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A REVIEW ON BIODEGRADABLE POLYMERS USED IN PHARMACEUTICAL NANO FORMULATIONS

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ABSTRACT
Biodegradable polymers have been used frequently as drug delivery vehicles owing to its ability to increase bioavailability, better encapsulation, control release and less toxic properties. The biodegradable polymers will slowly replace the use of existing non-biodegradable polymers in formulations because their distinct advantages. Use of biodegradable polymers in nanoparticulate drug delivery systems will also reduce the drug dosage frequency and will increase the patient compliance. In near future these systems can be used for exploiting many biological drugs which have poor aqueous solubility, permeability and less bioavailability. Various biodegradable polymers such as Polylactic acid (PLA), Poly (lactic-co-glycolic acid) (PLGA), Gelatin, chitosan, polyacrylamide, polycapro lactone were reviewed extensively for their different applications in drug delivery systems.

INTRODUCTION
Among various branches of research field, "Nanotechnology" is one of the most popularly used branches since last century. Nanotechnology produces product in nanometric range. [1] In general particle size of nanoparticles or ultrafine particles within the range of 10-1000 nm.[2] Now a day's nanotechnology has wide range of application in various fields such as in medicine, food, cosmetics, agriculture, space research, petroleum industry, renewable energy, home appliance etc.[3]

Polymeric nanoparticles have major contribution in medical field during last decade for treatment of various critical diseases like cancer, malaria, hepatic problem, AIDS, tuberculosis brain related disorder, ophthalmic problems etc.[4] Encapsulation of drugs into nonmaterial are preferred owning to its certain advantages over normal dosage form like enhancement of therapeutic index and its efficiency, safety, targeted drug delivery, sustained/controlled release of drug, increase in solubility of poorly water soluble drugs (BCS-II) which in turn leads to bioavailability enhancement etc.[5-8]

Polymer is one of the major components used in the manufacturing of polymeric nanoparticles.[9] Polymer used in polymeric nanoparticles either may be natural origin (albumin, gelatin, chitosan etc.) or derived synthetically (polyacrylate, polycapro lactone, poly lactide etc.).[10] Synthetic polymeric material are generally not preferred for manufacturing process due to its some hazardous impact on environment (do not degrade under natural condition).[11] Therefore, in recent days, biodegradable polymers (both natural and synthetic origin) are widely used for development of polymer based nanoparticulate drug delivery system for human use.

Use of biodegradable polymer has certain advantages over non-biodegradable polymer which includes (a) it does not degrade during usage period of product, (b) favors environment owning to its biodegradable property after expiry of product etc.[12] Microbial biodegradation (also known as biotic degradation) is a chemical degradation method. Biodegradation of polymer is facilitated by microbes present in natural environment such as algae, fungi, bacteria etc.[13] These microbes decompose polymer (either under aerobic or anaerobic condition) and convert them into bio-decomposable product such as methane, carbon dioxide, water and other inorganic compounds.[14] Production of these types of eco-friendly bio-decomposable biomass is the result of assimilation and degradation of polymer by naturally living microbes.[15] Biodegradation (one type of biological degradation activity) involves several types of abiotic chemical reaction such as redox reaction, photolytic degradation, hydrolysis etc.[16]

Aerobic biodegradation
Bio-degradable polymer + O_2 $\longrightarrow$ CO_2 + H_2O + biomass + residues (1)

Anaerobic biodegradation

Bio-degradable polymer $\longrightarrow$ $CO_2 + CH_4 + H_2O +$ biomass + residues (2)

The focus point of this present review will be on various biodegradable polymers used in nanoscale formulation based drug delivery system and to highlight their utility purpose in such formulations.

