraldehyde. Hydrogel microspheres have an average particle size of between 110 and 382 m. It was discovered that the concentration of pluronic F-127, the cross-linking agent, as well as the drug loading all had an effect on the drug release. The drug release could be prolonged for up to 24 hours and followed a non-Fickian release mechanism. N-isopropylacrylamide and Sodium alginate were used in a W/O emulsification process with the surfactant Tween 80 to create 5-fluorouracil semi-IPN microspheres that respond to stimuli. Drug distribution within the semi-IPN matrix was validated at the molecular level. Experiments on swelling and drug release at 25 and 37 degrees Celsius in varying buffer solutions verified the IPN matrix's thermoresponsive activity. Inverse suspension cross-linking was used to create drug-eluting semi-IPN microspheres from poly(2-

acrylamide-2-methylpropanesulfonic acid) and succinyl-modified chitosan.(17,18) The anticancer drug doxorubicin hydrochloride has been successfully administered using this technique by Sang et al. The relative mass increase of the finished product was used to calculate the amount of chitosan grafting. Micrographs of microspheres revealed that they were round and polished. Rapid drug loading and prolonged release have benefited from the incorporation of -COOH and SO_3H groups. Chitosan's biodegradability makes it useful for making anticancer medication drug-eluting microspheres.(19) 6-Thioguanine is used to help kids who have lymphoblastic leukaemia. To create the IPN microsphere, methyl cellulose and polyvinyl alcohol (PVA) were employed, and 6-thioguanine was added in situ. Up to 72% drug loading efficiency was observed. According to the findings of the in vitro dissolution, the concentration of the cross-linker, the drug loading, and the amount of PVA all played a part in the process of releasing 6-thioguanine from the microspheric core. Non-Fickian diffusion was revealed to be the mechanism responsible for the prolonged drug release up to 12 hours.(20,21)

5.2 Delivery of Antiviral Drugs

Zidovudine, an antiviral medicine, was investigated using a drug delivery system that was sensitive to both temperature and pH. Sodium alginate and guar gum-g-poly(N-vinyl caprolactam) were used to create hydrogel microbeads with the purpose of developing a delivery technique that is colon-specific. It was demonstrated that the drug release followed a non-Fickian route, and the highest rate of entrapment that was measured was 68%. For the purpose of administering the anti-HIV medicine abacavir sulphate, semi-IPN microspheres of dextran-grafted-acrylamide and poly(vinyl alcohol)were produced using an emulsification cross-linking process. The medication was released from the IPN matrix in a pH-dependent manner.(22) Hydrogel microspheres based on hydroxypropyl cellulose and chitosan were created to transport the anti-HIV medication valganciclovir hydrochloride. Biodegradable IPN microspheres cross-linked with glutaraldehyde were successfully developed. The microscopic analysis confirmed the flatness of the surface. Due to polymer matrix shrinkage, it was discovered that the microspheres shrank with increasing glutaraldehyde concentration. Controlled drug release was seen during in vitro testing in a 7.4 pH buffer solution. Researchers have looked into chitosan and acrylamide-g-dextran microspheres loaded with acyclovir using emulsification cross-linking technology and glutaraldehyde. Up to 79.6 percent entrapment efficiency was achieved. Drug release was found to be dependent on cross-linking intensity and acrylamide grafted dextran concentration in an in vitro study. Non-Fickian drug release behaviour was seen for up to 12 hours.(23) Acyclovir-loaded IPN hydrogel microparticles were studied by Jana et al., who

used the ionic cross-linked gelation process in the presence of Ca2+ to create the hydrogel from carboxymethyl tamarind polysaccharide and alginate. Various instrumental methods were used to characterise the manufactured hydrogels. Field emission scanning electron microscopy (FESEM) was used to characterise the surface morphology and elemental composition of IPN hydrogel microparticles, and the images indicated spherical microparticles with rough surfaces. A prolonged release of the medication was seen in an in vitro dissolution investigation conducted in an alkaline medium.(24)

