

Nano Technology in Ocular Drug Delivery

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ABSTRACT

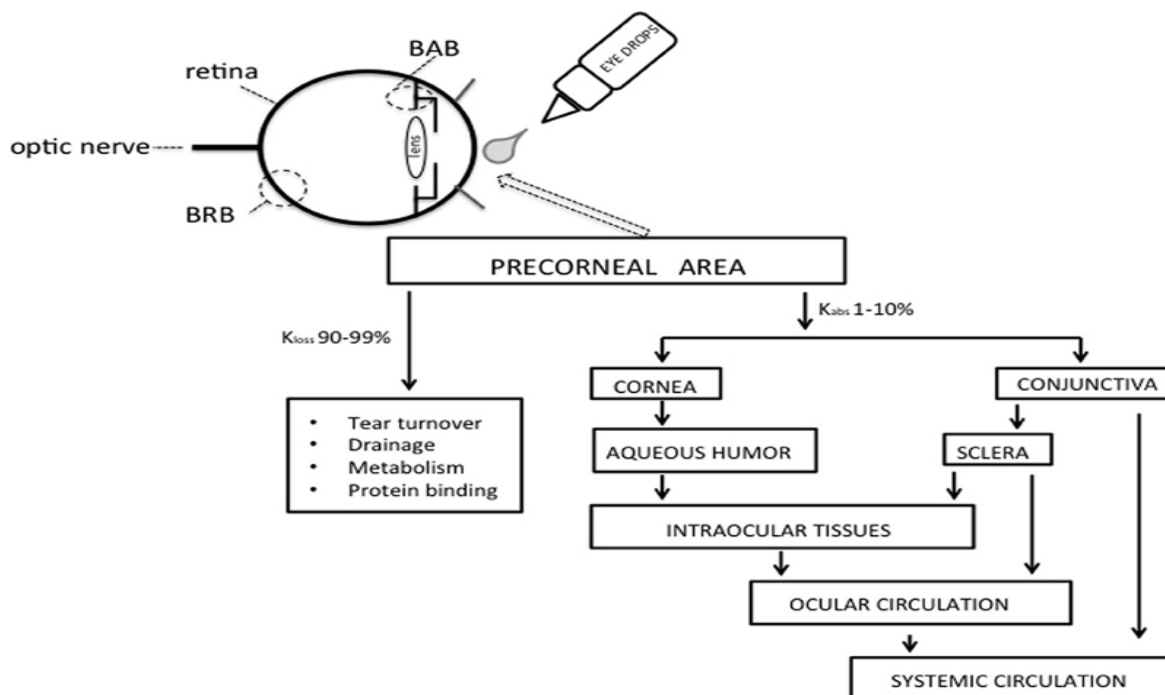
Nano technology is an emerging branch of science, with the tiny particles, which has wide range of application in medicine & molecular biology; etc. recent years have witnessed unprecedented growth of research & application in the area of nano science. The increasing optimism that nano technology, as applied medicine will bring significant advances in the diagnosis & treatment of disease. nano technology is effective in providing the regenerative for degenerative disorders. these particles bombarded by light and has a high rate of oxygen metabolism. Nano particles prevent 85% of the damage of retina. Nano particles are effective in regenerative anti oxidants due to catalytic property. nano technology is effective in gene delivery, there innovation have major impact on development in sight preserving and sight restoring. there nano particles have high residence time, more absorption rate and bio availability. It is more specific targeted drug delivery system with less adverse effects with therapeutic safety.

Keywords: Nano particles, ocular drug delivery, regenerative medicine, oxidative stress.