Classification of Biodegradable Polymers

Biodegradable polymers can be categorized in to mainly three different types such as (a) natural polymers, (b) chemically synthesized biodegradable polymers, (c) microbiologically synthesized polymers. Further basing on their origins, biodegradable polymeric materials can be divided into two categories e.g. (a) from petroleum resources, (b) from biological resources (also known as renewable resources).[17]

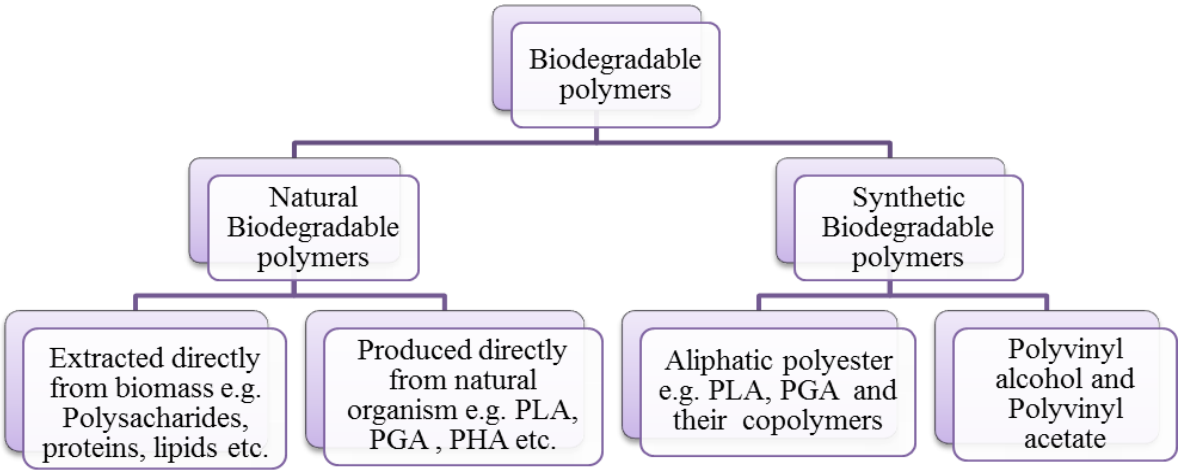

Fig 1: Hierarchical presentation on Classification of biodegradable polymers.

Table 1: Literature survey on PLA.

DRUG	METHOD	RESULT	REFERENCES
Catechin	Double emulsion solvent evaporation method	significant increase in antioxidant and metal chelation property of catechin nanoparticles	[21]
ScFv Her2 antibody	Double emulsion and bioconjugation	Nanoparticles show enhanced property for treatment of Her2+ breast cancer	[22]
2-hydroxyethyl methacrylate (HEMA)	Ring opening polymerization	In isotonic phosphate buffer solution PEGylated nanoparticles were stable and aggregation was not observed even after removal of sodium dodecylsulphate	[23]
Quercetin	Extraction	Nanoparticles helps in enhancement of therapeutic efficacy of the incorporated drug	[24]
Resiquimod	Polymerization	Modified PLA polymer based nanoparticles have no toxicity on immune cell and also deliver the immunoactive principle in a delayed manner	[25]
Daunorubicin	Electro spinning	Drug delivery system was efficient to enhance the cellular uptake of cancerous drug by cancer cell	[26]
2-hydroxyethyl methacrylate (HEMA)	Ring opening polymerization	PLA polymer enhances dissolving property of nanoparticles in the aqueous suspension	[27]
Recombinant human Growth Hormone (rhGH)	Ring opening polymerization	PLA polymer is responsible for sustained release of rhGH from nanoparticles	[28]
Hepatitis B vaccine	Double-emulsion solvent-evaporation	Nanoparticles exert enhancement of immune response	[29]
Pt(IV) prodrug	PEGylation and	PEGylation and dePEGylation of PLA based	[30]

	dePEGylation	nano carriers show enhanced antitumor activity	

Table 2: Literature survey on PLGA.