5.3 Delivery of Antibiotics

The antibiotic cefadroxil was encapsulated in a chitosan-based pH-sensitive microgel system for sustained release. Particles of microgel are dispersed uniformly in a solvent environment and are made of a polymer with intramolecular crosslinks. Chitosan and hydrolyzed acrylamide grafted poly(vinyl alcohol) (PVA) were utilized to create the system. Complete drug dissolution was shown to be slowed by the IPN matrix of the microgel device for times longer than 10 hours. Semi-IPN microspheres of chitosan and guar gum loaded with cefadroxil were created by Reddy et al. via a W/O emulsification cross-linking process. The SEM analysis revealed uneven and rough-surfaced microspheres. Research with XRD and DSC showed that cefadroxil molecules were spread out throughout the IPN matrix. Controlled release over 10 hours was seen during in vitro dissolution in a pH 7.4 buffer solution. Drug release from polymer matrices was shown to be affected by the entrapment percentage and polymer ratio.(25) IPN microspheres of ciprofloxacin hydrochloride were created using superabsorbent polymer and xanthan gum-based poly(vinyl alcohol). Hydrogel microspheres were created using W/O emulsification cross-linking technology by combining PVA with hydrolyzed superabsorbents and cross-linkers in varying ratios. Ciprofloxacin hydrochloride was shown to be continuously released from an IPN matrix by non-Fickian diffusion. Ofloxacin hydrochloride, a commonly prescribed antibiotic, was trapped in sodium alginate-chitosan IPN microbeads.(26) According to the microscopic analysis, the microbeads have a spherical shape and a smooth exterior. Ofloxacin hydrochloride was found to have a prolonged release time of up to 24 hours in an in vitro dissolution investigation. Boosting the sodium alginate concentration and cross-linking time was found to slow drug release by a higher percentage.(27,28)

5.4 Delivery of Antihypertensive Drugs

Semi-ionic polymer matrices of gellan gum and N-isopropylacrylamide were used to entrap the antihypertensive medication atenolol. Microspheres between 34 and 76 microns in diameter were the result of this process. The medication has been broken up into smaller molecules, as

shown by thermal analysis. The medication was released pulsatilely from the microsphere in response to temperature changes. Researchers found that IPN microspheres made with gellan gum and PVA by an emulsification cross-linking process effectively delivered carvedilol. The research indicate that the medication was dispersed crystalline in the IPN matrix. The finished microsphere was perfectly round and had a flawless surface. For the drug release test, we used both a gastric and an intestinal buffer solution. It was discovered that the polymer matrix may release drugs for up to 12 hours.(4) Semi-IPN microspheres based on chitosan and N,N'-dimethylacrylamide were created using a water/oil emulsification process and tested for their ability to deliver chlorothiazide. DSC and X-RD technique verified drug molecular dispersion. Up to 12 hours of controlled drug release has been achieved using a microsphere matrix. IPN microparticles containing the antihypertensive medication felodipine were created using the ionic cross-linking of tripolyphosphate and chitosan. Increases in tripolyphosphate concentration inhibit drug release from microparticle matrix. It was discovered that a higher level of cross-linking prolong drug release and slowed the swelling from the IPN matrix.(29,30)

5.5 Delivery of NSAIDs

The combination of polyacrylamide grafted gum ghatti (PAAm-g-GG) and ALG has allowed for the creation of pH-sensitive gastroprotective IPN microbeads. Microwave energy was used in PAAm-g-GG copolymer synthesis, with ceric ammonium nitrate serving as the activator. The PAAm-g-GG was then pH-sensitive by undergoing alkaline hydrolysis. Ketoprofen was employed to test the gastroprotective properties of the IPN microbeads. Phosphate buffer, pH 7.4, increased the swelling index of microbeads as compared to HCl buffer, pH 1.2. Using PVA and sodium CMC and emulsification cross-linking technique, Banerjee et al. have created IPN hydrogel microspheres loaded with diclofenac sodium. Non-Fickian drug release was seen when the matrix of microspheres was broken down.(31) When glutaraldehyde was utilised as the cross linker, it was discovered that the cross-linking density changed depending on the polymer composition. It has been observed that gum ghatti and chitosan IPN microparticles can transport diclofenac sodium across the intestinal wall. SEM was used to analyse the surface and characterise its morphology. Particle sizes ranged on average from 294 to 366 m. The medication was found to be released from the polymer matrix in a non-Fickian fashion in the in vitro dissolution assay. The simultaneous dissolution-absorption profile of the improved formulation was investigated in the rat gut. No notable differences were seen across groups, indicating that the targeted delivery of the drugs was effective.(32) IPN microspheres made of gelatin and sodium carboxymethyl cellulose were used to administer the NSAID ketorolac tromethamine.

