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# Interpenetrating Polymer Network (IPN): Novel Approach in Drug Delivery

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**Abstract**

Controlled release drug delivery System (CRDDS) is the major aspect of research in twentieth century into which Interpenetrating polymer network (IPN) based drug delivery system paying the important role in delivering the drug at predetermined rate. IPN is considered as one of the most useful novel biomaterial. Its biocompatible and biodegradable properties made this biomaterial as a novel excipient in the pharmaceutical industry. These systems are also used for tissue engineering such as cartilage scaffolds, bone substitutes etc. The excellent physiochemical attributes such as providing stability to the formulations, improves solubility of hydrophobic drugs, excellent swelling capacity and its biodegradability, impart bioavailability, drug targeting in a specific tissue and very weak antigenecity, made IPN the primary resource in both pharmaceutical and medical applications. IPN offers novel ways to formulator to formulate multiparticulate drug delivery system, tablets or transdermal delivery systems. IPN is highly effective for controlling the drug release of Biopharmaceutics Classification System (BCS) class I drugs.

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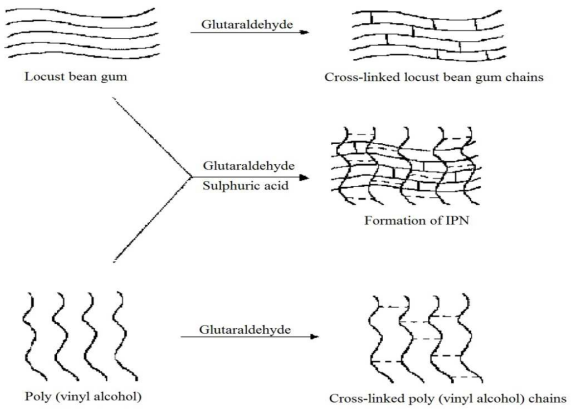
## INTRODUCTION:

An ideal dose regimen in the drug therapy of any disease is the one which immediately attains the desired therapeutic concentration of drug in plasma (or at the site of action) and maintains it constant for

the entire duration of treatment and this is the basic principle of pharmacotherapy. The frequency of administration or the dosing interval of any drug depends upon its half life or mean residence time (MRT) and its therapeutic index. Now day's extensive efforts have been focused on administering a drug delivery system at the site of action for maximizing drug availability and minimizing the dose related side effects and thus the effects of pharmacotherapy can be optimized [1]. When a drug is administered as a conventional dosage form such as tablet, the dosing interval is much shorter than the half life of the drug resulting in number of limitations such as poor patient compliance, typical peak-valley plasma concentration-time profile is obtained, and unavoidable fluctuations in the drug concentration may lead to precipitation of adverse effects. In order to overcome such a situation Controlled-release drug delivery system (CRDDS) are designed. They can improve the therapeutic efficacy and safety of drug by precise temporal and spatial placement in the body, thereby reducing both size and frequency. Several advantages include improved patient compliance, reduction of fluctuation in steady-state levels and reduction in health care cost [2].

Biocompatible and biodegradable polymers have been used as potential carriers for CRDDS. The natural as well as synthetic polymers alone are not always able to meet the complex demands of the delivery systems. The advantage of natural polymers are valuable in pharmaceutical industry due to their non-toxicity, low cost, biodegradability, biocompatibility and safety but some of their physical attributes are often poor while the success of synthetic polymers based on their broad range of mechanical properties. 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. Among these methods, considerable interest has been given to the development of IPN based drug delivery systems. This would open up new avenues to use IPN in designing the novel controlled release drug release systems [3,4]. A combination of natural and synthetic polymers has been found to be useful in enhancing the release of short half-lived drugs under physiological conditions. In order achieve this; the properties of natural and synthetic polymers have been modified by grafting, blending and other means. Grafting of vinyl monomers onto natural polymers such as cellulose has been widely accepted [5-7].