INTRODUCTION

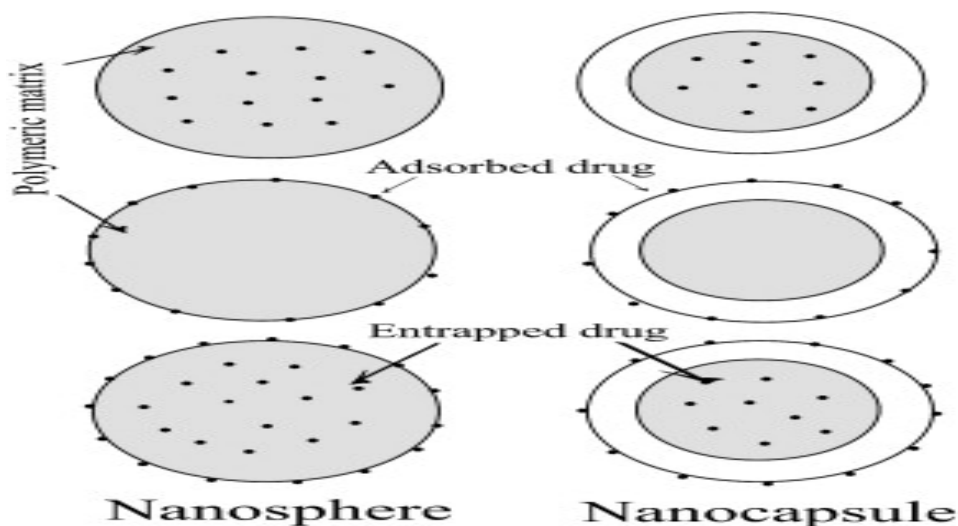
Nano technology is a branch of science with micron & submicron range particles. Nano technology has received considerable awareness in biomedical science over the past decade. nano particles are materials with over all dimensions in the nano scale under range

of 100nm. nano particles have number of properties that distinguish them from bulk materials, simply by virtue of their size, such as chemical reactivity, energy absorption, biological mobility. nano particles are also called as zero dimensional particles.



These nano particles could able to overcome the most of the disadvantages of ophthalmic drug delivery such as easy drainage of drug through the precorneal area, less contact time (or) residence time of medicament and less bioavailability & less drug absorption. In normal dosage forms the pre corneal drainage may cause the over flow of precorneal fluid which contain the medicament may absorb through the nasocomal system & gut may cause many toxic effects Interestingly pharmaceutical sciences are using nano

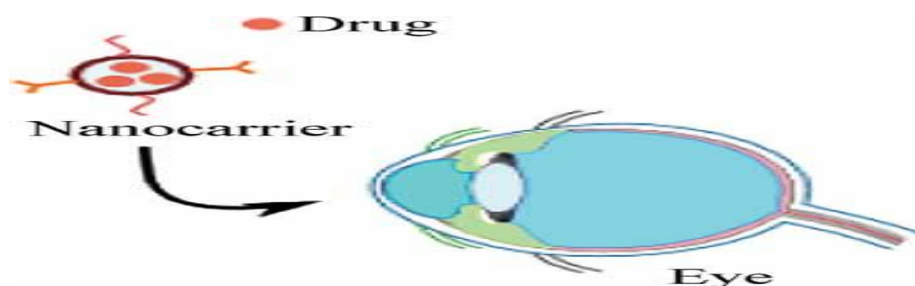
particles for reducing the toxicity & side effects. These nano particles have greater bio availability, long residence period, more absorption of drug due to the large surface and smaller particle size. nano technology is developing the regenerative medicine for the degenerative diseases .the nano particles have a major impact on the development of sight preserving and sight restoring treatment for conditions that currently lead to irreversible blindness¹⁻⁶.



Nano particles in ocular diseases

Nano particles ranging 10nm to 1µm are used effectively in the ocular drug delivery in nano particles drug is dissolved ,entrapped ,encapsulated. The recent promising drug carrier for ophthalmic application. These nano particles are further classified in to nano spheres ,nano capsules. The better efficiency of nano capsules is due to their bio adhesive

property resulting in increasing residence time of biological response, & improve the ocular bio availability and reduce dosing frequency. nano suspensions are sub micron colloidal particles with poor water soluble drug suspended in an appropriate dispersion medium stabilized by surfactants. Nano suspension improves the ocular bio availability its adhesion to the cornea⁷⁻¹⁰.