As a crosslinking agent, glutaraldehyde was employed. The in vitro drug release study found that, based on the NaCMC content and the cross-linker concentration, the release can be sustained for up to 10 hours. Sodium alginate and polyvinyl alcohol (PVA) were used to create a microsphere IPN delivery system for naproxen sodium. The microspheres were made with glutaraldehyde as the cross-linker, and the cross-linking procedure W/O emulsification type was utilized to create them. It was discovered that cross-linking density changes as a function of cross-linking time.(33)

5. 6 Delivery of Antidiabetic Drugs

The emulsification cross-linking and inotropic gelation method was used to successfully entrap repaglinide, an oral antidiabetic medication, in IPN microparticles of sodium alginate and sterculia gum. When diabetic rats were given microparticles treated with glutaraldehyde, their blood glucose levels dropped significantly within 3 hours.(34)

5.7 Delivery of Anticonvulsant Drugs

Oxcarbazepine, an anticonvulsant, was tested for administration using IPN beads manufactured from egg albumin and sodium alginate. The IPN microbeads were made by using ionic gelation, and calcium chloride served as the cross-linking agent. Because of how slowly the beads expanded, the drug was released consistently throughout time. Controlled drug release via non-Fickian diffusion was seen in an in vitro study.(35)

5.8 Delivery of Antiasthmatic Drugs

Methyl cellulose and chitosan were used to successfully entrap the antiasthmatic medication theophylline in cross-linked IPN microsphere. Hydrogel microsphere cross-linking density was found to change with cross-linker and methyl cellulose concentrations. The medication exhibited crystalline properties in the IPN matrices, as shown by DSC and XRD analysisThe in vitro drug release was discovered to be characterised by a Fickian process, and it was shown to be stable for up to 12 hours.

6. Conclusion

The creation of cutting-edge IPN systems has expanded dramatically in recent years. This article covered the evolution of microparticulate technologies and their uses in the controlled release pharmaceutical industry. Also proven is the usefulness of the IPN microparticulate system as a resource for the development of a tailored medication delivery system. The biological application of IPN microparticles is flourishing in many different fields, including tissue engineering. For IPN microparticles to be effectively administered in the therapeutic or biomedical field, much more research is needed on this potential subject.

7. References

1. Sperling LH, Hu R. Interpenetrating polymer networks. Polym Blends Handb. 2014;677–724.
2. Thapliyal PC. Interpenetrating polymer networks. Compos Interfaces. 2010;17(2–3):85–9.
3. Niu Y, Xia Q, Li N, Wang Z, (Lucy) Yu L. Gelling and bile acid binding properties of gelatin-alginate gels with interpenetrating polymer networks by double cross-linking. Food Chem. 2019;270(July 2018):223–8.
4. Interpenetrating A, Gelatin A, Cultures TC, Chen Q, Tian X, Fan J, et al. molecules. 2020;
5. Friedman GD, Udaltsova N, Chan J, Quesenberry CP, Habel LA. Screening pharmaceuticals for possible carcinogenic effects: Initial positive results for drugs not previously screened. Cancer Causes Control. 2009;20(10):1821–35.
6. James J, Thomas G V., Thomas S. Spectroscopic characterization protocols for interpenetrating polymeric networks [Internet]. Unsaturated Polyester Resins: Fundamentals, Design, Fabrication, and Applications. Elsevier Inc.; 2019. 233–241 p. Available from: http://dx.doi.org/10.1016/B978-0-12-816129-6.00010-7
7. Hago EE, Li X. Interpenetrating polymer network hydrogels based on gelatin and PVA by biocompatible approaches: Synthesis and characterization. Adv Mater Sci Eng. 2013;2013.
8. Rajivgandhi G, Saravanan K, Ramachandran G, Li JL, Yin L, Quero F, et al. Enhanced anti-cancer activity of chitosan loaded Morinda citrifolia essential oil against A549 human lung cancer cells. Int J Biol Macromol [Internet]. 2020;164:4010–21. Available from: https://doi.org/10.1016/j.ijbiomac.2020.08.169
9. Wadhera P, Jindal R, Dogra R. Synthesis of semi interpenetrating network hydrogel [(GrA-Psy)-cl-Poly (AA)] and its application for efficient removal of malachite green from aqueous solution. Polym Eng Sci. 2019;59(7):1416–27.
10. Qadri MF, Malviya R, Sharma PK. Biomedical Applications of Interpenetrating Polymer Network System. Open Pharm Sci J. 2015;2(1):21–30.
11. Devkar P, Nangare S, Zawar L, Shirsath N, Bafna P, Jain P. Design of polyacrylamide grafted sesbania gum-mediated pH-responsive IPN-based microbeads for delivery of diclofenac sodium: In-vitro-in-vivo characterizations. Int J Biol Macromol. 2023 Mar 1;230:123360.

