IPN based Drug Delivery System for Drug Delivery and Biomedical Application

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Abstract

Interpenetrating polymeric network (IPN) has been discussed for many years for its potential application in drug delivery area. They have been argued, patented and exploited for a long time. However, its applications are not wide still now. This review has tried to summarize some potential applications of IPN in drug delivery as well as in tissue engineering.

Keywords: Interpenetrating polymeric network; Drug delivery; Tissue engineering

INTRODUCTION

An interpenetrating polymeric network (IPN) is a type of newly developed active material used for delivery of drugs and other various purposes for pharmaceutical industry, biomedical industry and other chemical industry as well. IPN helps in increasing bioavailability, maintains safety profile and also have good swelling properties. They can be used for prolonged drug delivery, pH sensitive drug delivery and for targeted drug delivery. They increase the stability of the formulations containing active drugs and these IPN also increases solubility of hydrophobic drugs. They are targeted for tissue engineering.IPN get huge acceptability for their biocompatibility and biodegradability etc [1]. IPN have shown also other properties such as they are nontoxic in nature and non-immunogenic. IPN can be formulated with both natural and synthetic polymers and synergistic effect can be seen as the properties of both polymers are combined and the drawbacks are reduced [2]. Such a type of IPN with both synthetic and natural polymer shows to have better capability for controlled release of drug under different conditions.

Drug delivery, dialysis membrane, repairing dentures, artificial implants and burn dressing are some important application of IPN. Hydrogel IPN is one of the most important and has enormous potential and possibility. Hydrogels have the capability of delivering drug at a constant rate over a long time [3]. Hydrogels are generally three-dimensional figures, hydrophilic in nature and their polymeric network have the capability of incorporating large amount of water or biological fluids in the tissue [4]. Due to this property it is used in biomedical applications.IPN can also be used in repairing dentures [5]. Fibre reinforced composite structures are metal free adhesive and can be incorporated with IPN and which results in increasing the quality of the fibre reinforced composite and the desirable mechanical and physical property can be achieved [6]. In this

review, we have tried to summarize the potential uses of IPN with its preparation and characterization details.

SYNTHESIS, PROPERTIES AND APPLICATIONS OF IPN

Novel IPNs as biomaterials were tested for their potential in tissue engineering. IPN has the combination of polyethylene oxide (PEO) strength which is the mechanical stability along with characteristic advantages of the biological nanoscale polymerized fibrous fibrin network [7]. In-vitro cytotoxicity was evaluated in L929 fibro blast. The in vitro bioavailability was evaluated using chick embryo organotypic culture model while the in vivo bioavailability was determined by placing IPN matrix implant subcutaneously in nude mice. The biocompatibility was ascertained systematically using in vitro followed by ex vivo and in vivo methods [8]. The biological properties of fibrin matrix and the mechanical characteristics of the PEO were estimated in the advanced IPN product.

Advanced IPN biomaterials used for tissue engineering help in proliferation, migration and adhesion of several cell types was indicated, this highlighted their versatility. Although IPN is biocompatible when used as hydrogel in biomedical applications, it did not show promising results in its ease of promoting various cellular functions. IPNs can be used for biomedical applications like augmentation of soft tissue or wound healing. Moreover, their applications can be extended by altering their physical and biological properties. Gelatin (GL) and gellan gum (GG) was used to develop interpenetrating polymeric matrix (IPN) using maleic anhydride as the cross linker. Into the IPN micro particles Verapamil hydrochloride was encapsulated [9]. With varying ratio of GG & GL and the % of drug loading various formulations were prepared. FTIR was done on those micro particles for the understanding of the IPN structure formed and for confirming the chemical interaction between the drug, polymer and the cross linker. Morphology of the microparticles was studied using SEM, it showed slight rough surface to understand the crystallinity of drug encapsulated in IPN and also for the distribution of drug into the microparticles Differential Scanning Calorimetry (DSC) and XRD was performed. Using ultraviolet method drug encapsulation up to 90% was measured [10]. The effect of release rate on both of extent of cross linker and the amount of GL used was seen by in vitro study. The amount of swelling increase with that of increase in the content of GL was seen by selling kinetics. Non-Fickian type of behaviour was seen from release mechanism and this states that the microparticles obtained are useful as CR dosage form, to control the release of Verapamil from the matrix.

With the help of physical and chemical cross linking of deacylatedgellan gum innovative hydrogels are obtained. These hydrogels help in increase in the water uptake, compressibility and rheological properties also increasing the behaviour of the material to be tested depending on the various types of networks obtained [11]. Different gels of different loaded molecules which have different steric hindrance have been tested and the type of release of the product in association with the structure stated particularly for both the physical and chemical hydrogels are also investigated. The main purpose of this work was to obtain a gellan chemical hydrogel obtaining by the cross linking of polymer chain with L-Lysine ethyl ester moieties to change or to make the physicochemical properties better. Two types of physical and chemical hydrogels prepared by gellan gum polysaccharide were evaluated. The presence of tight junction

zones was present in physical hydrogels. Due to the Lys content physical hydrogels were stronger than that of chemical hydrogels. When networks are not formed properly then cross linker was added. With increase in Lys content the storage space increase in both the hydrogels. During drug delivery when high molecular weight products are used there is an influence of structural differences [12]. In physical gels steric hindrance doesn't plays any important role but in chemical gels it plays an important role and delivery of drug is affected and it occurs due to the Lys content and results in entrapment of drug in the network even after 8 days.