An IPN is a combination of at least two polymers, exhibiting different characteristics, it is prepared when at least one polymer network is synthesized or crosslinked independently in the presence of the other without any covalent bonds between them **[8,9]** Figure 1. IPN can produce synergistic effect by sharing the properties of both the polymers consequently avoiding the limitations of natural as well as synthetic polymers. IPN is regarded as one of the most valuable novel biomaterials [10]. Interpenetrating polymer network (IPN) is not formed from normally mixing of two or more polymers and also does not produce from copolymers. IPN based drug delivery system is designed to deliver drugs in zero-order pattern with minimum fluctuation



**CLASSIFICATION OF IPN:** [11]

**BASED ON CHEMICAL BONDING**

**Covalent Semi IPN:** It contains two separate polymer systems that are crosslinked to form a single polymer network.

**Non Covalent Semi IPN:** In this only one of the polymer systems is crosslinked.

**NonCovalent Full IPN:** In which the two separate polymers are independently crosslinked [11].

**BASED ON ARRANGEMENT PATTERN**

**Novel IPN:** Polymer comprising two or more polymer networks which are at least partially inter-locked on a molecular scale but not co-valently bonded to each other and cannot be separated unless chemical bonds are broken.

**Sequential IPN:** In sequential IPN the second polymeric component network is polymerized following 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 concurrently, the IPN may be referred to as a simultaneous IPN.

**Semi IPN:** If only one component of the assembly is cross linked leaving the other in a linear form, the system is termed as semi-IPN [12].

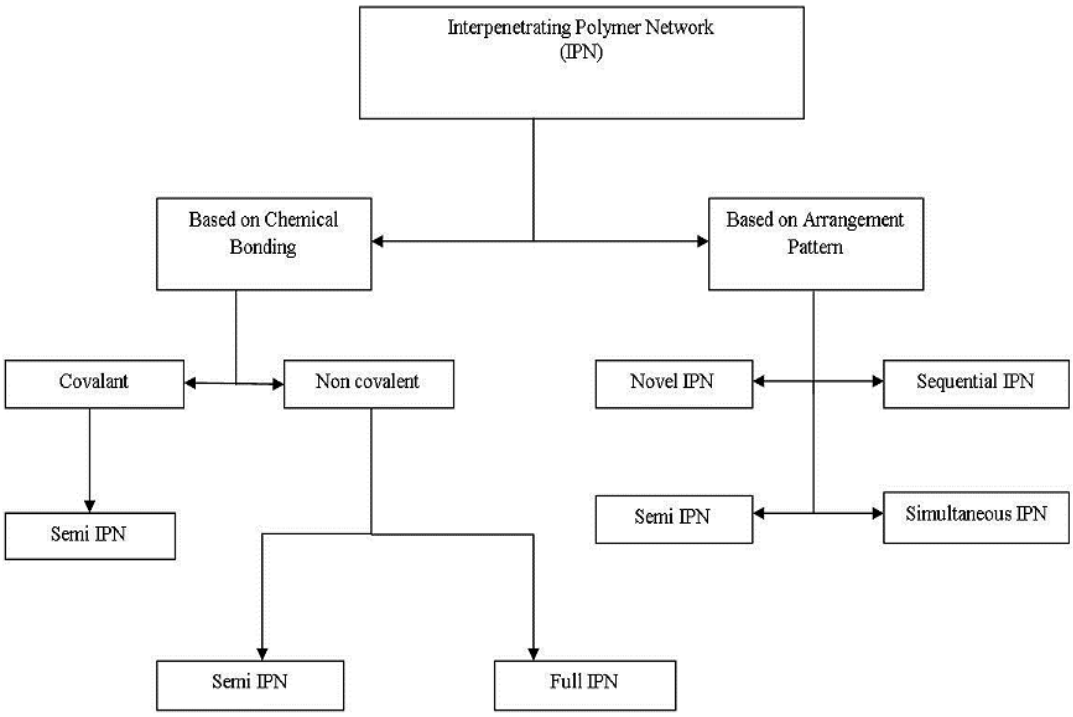



**Figure 2:** Classification of IPN

**ADVANTAGES OF IPN:** [13-16]

- Whenever an IPN hydrogel is formed from two polymers at a given temperature, the physical phase separation between the component polymers would be almost impossible because of the infinite zero-viscosity of the gel.
- IPN enhance the mechanical properties and phase stability of the final product.
- As long as the reacting ingredients are blended thoroughly during the synthesis, thermodynamic incompatibility is overcome due to the permanent interlocking of the network segments.
- When the blends are subjected to stress, they can keep the separate phases together.
- Due to the infinite zero-viscosity of the gel phase separation between the component polymers is almost impossible.