DRUG	METHOD	RESULT	REFERENCES
Nimodipine	Modified precipitation method	Nanoparticles release the drug in a sustained manner for prolonged period of time	[31]
Dexketoprofen trometramol	Double emulsion solvent evaporation method	Nanoparticles show sustained and controlled release of drug	[32]
Hepatocyte growth factor	W/O/W emulsion – Solvent evaporation method	Nanoparticles exert greater therapeutic effect on CCL_4 induced acute liver injury	[33]
Doxorubicin	Modified O/W nano precipitation method	Nanoparticles show controlled release of active medicament in a P^H dependent manner and also was effective for treatment of breast cancer	[34]
Doxorubicin	Nanoprecipitation method	Nanoparticles show enhanced anticancer activity	[35]
Coumarin based MAO-B inhibitor	Nanoprecipitation method	Nanoparticles helps to enhance cellular uptake of coumarin based MAO B inhibitor	[36]
Curcumin	Nanoprecipitation method	Nanoparticles have greater permeability through pulmonary human mucus	[37]
Ferulic acid	Emulsion evaporation technique	Chitosan coated PLGA act as a promising carrier for oral delivery of Ferulic acid	[38]
Calcitriol	Emulsion- solvent evaporation technique	Nanoparticles act as a potential anticancer agent	[39]
Doxorubicin	Double emulsion- solvent evaporation technique	Nanoparticles have potential antitumor activity	[40]
Hydrophobic drug	Emulsion- solvent evaporation technique	Nanoparticles provide sustain release and targeted release of drugs	[41]

Table 3: Literature survey on Gelatin.

DRUG	METHOD	RESULT	REFERENCES
Anti-CD3 antibodies	Desolvation process	Nanoparticles act as a promising carrier for lymphocytic uptake	[42]
Methotrexate	Solvent evaporation technique	Nanoparticles release the drug by diffusion controlled mechanism	[43]
TMR-dextran	solvent displacement technique,	Nanoparticles have long in vivo circulating time	[44]
FITC-dextran	Desolvation	Thiolated gelatin nanoparticles were biocompatible for intracellular drug delivery and release the drug in a highly reducing environment	[45]
Plasmid DNA	Desolvation	Nanoparticles serve as a vector for systemic DNA delivery to solid tumors	[46]
Bovine serum albumin	Phase separation method and solvent extraction method	The proteinacious drug delivery system possesses sustained release characteristics and also prevent the denaturation of protein drugs	[47]
Vancomycin	Desolvation method	Nanoparticles were effective against bacterial infection with low dose	[48]
Fluorescein isothiocyanate dextran	Desolvation technique	Nanoparticulate system was suitable for oral delivery of therapeutic agent such as protein, peptide, nucleic acid etc. in an effective manner	[49]
Rutin	Desolvation technique	Nanoparticles act as a SPF enhancer in sunscreen products	[50]
Epigallocatechin gallate (EGCG)	Layer -by-layer technique	EGCG retained its biological activity and blocked hepatocyte growth factor (HGF) induced intracellular signaling in breast cancer cell	[51]
NeutrAvidin	Desolvation method	Nanoparticles were effective against lung cancer	[52]

Cisplatin	Desolvation method	Nanoparticulate were effective against cancer	[53]
FITC-BSA	Desolvation method	Nanoparticles were suitable for delivery of protein drug with minimal toxicity	[54]
CpG Oligonucleotides	Desolvation method	Nanoparticles act as a carrier to deliver CpG oligonucleotides (CpG ODN) into target cell which in turn enhances its uptake and immunostimulatory activity both in vivo and in vitro	[55]

Table 4: Literature survey on Chitosan.

DRUG	METHOD	RESULT	REFERENCES
Ovalbumin antigen	Emulsification/solvent extraction ionic complexation	Nanoparticles show improved antibody response after nasal administration	[56]
Alprazolam	Heat coagulation method	Developed chitosan-egg albumin-PEG nanoparticles were found to be a promising vehicle for sustained release delivery of lipophilic drugs.	[57]
Protophorphyrin IX (PpIX)	Self-assembling amphiphilic glycol chitosan – 5b-cholanic acid conjugates in an aqueous environment	Nanoparticles exhibit enhanced specificity towards tumor cell and improved efficacy for clinical photodynamic therapy	[58]
Tripolyphosphate	Spray-coating	CS(42)-TPP nanoparticles has the potency for a fast release of unmodified BMP-2 at the implant surface	[59]
Paclitaxel	Double emulsion method together with programmed- temperature solidification method	HNP:PTX remarkably inhibited tumor growth in a synergistic manner and held great potential as a facile nano-platform for hydrophobic drug co delivery in anticancer applications	[60]
Bovine serum albumin	Ionic gelation method	OREC made these nanoparticles effective carriers to encapsulate drug and slow the drug controlled release of nanoparticles	[61]
Paclitaxel	Graft copolymerization	PTX-LMC showed significantly potent tumor inhibition efficacy	[62]

Table 5: Literature survey on polyacrylamide.