MECHANISM

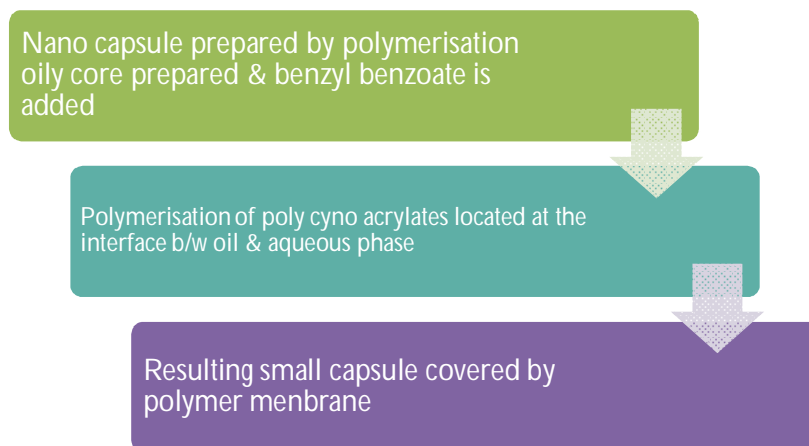
The nano particles has prolong residence time by trapping the ability to prolong drug residence time by trapping the drug in ocular mucous layer, which is considered to be a

diffusion barrier and to protect the epithelial layer of cornea. when these nano particles are installed in conjunctive sac. It could inhibit the inflammatory response after surgical trauma, secondly nano particles increases the levels of

vitreous humor, which arise from the longer residence time of the drug. certain disease conditions such as cytomegalovirus, retinitis require administration of drug to the retinal region of eye. Infection with cytomegalo virus

can lead to permanent damage of retina, choroid, iris, and adjacent tissue. nano particles have effective drug delivery of ganciclovir in treatment of cytomegalovirus infection⁷⁻¹⁰.

Nano capsule



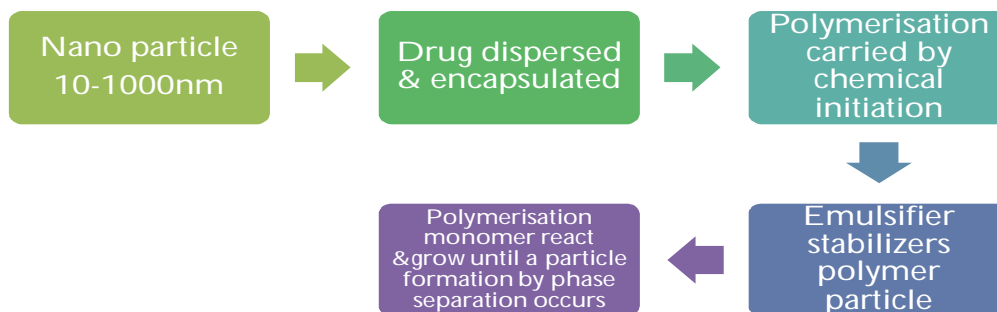
MANUFACTURING OF NANO PARTICLES

There are many production methods exists for microspheres, microcapsules & nanoparticles.

- 1) Some of the manufacturing processes are: Denaturation (or) cross linking of macro molecules in emulsion form
- 2) Interfacial polymerization

- 3) Formation in an aerosol phase desolvation
- 4) Aggregation by PH adjustment & heat treatment formulation of nano particles via microcapsules

Preparation method



Nanoparticles for ophthalmic drug delivery prepared from synthetic polymers have been mainly prepared by emulsion polymerization. In this process, a poorly soluble monomer is dissolved in the continuous phase. This continuous phase can be aqueous or organic. Additional monomer may be emulsified in emulsion droplets that are stabilized by emulsifiers. The polymerization is started by chemical initiation, pH shift, or by irradiation with gamma-rays, ultraviolet (UV) or visible light. The location of the polymerization is in the continuous phase where dissolved monomer molecules react with each other and grow until particle formation by phase separation occurs. Additional monomer molecules diffuse to the resulting growing polymer particles and maintain the polymerization. The emulsion droplets mainly act as monomer reservoirs. In later stages, the emulsifiers stabilize the resulting polymer particles. It has to be noted, that the nanoparticles are not formed by one single polymer molecule but consist of a large number of macromolecules. Nanocapsules with an oily core were prepared mainly by the

addition of benzyl benzoate or mineral oils. In this case, the polymerization of the poly(alkyl)cyanoacrylates (i.e. poly(isobutyl)cyanoacrylate) is located at the interface between the oily and the aqueous phase resulting in a small capsule covered by a polymer membrane. A number of studies deal with the preparation and application of ophthalmic drugs loaded to micro- and nanospheres. Pilocarpine instill among one of the most important drugs for ocular delivery and glaucoma Therapy. Also, beta-blockers like timolol and more recently betaxolol were investigated as Potent candidates for particulate ophthalmic drug delivery systems. In most cases, the drug is present during the polymerization- or particle manufacturing process leading to an incorporation of the drug in form of a solid solution or solid dispersion. Alternatively, a drug can be adsorbed onto the particle surface after the manufacturing process. In the case of hydrocortisone it was shown that a very high loading capacity can be reached. Similar results were observed for other steroids like progesterone¹.