**IPN-BASED DRUG DELIVERY SYSTEMS:**

**Microspheres:**

Interpenetrating polymer network (IPN) is primarily used for the controlled release of the drugs. Ray *et al.,* developed novel IPN microspheres based on xanthan gum (XG) and polyvinyl alcohol (PVA) by an emulsion cross-linking method using glutaraldehyde as a cross-linker to deliver an anti-inflammatory drug, Diclofenac sodium (DS) to the intestines [17]. Several formulations were prepared by varying the ratio of polymer, extent of cross-linking in order to optimize the formulation variables on drug encapsulation efficiency, and release rate. FTIR spectroscopy was done to confirm the formation of IPN and the chemical stability of DS after penetration of microspheres. Upto 83% drug encapsulation efficiency was achieved. *In-vitro* release studies were carried out at pH 1.2 and 6.8 dissolution media. Release study showed a Fickian trend of drug release that depends on the ratio of polymer present in the microsphere and the extent of cross-linking. *In-vivo* pharmacokinetic evaluation was performed in rabbits and indicated that microparticles showed slow as well as prolonged drug release when compared with a DS solution. Depending upon the results of *in-vitro* and *in-vivo* studies it was concluded that these IPN microspheres offer a potential candidate for oral controlled release of watersoluble DS. Banerjee *et al.,* developed an IPN based microspherical formulation consisting of sodium alginate and polyvinyl alcohol by the emulsion crosslinking method using glutaraldehyde as cross-linking agent [18]. This IPN based formulation was used for the controlled release of Diclofenac sodium. Drug entrapment efficiency was found to be 72% depending upon the extent of crosslinking. It was observed that as the concentration of the crosslinking agent increases, drug entrapment efficiency also increased. *In-vitro* drug release study was demonstrated both in acid as well as in alkaline media. This study concluded that the release behavior was slower for formulations with a higher amount of crosslinking agent than those for a lower amount of glutaraldehyde which is mainly attributed to an increase in concentration of crosslinking agent. Aminabhavi *et al.,* prepared semi-IPN hydrogel microspheres composed of chitosan and hydroxypropyl cellulose (HPC) by emulsion crosslinking method for controlled release of Chlorthiazide [19, 20].

**Transdermal Membranes:**

Kulkarni *et al.,* developed IPN hydrogel membranes consisting of sodium alginate and polyvinyl alcohol by solvent casting method for the transdermal delivery of Prazosin hydrochloride, an antihypertensive drug through skin [21]. Glutaraldehyde was used as a crosslinking agent. Differential scanning calorimetric (DSC) analysis was done to confirm the formation of IPN and showed that as the concentration of glutaraldehyde increases, the stiffness of membrane increased. The *in-vitro* drug release study was demonstrated through excised rat abdominal skin and indicated that drug release depends upon the amount of glutaraldehyde in membranes. The slow drug release was extended up to 24 hr, whereas sodium alginate and polyvinyl alcohol membranes frequently discharged the drug. The developed IPN membranes were safe and less irritant as showed by primary skin irritation and skin histopathology study. Another successful approach was the incorporation of antiasthmatic drug i.e. Salbutamol sulphate into IPN membranes consisting of polyvinyl alcohol, chitosan and sodium alginate using glutaraldehyde as a crosslinker [22]. Membranes were evaluated for its mechanical properties like elongation and tensile strength along with its permeability properties and drug entrapment efficiency. *In-vitro* drug release study was performed using Keshary-Chien diffusion cell. The prepared membranes were found to be smooth, thin and transparent and have high tensile strength and

elongation. Pure polyvinyl alcohol (PVA) membranes has high rate of swelling and water vapor transmission as compared to their IPNs. The study concluded that crosslinking of PVA with glutaraldehyde and blending with other polymers has higher entrapment efficiency. The drug release study indicated that the permeation of drug through the membranes was up to 20 hrs.