DRUG	METHOD	RESULT	REFERENCES
Ascorbic acid	Nucleation method	Silver nanoparticles/ polyacrylamide nanosphere were effective carrier for DNA delivery	[63]
Methylene blue	Reverse Microemulsion polymerization method	Nanoparticles were effective for tumor targeted photodynamic therapy with no dark toxicity	[64]
Phosphinite ligand	Cross-coupling reactions	Effective for used as a catalyst in a repeated cyclic manner without loss of their activity.	[65]
Methylene blue	Enzymatic reduction	Effective in terms of in vitro photodynamic therapy	[66]

Table 6: Literature survey on Polycapro lactone.

DRUG	METHOD	RESULT	REFERENCES
Cyclosporine	Water precipitation	Enhancement of oral bioavailability, uptake capacity by lymphocyte, immunosuppressant effect of cyclosporine along with reduction of its adverse effect	[67]
Anticancer agent	Emulsion solvent extraction method Nano-precipitation method Dialysis method	Suitable carrier for delivery of anticancer agent against tumor cells	[68]
Tetracycline	Electro spraying process & electro spinning	Inclusion of tetracycline hydrochloride into polycapro lactone nanoparticles results in extended release of drug due to hydrophobic nature of polycapro lactone fibers	[69]

	process		
Cyclosporine A	Solvent displacement process	Enhancement of bioavailability as well as higher percentage of drug loading into the formulation	[70]
Doxorubicin	Nanoprecipitation method	Enhancement of therapeutic index of the drug for the treatment of cancer	[71]
Curcumin	Two step mixing method	Effective for hepatic disorder with improved bioavailability	[72]

Literature Survey on Different Types of Biodegradable Polymers

Based on literature survey, it was revealed that biodegradable polymers such as PLA, PLGA, gelatin, chitosan, polyacrylamide, polycapro lactone etc. were widely used for the preparation of various drug delivery systems.

A. Polylactic acid (PLA)

It is also called as polylactide.It is a thermoplastic polyester having empirical formula $(C_3H_4O_2)_n$. It can be obtained by condensation of lactic acid with loss of water molecule.PLA can be economically produced from renewable resources.PLA polymers may be crystalline or amorphous in nature having glass transition temperature of 60-65°C.[18] Melting point of PLA is 130-180°C.[19]Due to chiral nature of Lactic acid, PLA also exist in several polylactide form e.g. Poly-L-Lactide (Polymerization product of L, L-lactide).It is soluble in hot benzene, tetrahydrofuran and dioxane.[20]

From literature survey on PLA, It was observed that PLA can be incorporated into various formulations because of its beneficial effects such as antioxidant and metal chelation property, controlled and sustain release property, stability enhancing property, enhances therapeutic efficacy and immune response, enhances dissolution potency, improved drug delivery etc. **Singh et *al.*, 2017**[21] reported significant increase in antioxidant and metal chelation property of catechin nanoparticles. **Shuang Douet.*al*, 2014**[22] reported PLA based nanoparticles show enhanced property for treatment of Her2+breast cancer. **Raffaele Ferrari et.*al*, 2012**[23] reported that in isotonic phosphate buffer solution PEGylated nanoparticles were stable and aggregation was not observed even after removal of sodium dodecylsulphate. **Avnesh Kumari et.*al*, 2012**[24] reported that PLA based developed nanoparticles helps in enhancement of therapeutic efficacy of the incorporated drug. **Cedric Thauvin et.*al*, 2019**[25] reported that developed modified PLA polymer based nanoparticles have no toxicity on immune cell and also deliver the immunoactive principle in a delayed manner. **Chen et.*al*, 2007**[26] reported that the developed drug delivery system was efficient to enhance the cellular uptake of cancerous drug by cancer cell which leads to early recovery from cancer. **Yingchun Yu et.*al*, 2012**[27] reported that PLA polymer enhances dissolving property of nanoparticles in the aqueous suspension. **Rohollah Ghasemi et.*al*, 2018**[28] reported that PLA polymer is responsible for sustained release of rhGH from nanoparticles. **Chandan Thomas.et.*al*, 2010**[29] reported that the developed inhalable nanoparticles exert enhancement of immune response. **Yueqiang Zhu et.*al*, 2019**[30] reported that PEGylation and dePEGylation of PLA based nano carriers show enhanced antitumor activity. The various applications of PLA are presented in **table 1**.