12. Roy D, Bal T, Swain S. Fabrication and evaluation of pH-sensitive biocompatible microwave irradiated moringa barkgum-carrageenan (MOG-CRG-IPN) interpenetrating isotropic polymeric network for controlled delivery of pharmaceuticals. Sustain Chem Pharm [Internet]. 2020;18(August):100325. Available from: https://doi.org/10.1016/j.scp.2020.100325
13. Mallikarjuna B, Rao K, Pallavi K, Rao K, Subha MCS. Biodegradable interpenetrating polymer network hydrogel membranes for controlled release of anticancer drug. Asian J Pharm. 2015;9(2):129–36.
14. Shaikh MAJ, Gilhotra R, Pathak S, Mathur M, Iqbal HMN, Joshi N, et al. Current update on psyllium and alginate incorporate for interpenetrating polymer network (IPN) and their biomedical applications. Vol. 191, International Journal of Biological Macromolecules. Elsevier B.V.; 2021. p. 432–44.
15. Koul V, Mohamed R, Kuckling D, Adler HJP, Choudhary V. Interpenetrating polymer network (IPN) nanogels based on gelatin and poly(acrylic acid) by inverse miniemulsion technique: Synthesis and characterization. Colloids Surfaces B Biointerfaces [Internet]. 2011;83(2):204–13. Available from: http://dx.doi.org/10.1016/j.colsurfb.2010.11.007
16. Upadhyay M, Vardhan H, Mishra B. Natural polymers composed mucoadhesive interpenetrating buoyant hydrogel beads of capecitabine: Development, characterization and in vivo scintigraphy. J Drug Deliv Sci Technol [Internet]. 2020;55(August 2019):101480. Available from: https://doi.org/10.1016/j.jddst.2019.101480
17. Eswaramma S, Reddy NS, Rao KSVK. Carbohydrate polymer based pH-sensitive IPN microgels: Synthesis, characterization and drug release characteristics. Mater Chem Phys [Internet]. 2017;195:176–86. Available from: http://dx.doi.org/10.1016/j.matchemphys.2017.04.018
18. Mallikarjuna Reddy K, Ramesh Babu V, Krishna Rao KSV, Subha MCS, Chowdoji Rao K, Sairam M, et al. Temperature sensitive semi-IPN microspheres from sodium alginate and N-isopropylacrylamide for controlled release of 5-fluorouracil. J Appl Polym Sci [Internet]. 2008 Mar 5 [cited 2021 Jul 1];107(5):2820–9. Available from: https://onlinelibrary.wiley.com/doi/full/10.1002/app.27305
19. Huang FYJ, Hung CC, Chang CW, Chao JH, Hsieh BT. Evaluation of injectable chitosan-based co-crosslinking hydrogel for local delivery of 188Re-LIPO-DOX to breast-tumor-bearing mouse model. Anticancer Res. 2018;38(8):4651–9.
20. Kulkarni R V., Baraskar V V., Alange V V., Naikawadi AA, Sa B. Controlled Release of

an Antihypertensive Drug through Interpenetrating Polymer Network Hydrogel Tablets of Tamarind Seed Polysaccharide and Sodium Alginate. J Macromol Sci Part B. 2013;52(11):1636–50.