**Tablets:**

Sa *et al.,* prepared interpenetrating network (IPN) matrix tablets composed of polyacrylamide grafted-sodium alginate (PAam-g-SAL) copolymer and sodium alginate (SAL) by wet granulation method for the sustained release of Diltiazem HCl (DTZ) [23]. Ca2+ ion was used to crosslink both copolymer and SAL. FTIR was performed to confirm the formation of IPN structure and DSC, XRD analysis was done to demonstrate compatibility of the drug with the polymers. The effect of polymer ratios, drug loading and total polymer and calcium gluconate (CG) ratios on drug release in acidic and phosphate buffer solutions was demonstrated. The drug release was primarily controlled by viscosity of the gel formed and the relative magnitude of swelling capacity of IPN matrix followed by dissolution of the polymers. The formation of calcium alginate gel structure governed the swelling capacity of the matrix and the co-polymer was used to impart the rigidity. The study concluded that IPN matrix tablets of PAam-g-SAL and SAL can be used for sustained release of DTZ. Kulkarni *et al.,* studied interpenetrating polymer network (IPN) matrices of sodium alginate and carrageenan for controlled release of Propranolol HCl. The Propranolol-resin complex (resinate) loaded matrices were prepared by wet granulation/covalent cross-linking method and subsequently compressed into tablets. The pure drug showed rapid and complete dissolution within 60 min, while drug release from resinate was extended for 2.5 h and that from IPN tablets was still slower and drug release prolonged over 18 h. The study concluded that the cross-linking time of granules affected the release of drug from IPN matrix [24].

**Capsules:**

Ramaraj *et al.,* synthesized interpenetrating polymer networks (IPNs) hydrogel capsules consisting of polyacrylamide and polyvinyl alcohol for sustained drug release [25]. These networks were then evaluated as drug-delivery devices by means of Crystal violet and Bromothymol blue as model compounds. The drug release study showed that the release rate is higher for semi-II-IPN as compared to full-IPN and the drug release from the capsules follows the Non-Fickian diffusional model. The mechanical behavior of hydrogel disks was also Demonstrated

**Nanoparticles:**

Peppas *et al.,* synthesized and characterized a thermally responsive polymer-metal nanocomposite system which consist of a solid gold nanoparticle core and thermally responsive interpenetrating polymer network (IPN) shell, which was PEGylated with a covalently bound linear poly(ethylene glycol) chain layer [26]. The main aim of this study was to prepare Gold nanoparticles (GNPs) having a range of 50 nm diameter using standard gold chloride and citrate reduction method. These nanoparticles were then incorporated inside a polyacrylamide (PAAm)/poly(acrylic acid) (PAA) IPN shell by an *in-situ* inverse emulsion polymerization. The surface of the nanocomposite system was then PEGylated by means of covalent grafting of a linear methoxy-PEG-N-hydroxysuccinimide to the primary amine groups of the PAAm network. Scanning electron microscopy (SEM) and transmission electron microscopy (TEM) were perfomed to confirm the successful synthesis and incorporation of gold nanoparticles within the IPN shell. The temperature swelling response of the IPN particles were demonstrated by dynamic light scattering. The successful PEGylation of the nanocomposite system was confirmed by zeta-potential analysis. Wang *et al.,* studied novel quasiinterpenetrating network/gold nanoparticles