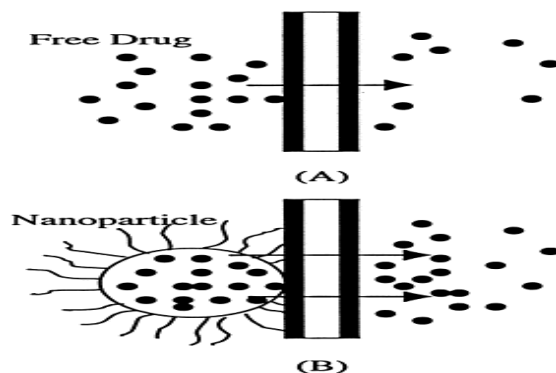
Polymers used in synthesis of nano particles

POLYMERS	DRUG	OBSERVATION
Albumin	piroxicam	Increased bioavailability compared to commercial eye drops
Albumin	gancyclovir	The residence time is prolonged
chitoson	Cyclo sporine A	Therapeutic conc in cornea & cojectva during at least 48 hr
Carrageenan gelatin	timolol	Higher bioavailability in aqueous humor compared to commercial eye drops
eudragit	ibuprofen	Improved ocular bioavailability

Distribution & penetration of Nano particles

The nano particles have effective distribution and penetration. About 1% of applied dosage remained in ocular tissue for about 4hr. Interestingly, in inflamed eyes the tissue

concentration were about 3 to 5 times normal eyes with the exception of conjunctiva. These are well tolerated & significantly less histotoxicity. nano particles are biodegradable within few hr's¹⁻⁴.

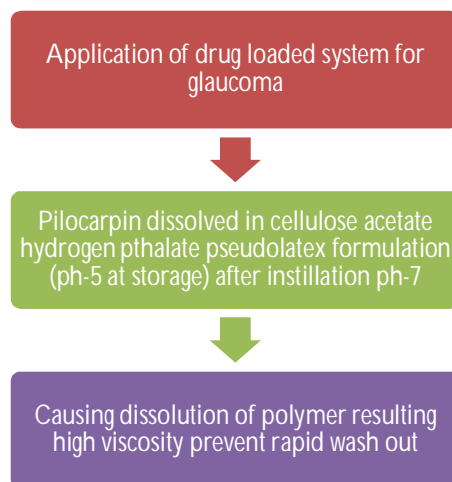


Nano particles preventing eye damage

These particles bombarded by light and have a high rate of oxygen metabolism, cells in the retina encounter relatively high number of reactive species of oxygen. nano particles

prevent 85% of the damage to the retina. nano particles are used for genetic disease retinitis, pigmentosa, age related macular degeneration & diabetic retinopathy¹².

Applications of drug loaded particles



Nano particles in oxidative stress

Oxidative stress leads to many retinal diseases. this stress has been implicated as cause of arthritis heart diseases & aging. It also plays a role in several incurable blinding diseases such as diabetic retinopathy, age related macular degeneration, and retinal degeneration. The nano particles are powerful molecules have generated by exposure to ionizing radiation and by common place reduction. Nano ceria are effective in regeneration anti oxidants' due to catalytic property. Nano particles are effective in treating macular edema in diabetic eye¹²⁻¹³.

Nano particles in gene delivery:

Nano particles are effective in gene delivery, in the treatment and diagnosis of ocular diseases. These innovation have major impact on development in sight preserving and sight restoring treatment⁷⁻⁹.

Applications of nano particles in other diseases

Nano particles in Alzheimer's disease

Nano technology has improved in the development of techniques for easy diagnosis and treatment of methods for Alzheimer's

disease. Nano treatments for Alzheimer's methods are numerous. nano ceria protects neurons from cyto toxic effects of antibody via modulating the intracellular signaling pathways

involved in cellular death and neuron protection¹³.