B. Poly (lactic-co-glycolic acid) (PLGA)

PLGA is a co-polymer and used as a carrier in many therapeutic treatment formulations owing to its biocompatible as well as biodegradable nature. PLGA is synthesized by ring opening co-polymerization method of two different monomer e.g. glycolic acid and lactic acid. Glass transition temperature of PLGA is in the range of 40- 60°C and can be dissolved in wide range of solvents. Hydrolytic product of PLGA e.g. glycolic and lactic acid is by-products of various metabolic pathways in the body.

Literature survey of PLGA revealed that, it can be used as a biodegradable polymer in various pharmaceutical formulations owing to its some beneficial property like sustain and control release, improved permeability, enhancement of therapeutic activity, high encapsulation property etc. **Ashish K. Mehta et *al.*, 2007**[31] reported that PLGA based NIM loaded nanoparticles release the drug in a sustained manner for prolonged period of time. **A. Alper Öztürk et *al*. 2019**[32] reported that DT loaded PLGA polymer based nanoparticles show sustained and controlled release of drug. **Chuxi lin et*al*. 2019**[33] reported that HGF- loaded PLGA nanoparticles exert greater therapeutic effect on CCL_4 induced acute liver injury. **Tania Betancourt et *al.*, 2007**[34] reported that doxorubicin loaded PLGA nanoparticles show controlled release of active medicament in a P^H dependent manner and also was effective for treatment of breast cancer. **Lakshmi Priya Krishnamoorthy et *al.*, 2017**[35] reported that doxorubicin loaded PLGA nanoparticles show enhanced anticancer activity. **Carlos Fernandes et *al.*, 2018**[36] reported that PEGylated PLGA nanoparticles helps to enhance cellular uptake of coumarin based MAO B inhibitor. **Nashrawan Lababidi et *al.*, 2019**[37] reported that curcumin loaded PLGA NPs have greater permeability through pulmonary human mucus. **Isabela Angeli de Lima et *al.*, 2018**[38] reported that chitosan coated PLGA act as a promising carrier for oral delivery of Ferulic acid. **M J Ramalho et *al.*, 2015**[39] reported that Calcitriol loaded PLGA nanoparticles act as a potential anticancer agent. **Juqun Xi et *al.*, 2017**[40] reported that PLGA based doxorubicin loaded nanoparticles have potential antitumor activity. **Hu yan et *al.*, 2015**[41] reported that hydrophobic drug loaded PLGA nanoparticles provide sustain release and targeted

release of drugs. The summarized literature survey table for PLGA is presented in **table 2**.

C. Gelatin

Gelatin is a translucent, colorless product derived from irreversible hydrolytic extraction of animal collagen. Generally it is used as a gelling agent in food, cosmetics, medicines etc. Gelatin readily dissolves in hot water and most of organic solvents. Gelatin solution has property of viscoelastic flow and streaming. The strength of gelatin molecule is measured in terms of "Bloom strength".