composite matrices for DNA sequencing by means of capillary electrophoresis (CE) technique [27]. The objective of the study is to improve ssDNA sequencing performances by quasi-IPN as a matrix consisting of linear polyacrylamide with poly(*N*,*N*-dimethylacrylamide), which has lower viscosity. Gold nanoparticles (GNPs) were prepared and incorporated into the quasi-IPN to produce polymer/metal composite sieving matrices. Differential scanning calorimetry (DSC) and intrinsic viscosity studies was done on quasi-IPN and quasi-IPN/GNPs and it was observed that there was an interaction between gold nanoparticles and polymer chains. At different temperatures, comparison was done by means of CE to analyze the sequencing performances on ssDNA using quasi-IPN and quasi-IPN/GNPs with different GNPs concentrations as sieving matrices. The study concluded that resolutions of quasi- IPN/GNPs were higher as compared to quasi-IPN without GNPs and approximated than those of quasi-IPN consisted of linear polyacrylamide with higher molecular weight and PDMA without GNPs in the bare fused-silica capillaries. Moreover, under the same sequencing conditions, the sequencing time of quasi-IPN/GNPs was shorter as compared to quasi-IPN. In their study, they also discussed the influences of GNPs and sequencing temperature on the sequencing performances of ssDNA. Quasi-IPN/GNPs solution has tremendous separation reproducibility and its shelf life was more than 8 months.

**Hydrogels:**

Several combinations of polymers were prepared into hydrogel formulations to determine their potential as a drug delivery system. An attempt of combining two natural polymers such as collagen and hyaluronic acid and two synthetic polymers such as polyvinyl alcohol and polyacrylic acid into IPN hydrogels to improve the mechanical strength of natural polymers and to overcome the limitations of synthetic polymers [28]. Dinda *et al.,* studied the efficacy of antibiotics loaded interpenetrating network (IPNs) hydrogel composed of poly(acrylic acid) and gelatin for treatment of experimental osteomyelitis [29]. The main objective of the study to evaluate the safety and efficacy of Vancomycin hydrochloride (Vcl) or Gentamycin sulphate (GS) loaded polymer devices by varying the concentration of drug onto the devices. N,N'-methylene bisacrylamide and glutaraldehyde were used as a crosslinking agent. An *in-vivo* study was performed on rabbits employing placebo and drug loaded device of acrylic acid and gelatin for the treatment of experimental osteomyelitis. After the treatment macroscopic evaluation was done which indicated that depending upon the drug loading of implants; redness, swelling, local warmth and drainage decreased. It was observed that there is no significant difference in the rate of healing between GS and Vcl loaded devices and no implant showed toxic level at any particular time in serum. Rao *et al.,* developed collagen and poly(HEMA) hydrogel matrices for the controlled release of anticancer drugs [30]. The main aim of the study was the incorporation of three potent anticancer agents i.e. 5-Fluorouracil (5-FU), Bleomycin A2 (BLM) and Mitomycin C (MMC) into hydrogel matrices. It was observed that the drug entrapment efficiency was varied in the order of MMC>5-FU>BLM. *In-vitro* drug release studies were performed in phosphate buffer (pH 7.4) at 37$^{o}$C. The study concluded that release profiles followed zero-order kinetics and rates of release were independent on time. The results concluded that the collagen-poly (HEMA) hydrogel offers excellent potential as a carrier for the controlled release of anticancer drugs. Shantha *et al.,* prepared biocompatible and biodegradable hybrid copolymeric implants based on collagen and poly(ethylene glycol) for the controlled release of contraceptive steroids i.e. Testosterone [31]. Poly(vinyl pyrrolidone) was used to impart biocompatibility as well as bioactiveness to the implant. The *in-vitro* release studies of testosterone entrapped within the

hybrid were performed at physiological pH and temperature. It was observed that the testosterone showed initially a large release and then levelled off to release the same quantity everyday following a zero-order pattern. The study concluded that about 44% of the steroid was released in the first 10 days and after that the release was found to be very slow. The total amount of drug released was about 66% by 90 days. Kundu *et al.,* synthesized semi-IPN hydrogels using silk fibroin and polyacrylamide mixtures crosslinked by N,N-methylenebisacrylamide for the controlled release of two model compounds i.e. trypan blue dye and FITC-inulin [32]. Vaghani *et al.,* developed pH-sensitive hydrogels based on semi-IPN of chitosan and poly(vinyl pyrrolidone) crosslinked with glutaraldehyde for the controlled release of Clarithromycin [33].