With the help of IPN method the starch was modified with poly (N-vinyl- pyrolidone). Tests were carried out to find out its properties as a floating drug [13]. Modified starch hydrogels of three types were prepared which were- cross linked starch, full-IPN & semi-IPN, for standardising a non-modified starch hydrogel was prepared. The materials used were all tested for swelling, DSC, Thermogravimetric Analysis (TGA), buoyancy test and FTIR. New property for drug delivery system, additional strength is provided by IPN hydrogel. Hydrogels helps in targeting drug delivery such as intestine colon, etc. In this the drugs present in the hydrogels is release into the system/body gradually. Here the absorption in the body is increased so the function of the drug can be optimized even when a low dose is used. In this study it is seen that better structures are observed in non-floating hydrogels, but the use of floating character for the delivery of drug is more useful [14]. The various tests done here shows that the most suitable characteristics as an encapsulatoris shown by full-IPN in floating delivery. Thus it's concluded that for the drug delivery full-IPN floating hydrogels is can be of more importance.

In this study tartaric acid was used as a cross linker to synthesize chitosan & poly (vinyl alcohol) base hydrogel. The films were then denoted by CVT and different tests were performed such as FTIR, NMR, and SEM & XRD. In this study a biodegradable PVA-chitosan hydrogel film with TA cross linked was prepared and it's seen that according to chitosan the CVT hydrogel film breaks down more slowly [15]. The amount of cross linker used and the pH affect the swelling property of the hydrogel. With a decrease in the surrounding pH value the swelling ratio increases, but when a PVA based film was used these values were increased three times. A high swelling ratio at high temp and same reversible temperature- dependent swelling nature was observed all the films. By changing the content of PVA the swelling rate can be controlled. Also, the hydrogels can be pH sensitive system can be demonstrated by their reversible swelling property. Hydrogels containing lower cross linker content exhibited highest swelling degree and better rate of release [16]. The pH of the medium also affects the release behaviour of amoxicillin and also it was observed that at pH 1.2, the release of amoxicillin was very high.

Hydrogels are 3-dimensional structure of hydrophilic polymers that can retain high quantity of water. Hydrogels can be used in different sectors like biomedical, pharmaceutical, and mechanical engineering and developments are done for better cross-linking structures. Poly acrylic acid (PAA), also known as smart hydrogels, is sensitive to both temperature and pH. PAA when crosslinked in cellulose nanocrystals (CNC) suspension results in a semi- interpenetrating polymer network [17]. The crosslinking agent, N, N-methylenebisacrylamide (MBA) entraps the CNC in the smart hydrogel PAA matrix. Combination of both these polymers gives the desired mechanical strength and crystalline. Characterisation studies like Fourier transform

Infra-Red Spectroscopy (FTIR), Scanning Electron Microscopy (SEM) and X-ray diffraction (XRD), along with several other rheological tests demonstrated an increase in crystallinity and storage capacity Moreover, hydrogels were observed to have the desired swelling in pH 7 solution [18]. Hence, hydrogels can be the potential drug carrier, was clearly demonstrated based on the drug release studies, drug loading performance and encapsulation efficiency test which were conducted, where theophylline was the model drug that was used.

The purpose of this study was to investigate and know about the evaluation and different formulation studies about the using of Locust bean gun (LBG) and sodium alginate and gluatalaldehyde as the cross-linking agent for controlled release of the anti-inflammatory drug Nimesulide [19]. The two polymers LBG and Sodium alginate were blended to make hydrogel beads by extrusion method. Nimesulide, an anti-inflammatory agent was incorporated or rather encapsulated into the matrix of the hydrogels beads. Several evaluation tests include morphology, size, encapsulation efficiency and drug release studies were done. Also, other characterization techniques such as FTIR, DSC, XRD, SEM studies were also conducted. The beads thus formed were through ionic gelation technique and encapsulation efficiency of the beads confirms the formation of the IPN Between the polymer and the drug [20]. The DSC study showed the dispersion of drug in molecular level. The results obtained clearly showed the ability of the newly formed IPN containing the drug can be possibly used as sustained release drug formulation.

The interpenetrating polymeric network (IPN) was prepared using chitosan, poly N- vinyl pyrolidine and poly acryl amide polymers [21]. Acryl amide monomers were used in radical polymerization, while, crosslinking was made by the crosslinking agents, MBA and glutaraldehyde. Different concentrations of glutaraldehyde were used to check the network porosity of the IPNs. Several evaluation studies like spectroscopic and thermal analysis with FTIR, thermo gravimetric analysis and thermo chemical analysis. Also swelling studies were conducted with pH 1.1 and pH 7.4 medium at 37^{o}C [22]. The studies were conducted in these solutions. Amoxicillin, an antibiotic, was entrapped in the IPN during the synthesis process. The in-vitro release kinetics was evaluated and the data obtained clearly demonstrated that the swelling and the release studies obeyed second order kinetics. The entrapped drug release rate is dependent on two factors which are the pH of the medium, at 37 ^{o}C, used for the release rate studies and the degree of polymer crosslinking. The experiment clearly demonstrated that the release was better at pH 1.1 and thus the formed IPN could be a better carrier for oral gastrointestinal delivery system.

CONCLUSION

In summary, IPN provides the opportunity to regenerate targeted and prolonged drug delivery system. They play an important role in pharmaceutical industry. Different types of polymers can be exploited for invention of IPN based drug delivery system. They come up with good thermal and mechanical properties. They also get importance in tissue engineering.

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