From literature survey it was found that gelatin can be used as a biodegradable polymer in various pharmaceutical formulations due to its beneficial effect such as enhanced cellular uptake, sustained and controlled release feature, antibacterial activity, prolong circulation time, effective in genetic engineering, enhancement of protein based drug delivery and prevent their denaturation, skin protection factor enhancer, antitumor property, act as immune booster etc. **Sabine Balthasar et*al.*, 2005**[42] reported that antibody loaded nanoparticles containing gelatin as a biodegradable polymer was less toxic and biodegradable in nature and also act as a promising carrier for lymphocytic uptake. **Maria Grazia Cascone et *al.*, 2002**[43] reported that methotrexate loaded gelatin based nanoparticles release drug by diffusion controlled mechanism. **Goldie Kaulet.*al*, 2002**[44] reported that PEGylation of gelatin based nanoparticles have long circulating time in vivo. **Sushma Kommareddy et*al.*, 2005**[45] reported that thiolated gelatin nanoparticles were biocompatible for intracellular drug delivery and release the drug in a highly reducing environment. **Sushma Kommareddy et *al.*, 2006**[46] reported that PEG-modified thiolated gelatin nanoparticles serve as a vector for systemic DNA delivery to solid tumors. **JIA K. LI et *al.*, 1997**[47] reported that drug release from gelatin nanoparticles based protein and peptide drug delivery system follow sustained release characteristics. **Li-Li Li et *al.*, 2014**[48] reported that vancomycin loaded gelatin nanoparticles were effective against bacterial infection with low dose. **Kenneth Ofokansi et *al.*, 2010**[49] reported that the developed gelatin based nanoparticulate system was suitable for oral delivery of therapeutic agent such as protein, peptide, nucleic acid etc. in an effective manner. **Camila Areias de Oliveira et al., 2015**[50] reported that rutin loaded gelatin based nanoparticles act as a SPF enhancer in sunscreen products. **Tatsiana G. Shutava et *al.*, 2009**[51] reported that nanoparticles encapsulated epigallocatechin gallate (EGCG) retained its biological activity and blocked hepatocyte growth factor (HGF) induced intracellular signaling in breast cancer cell. **Ching-Li Tseng et *al.*, 2007**[52] reported that gelatin nanoparticles modified with neutravidin biotinylated epidermal growth factor (EGF) was effective against lung cancer. **Ching-Li Tseng et al., 2009**[53] reported that gelatin nanoparticles loaded with cisplatin and decorated with epidermal growth factor tumor specific ligand were developed successfully having anticancer activity. **Young-Wook Won et *al.*, 2008**[54] reported that the developed recombinant human gelatin nanoparticles were suitable for delivery of protein drug with minimal toxicity. **Klaus Zwiorek et *al.*, 2007**[55] reported that gelatin nanoparticles act as a carrier to deliver CpG oligonucleotides (CpG ODN) into target cell which in turn enhances its uptake and immunostimulatory activity both in vivo and in vitro. The summarized literature survey table for gelatin is presented in **table 3**.

D. Chitosan

Chitosan is a linear polysaccharide consisting of randomly distributed β (1-4) linked D-glucosamine (deacylyted unit) with N-acetyl-D-glucosamine (acetylated unit).Commercially chitosan is produced by deacetylation of chitin which is the structural element in the exoskeleton of crustaceans (such as crab and shrimp) and cell walls of fungi. Chitosan is water soluble and binds to negatively charged surfaces owning to its bioadhessive nature. Chitosan has a number of commercial and biomedical uses.

Chitosan literature survey reveals that it has number of biomedical application such as improved antibody response, sustained drug release pattern, clinical importance in photodynamic therapy, anticancer activity etc. **Bram Slütter et *al.*, 2010**[56] reported that nanoparticles show improved antibody response after nasal administration. **Sougata Jana et *al.*, 2013**[57] reported that the drug release from developed chitosan-egg albumin-PEG nanoparticles follow sustained pattern. **So Jin Lee et *al.*, 2009**[58] reported that protophorphyrin IX loaded chitosan based nanoparticles exhibit enhanced specificity towards tumor cell and improved efficacy for clinical photodynamic therapy. **Nils Poth et *al.*, 2015**[59] reported that biodegradable chitosan coated tripolyphosphate nanoparticles have the potency for both fast release along with high release efficiency of unmodified bone morphogenetic protein 2 (BMP 2) at the implant surface. **Wei Wei et *al.*, 2013**[60] reported that co delivery of mTERT SiRNA and paclitaxel by chitosan based nanoparticles synergistically inhibit tumor growth. **Ruifen Xuet *al.*, 2012**[61] reported that inclusion of organic rectorite intercalated composites into quaternised chitosan based nanoparticles make these nanoparticles effective for encapsulation of protein drugs and release the drug in a controlled manner. **Ziming Zhao et *al.*, 2008**[62] reported that paclitaxel loaded chitosan based nanoparticles exhibit potent action against tumor cell and also drug release was in sustained manner for a period of 24 hour. The summarized literature survey table for chitosan is presented in **table 4**.