**Sheet:**

Sheets are mainly used in several types of wound dressings and scar management products [34]. A most promising method of developing IPN based drug delivery system is sheeting. An interpenetrating network (IPN) composed of polymeric material like polyol(allyl carbonate) e.g. nouryset®200 and epoxy resin is developed by polymerizing 70 to 95 parts by weight of the polyol(allyl carbonate) by means of radical initiation and polymerizing partially or completely concurrently an epoxy resin forming mixture by acid catalysis. The epoxy resin forming mixture composed of 10 to 90 wt. % of aliphatic or cycloaliphatic polyepoxide and 90 to 10 wt. % of a polyol/anhydride adduct [35].

**Sponges:**

IPN based sponges were mainly used in wound dressings and hemostyptics [36]. These sponges are also very helpful in the treatment of severe burns [37]. Collagen-based materials can be produced into a three-dimensional sponge for use as a wound dressing and as a support for cell cultured skin components [38]. Additionally, collagen is used in combination with other materials like elastin, glycoaminoglycans or fibronectin [39, 40]. The most important advantages of collagen include their capacity to easily take up large quantities of tissue exudates and provide smooth adherence to the wet wound bed with preservation of moist climate as well as its protection against mechanical harm and secondary bacterial infection [41]. Moreover, collagen promotes growth, cellular mobility and inflammatory cells that actively penetrate the porous scaffold. This allows a highly vascularized granulation bed to form which encourages the creation of new granulation tissue and epithelium on the wound. Therefore, collagen sponges can be considered as active dressings which help in the process of healing. Collagen in combination with glycosaminoglycan (GAG) polymers is capable of controlling differentiation and proliferation of cells [42]. Cho *et al.,* prepared semi-interpenetrating polymer networks (semi-IPNs) composed of poloxamer and chitosan sponge for wound dressing application [43]. Poloxamer was used to increase the mechanical properties of chitosan sponge. 1H NMR spectroscopy was done to confirm the synthesis of poloxamer macromer. The study concluded that formation of SIPNs with poloxamer and increasing the amount of poloxamer in CS/poloxamer SIPNs can increased the mechanical strength of CS sponge as compared to CS/poloxamer blend. It could also increase the water content of CS because of the hydrophyllicity of CS and poloxamer. Consequently these results indicated that CS/poloxamer sponges prepared by SIPNs method have good possibility for wound dressing application due to rapid water adsorption, high mechanical strength, and interconnected cross-sectional morphology of SIPNs.

**Films:**

Athawale *et al.,* synthesized semi and full IPNs basedfilm composed of uralkyd/poly(glycidyl methacrylate) bysequential technique [44]. Mechanical properties such atensile strength and

elongation percentage were evaluated. The study concluded that the tensile strengths of semi as wellas full IPNs went on decreasing with the decrease in the MPGMA content since PGMA homopolymer exhibited higher tensile strength as compared to the UA homopolymer. The full-IPNs exhibited higher tensile strengths than those ofsemi-IPNs due to better interpenetration in the full-IPNs as compared to the semi- IPNs. Moreover, it was showed that the semi-IPNs exhibited higher values of elongation percentage as compared to the full-IPNs. Consequently, it was indicated that IPNs of UA and PGMA can lead to the production of tough films. Biodegradable collagen films or matrices have served as scaffolds for a survival of transfected fibroblasts [45]. Suh *et al.,* studied the graft copolymerization of type I atelocollagen onto the surface of polyurethane (PU) films treated with ozone [46]. It has been observed that they could enhance an attachment and proliferation of fibroblasts and growth of cells. Films composed of collagen and polyvinylalcohol mixtures crosslinked with glutaraldehyde vapor have been investigated as a depot formulation for recombinant human growth hormone [47].

**Calcifiable Matrix System:**

Calcification is one of the problems encountered with implantable biomaterials which is influenced by the structure of the implantable system and determines its *in-vivo* therapeutic efficiency and clinical fate [48]. Calcification of tissue or systems mainly depends upon chemical factors that can operate at the cellular level around different tissues or biomaterials [49]. Elastin and collagen both are chief components of connective tissues that possess a structure which compromises collagen fibers closely associated with a remarkably stable elastin network. The suitability of collagen and elastin in numerous potential medical applications in reconstructive and plastic surgery as well as controlled delivery of bone morphogenetic protein has been studied [50]. IPN based matrix films composed of various combinations of collagen and elastin were developed and evaluated for their suitability as drug delivery systems as well as in tissue calcification. Biomaterials should possess good mechanical properties able to withstand with the forces and motions experienced by the normal tissues and have adequate fatigue strength to ensure a long life of the implant *in-vivo* [51].