21. Rao KM, Rao KSVK, Ramanjaneyulu G, Rao KC, Subha MCS, Ha C. Biodegradable sodium alginate-based semi-interpenetrating polymer network hydrogels for antibacterial application. 2013;3196–206.
22. Eswaramma S, Rao KSVK. Synthesis of dual responsive carbohydrate polymer based IPN microbeads for controlled release of anti-HIV drug. Carbohydr Polym [Internet]. 2017 Jan 20 [cited 2021 Jul 3];156:125–34. Available from: https://pubmed.ncbi.nlm.nih.gov/27842806/
23. Mallikarjuna B, Madhusudana Rao K, Siraj S, Chandra Babu A, Chowdoji Rao K, Subha MCS. Sodium alginate/poly (ethylene oxide) blend hydrogel membranes for controlled release of valganciclovir hydrochloride. Des Monomers Polym. 2013;16(2):151–9.
24. Jana S, Sharma R, Maiti S, Sen KK. Interpenetrating hydrogels of O-carboxymethyl Tamarind gum and alginate for monitoring delivery of acyclovir. Int J Biol Macromol [Internet]. 2016;92:1034–9. Available from: http://dx.doi.org/10.1016/j.ijbiomac.2016.08.017
25. Kulkarni AR, Soppimath KS, Aminabhavi TM, Rudzinski WE. In-vitro release kinetics of cefadroxil-loaded sodium alginate interpenetrating network beads. Eur J Pharm Biopharm. 2001;51(2):127–33.
26. Singh B, Kanwar JS, Kumari P. Modification of Dietary Fiber Psyllium with Poly(vinyl pyrrolidone) through Network Formation for Use in Slow Drug Delivery Application. Polym Sci - Ser B. 2018;60(3):331–48.
27. Kulkarni P V, Keshavayya J. CHITOSAN-SODIUM ALGINATE BIODEGRADABLE INTERPENETRATING POLYMER NETWORK (IPN) BEADS FOR DELIVERY OFOFLOXACIN HYDROCHLORIDE.
28. Rajesh AM, Popat KM. In vivo and in vitro taste masking of ofloxacin and sustained release by forming interpenetrating polymer network beads. Pharm Dev Technol. 2017;22(1):26–34.
29. Jana S, Sen KK. Gellan gum/PVA interpenetrating network micro-beads for sustained drug delivery. Mater Today Proc [Internet]. 2019;11:614–9. Available from: https://doi.org/10.1016/j.matpr.2019.03.018
30. Upadhyay M, Vardhan H, Mishra B. Natural polymers composed mucoadhesive

interpenetrating buoyant hydrogel beads of capecitabine: Development, characterization and in vivo scintigraphy. J Drug Deliv Sci Technol [Internet]. 2020;55(December 2019):101480. Available from: https://doi.org/10.1016/j.jddst.2019.101480

31. Boppana R, Krishna Mohan G, Nayak U, Mutalik S, Sa B, Kulkarni R V. Novel pH-sensitive IPNs of polyacrylamide-g-gum ghatti and sodium alginate for gastro-protective drug delivery. Int J Biol Macromol [Internet]. 2015;75:133–43. Available from: http://dx.doi.org/10.1016/j.ijbiomac.2015.01.029
32. Bhattacharya SS, Ghosh AK, Banerjee S, Chattopadhyay P, Ghosh A. Al3+ ion cross-linked interpenetrating polymeric network microbeads from tailored natural polysaccharides. Int J Biol Macromol [Internet]. 2012;51(5):1173–84. Available from: http://dx.doi.org/10.1016/j.ijbiomac.2012.08.029
33. Kondolot Solak E, Er A. pH-sensitive interpenetrating polymer network microspheres of poly(vinyl alcohol) and carboxymethyl cellulose for controlled release of the nonsteroidal anti-inflammatory drug ketorolac tromethamine. Artif Cells, Nanomedicine Biotechnol. 2016;44(3):817–24.
34. Awasthi R, Kulkarni GT, Ramana MV, de Jesus Andreoli Pinto T, Kikuchi IS, Molim Ghisleni DD, et al. Dual crosslinked pectin–alginate network as sustained release hydrophilic matrix for repaglinide. Int J Biol Macromol [Internet]. 2017;97:721–32. Available from: http://dx.doi.org/10.1016/j.ijbiomac.2017.01.050
35. Prajapati VD, Gandhi AK, Patel KK, Patel BN, Chaudhari AM, Jani GK. Development and optimization of modified release IPN macromolecules of oxcarbazepine using natural polymers. Int J Biol Macromol [Internet]. 2015;73(1):160–9. Available from: http://dx.doi.org/10.1016/j.ijbiomac.2014.11.016