E. Polyacrylamide

Polyacrylamide is a polymer formed from acryl amide monomer subunits. It can be synthesized as a simple linear-chain structure or cross-linked, typically using N, N'-methylenebisacrylamide. It is highly water absorbent and forms soft gels when gets hydrated. Linear

polyacrylamide is a water-soluble polymer. Polyacrylamide is used to flocculate solids in a liquid.

Literature survey on polyacrylamide polymer revealed that it can also be used in different fields owning to its some beneficial action like genomic application, antitumor activity, catalytic action etc. **Vasim Ahmed et *al.*, 2013**[63] reported that ascorbic acid loaded silver nanoparticles/ polyacrylamide nanosphere were effective carrier for DNA delivery. **Ming Qin et *al.*, 2011**[64] reported that polyacrylamide polymer based Methylene blue loaded nanoparticles were effective for tumor targeted photodynamic therapy with no dark toxicity report. **Bahman Tamami et *al.*, 2010**[65] reported that modified cross linked polyacrylamide polymer supported palladium nanoparticles loaded with phosphinite ligand were effective for used as a catalyst in a repeated cyclic manner without loss of their activity. **Wei Tang et *al.*, 2008**[66] reported that Methylene blue containing polyacrylamide nanoparticles were effective in terms of in vitro photodynamic therapy. The summarized literature survey table for polyacrylamide is presented in **table 5**.

F. Polycapro lactone

Polycaprolactone is biodegradable polyester with a low melting point of around 60^0C. Polycaprolactone is prepared by ring opening polymerization of ε-caprolactone using a catalyst such as stannous octoate. Polycaprolactone is degraded by hydrolysis of its ester linkages in physiological conditions (such as in the human body). The most common use of polycaprolactone is in the production of polyurethanes.

Literature survey on polycapro lactone biodegradable polymer reveals that it has wide range of application in nanoformulations owning to its beneficial effect such as enhances bioavailability, immunosuppressant effect, increases lymphocytic uptake capacity, antitumor properties, extended release property, enhances drug loading capacity, enhances therapeutic index of drug, useful for hepatic disorder etc. **M. Carmen Varela et *al.*, 2000**[67] reported that polycapro lactone nanoparticles enhance oral bioavailability, uptake capacity by lymphocyte, immunosuppressant effect of cyclosporine along with reduction of its adverse effect. **MaLing Gou et *al.*, 2011**[68] reported that Polycapro lactone – Polyethylene glycol copolymer based nanoparticles were suitable carrier for delivery of anticancer agent against tumor cells. **WK Wan Abdul Khodir et *al.*2013**[69] reported that inclusion of tetracycline hydrochloride into polycapro lactone nanoparticles results in extended release of drug due to hydrophobic nature of polycapro lactone fibers. **Jesus Molpeceres et *al.*, 1995**[70] reported that cyclosporine A loaded polycapro lactone based nanoparticles made by central composite design method result in enhancing bioavailability as well as higher percentage of drug loading into the formulation. **Awesh Kumar Yadav et *al.*, 2008**[71] incorporation of doxorubicin into combined hyaluronic acid- polyethylene glycol- polycapro lactone nanoparticles enhances therapeutic index of the drug for the treatment of cancer. **Nuo Zhou et *al.* 2013**[72] reported that curcumin loaded glycosylated chitosan – polycapro lactone nanoparticles were effective for hepatic disorder with improved bioavailability. The summarized table on literature survey of polycaprolactone is presented in **table 6**.

CONCLUSION

The present review article focused on various applications of biodegradable polymers in drug delivery systems. The use of biodegradable polymers will improve the drug delivery potential of drugs. The biodegrable polymers will slowly replace the use of existing non-biodegradable polymers in formulations because their distinct advantages. Use of biodegradable polymers in nanoparticulate drug delivery systems will also reduce the drug dosage frequency and will increase the patient compliance. In near future these systems can be used for exploiting many biological drugs which have poor aqueous solubility, permeability and less bioavailability.

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