**BIOMEDICAL APPLICATIONS OF IPN BASED DRUG DELIVERY SYSTEM:**

**Bioengineered Tissue:**

Tissue engineering is a promising field with the view to provide functional replacement of impaired tissues or organs to patients. Tissue engineering requires a mechanically stable, biocompatible and biodegradable scaffold that permits cell adherence and proliferation and allows protection of cell-specific properties and also appropriate for surgical implantations [52]. Synthetic and naturally derived biodegradable polymers such as PGA, PLGA, PLA and collagen based porous three-dimensional scaffolds have been extensively used in the tissue engineering of bone, cartilage, skin and ligament etc [53]. Recent development in tissue engineering may lead to well characterized and reproducible biomaterials from natural IPN based materials. Collagen gel as human skin substitutes have confirmed its usefulness in tissue engineering and led to the development of bioengineered tissues such as heart valves, blood vessels and ligaments [54]. Collagen also shows hemostatic properties that can promote blood coagulation and play an important role in tissue repair process. Liu *et al.,* prepared highly porous scaffolds based on collagen and hydroxyapatite composite by solid-liquid phase separation method for bone tissue engineering [55]. The cell proliferation and attachment on the scaffolds *in-vitro* were examined. The study concluded that collagen-hydroxyapatite composite showed good

biocompatibility and hydroxyapatite does not affect the histocompatability of the scaffold materials. The porous collagen-hydroxyapatite composite is suitable as scaffold for bone tissue engineering.

**Bone Substitutes:**

Bone has been considered as a powerful marker for regeneration among various tissues in the human body and its formation serves as a prototype model for tissue engineering based on morphogenesis. Combination of collagen with other polymers was also used for the treatment of orthopaedic defects. Demineralized bone collagen itself as well as in combination with porous hydroxyapetite was used as a bone graft material for the treatment of acquired and congenital orthopaedic defects [56]. The result of this study showed that grafted demineralized bone collagen in combination with hydroxyapatite was an excellent osteoinductive material and could be used as a carrier of bone morphogenetic protein (BMP) for expression of biological activity *in-vivo* and also used as bone substitute. One of the attempts was successfully developed by Healy *et al.,* [57]. The main aim of their study was to develop a nonfouling, enzymatically degradable IPN (edIPN) composed of poly(AAmcoEG/AAc) amenable to present the cell signaling domain Arg-Gly-Asp (RGD), to evaluate the relative effects of implant surface chemistry and topography on osseointegration inside the rat femoral ablation implant model. The result showed that moderate enhancement of peri-implant bone formation was observed after 28 days using the enzymatically degradable IPN (edIPN) devoid of peptide modification. Another successful attempt was developed by Barber *et al.,* [58]. The main objective of the study is to modulate bone formation in the peri-implant region in the rat femoral ablation model by means of peptide modified IPNs of poly(acrylamide-coethylene glycol/acrylic acid) functionalized with an Arg-Gly-Asp (RGD) containing 15 aminoacid peptides, derived from rat bone sialoprotein which were grafted to titanium implants.

**Cartilage Scaffolds:**

Rao *et al.,* developed a biodegradable polymer scaffold composed of collagen and chitosan in the form of interpenetrating polymeric network (IPN) for *in-vitro* culture of human epidermoid carcinoma cells (HEp-2) using glutaraldehyde as a cross-linking agent [59]. *In-vitro* culture studies were perfomed using HEp-2 cells, over the selected scaffold and its growth morphology was examined through optical photographs taken at different magnifications at various days of culture. The results of the study indicated that the scaffolds prepared from collagen and chitosan can serve as a substrate to culture HEp-2 cells and can also be used as an *in-vitro* model to test anticancerous drugs. Tigli *et al.,* prepared semi IPN scaffolds composed of alginate and chitosan by freeze-drying process. CaCl2 was used as a crosslinking agent [60]. Their cellular and structural responses were analyzed. The results of the study revealed the potential utility of chitosan semi IPNs in alginate scaffolds. Comparative results were observed in relation to alginate scaffolds support the necessity for alginate: chitosan scaffolds for improved cartilage tissue engineering.

**THERAPEUTIC APPILICATIONS OF IPN:**

**Infectious diseases:**

Full and semi-IPN based on polyacrylic acid and gelatin loaded gentamicin sulphate were evaluated in rats for the tissue response, no additional local and systemic reaction occurred suggesting use of hydrogels as a potential carriers of drugs[61].

**Cancer:**

Biodegradable polymer scaffold composed of collagen and chitosan in the form of IPN for *in-vivo* culture of human epidermoid carcinoma cells (HEp-2).The result showed that scaffolds prepared from collagen and chitosan can be utilised as a substrate to culture HEp-2 cells and can also be used as an *in-vitro* model to test anti-cancerous drugs[62].

**Chronic Pain:**

Control release systems for local applications of analgesics morphine, hydromorphone and codeine and a local anasthetic bupivacaine loaded interpenetrating network system was prepared using biocompatible, biodegradable copolyester, poly(3-hydroxybutyrate-co-3-hydroxyvalerate) and other biocompatible but synthetic, nondegradable polymer, poly (2-hydroxyethyl methacrylate), shows prominent relief from chronic pain[63].

**Cardiac Diseases:**

Cell surface interactions between poly(acrylamide-copolyethylene glycol/ acrylic acid) IPN hydrogel and aortic endothelial cells(ECs) were studied. The result concluded that IPN can be used to promote endothelialization of vascular implants made of polymeric and metal materials for cardiovascular applications[64]. Various combinations of collagen and elastin were used as a control delivery device for cardio-vascular drugs. They stimulate the calcification process of implantable biomaterials, such as bioprosthetic heart valve (BHV) [65].

**Immunotherapy:**

Novel homogeneous surfaces consisting of N-(2 aminoethyl)-3-amino propyltrimethoxysilane (EDS) and an IPN of polyacrylamide and poly(ethylene glycol) are used to mediate adhesion. The EDS surface promotes cell adhesion and IPN minimises protein adsorption and subsequent cell adhesion. These surfaces were designed to control cell adhesion and morphology and mediate cell differentiation, activation, metabolic ability, and apoptosis, resulting in a reduced or controlled inflammatory response [66].

## FUTURE ASPECTS:

In 21 ST Century researchers mostly emphasizes on the CRDDS into which IPN Based drug delivery system can the option for providing extended release drug delivery system. By using the IPN based systems to eradicate diseases like cancer, AIDS, cardiac disease, celiac diseases like ulcerative colitis, etc, inflammatory diseases like meningitis, rheumatoid arthritis, Osteo arthritis etc and infectious diseases. The preparation of IPN system is very challenging on technological grounds so the safety aspects with IPN based delivery approaches will be high, with exact evaluations. The IPN technology is stable, economical, require fewer doses and can easily be administered via oral route are a world-wide priority. Currently, various formulation techniques involving single unit dosage form, muliparticulate unit dosage form, transdermal drug delivery systems etc are being developed and evaluated.

## CONCLUSIONS:

IPN can be used as a carrier system for drug delivery as well as for tissue engineering such as bone substitutes and cartilage scaffolds etc due to its advantages as a biomaterial. Extensive efforts have been emphasized to provide prolonged drug delivery to eradicate critical diseases like AIDS, cancer and cardiac diseases etc as well as inflammatory diseases like rheumatoid arthritis, osteoarthritis and meningitis etc. IPN is mainly designed to deliver drugs to a specific site of action with minimum fluctuation at a predetermined rate for maximizing drug availability and minimizing the dose related side effects and thus the effects of pharmacotherapy can be optimized. Moreover, it will provide better treatment options. It can be concluded from its utilization as a drug delivery matrix system *(in-vitro)* as well as in tissue engineering that these systems may lead to better understanding of numerous pathological diseases and can serve as a potential candidate for various therapeutic applications in future.

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