APPLICATIONS OF NANO PARTICLES

POLYMERIC COMPOUNDS	TRADE NAME	STATUS	TARGET DISEASE
Polyglutamate paclitaxel	CT-2103 XYOTAX	Phase-3	Cancer, ovarian cancer, lung cancer
Albumin nano particle containing paclitaxel	Abraxane	marketed	Breast cancer
PEG-L-asparaginase	onasper	marketed	Lymphoblastic leukemia
Poly calanine, lysin glutamic acid tyrosine	copaxone	marketed	Multiple sclerosis

Nano particles in HIV/AIDS

The therapeutic efficacy of anti HIV agents often hampered by poor bio availability and lack drug penetration in infected targeted tissues using different types of nano particles based drug delivery system nano particles improve the therapeutic efficacy in HIV drugs to cellular and anatomical viral reservoirs¹⁶.

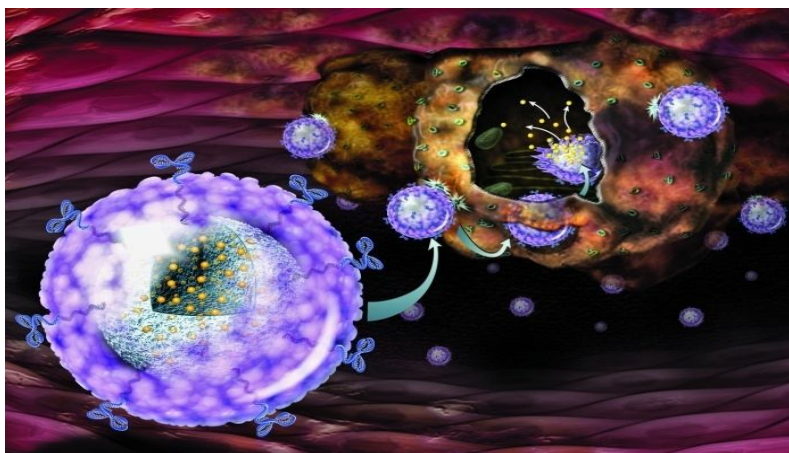
Nano particles in neuro degenerative diseases

Drug delivery to CNS remains a challenge in development for neuro degenerative diseases. These nano particles with their small particle

size and large surface area. nano particles are effective in the treatment of neurodegenerative disorders⁹.

Nano particles in cancer

Nano particles are effective in drug delivery of cancer due to its specific targeting ability of tumor cells, nano particles with optical properties & Plasmon binding ability. These nano particles are effective in degenerating the specific tumor cells with out damaging surrounding tissue¹⁴.



Nano particles in diabetes

Blood glucose level, lipid & serum biochemical profiles in diabetes provokes their effective role in controlling and increasing the organ function for better utilization of blood glucose . the gold nano particles are anti oxidative agents by inhibiting the formation of free radicals thus increasing the antioxidant enzyme and creating a sustained control over hyperglycemic conditions¹⁵ .

Nano particles in respiratory diseases

The application of nano particles based drug delivery approaches in respiratory diseases has been somewhat limited⁹.

Nano particles in skin care

Nano particles that absorb and reflect in different wave lengths could alleviate uncoated

red tones from the face more effectively than current facial foundations. nano particles have tremendous opportunity for the drug delivery of active agent to the skin¹² .

Environmental considerations of nano particles

Nano particles has set a new trend in targeted drug delivery system, the impact of nano particles on environment and public health care has received considerable attention in recent year⁹.

Future challenges

Most of the marketed ocular drug were initially developed for non ocular application. faster development of new drugs and safe medicine. ocular bioavailability must be increased from <1%-20% of administered dose¹¹ .

**Table 1: Nano technology products of ocular drug delivery¹⁷
Successful formulations of ocular drug delivery**

PRODUCT	Active ingredient	Indication	Status
Cationorm ®	Medical device	Dry eye	Marketed
Cyclokot®	0.1% cyclosporine A	Severe Dry eye	Phase III
Vekacia®	0.1% cyclosporine A	Vernal keratoconjunctivitis	Phase III
Catioprost®	0.005% latanoprost	Glaucoma associated with ocular surface disease	Phase II

CONCLUSION

Nano particles are effective in treatment of the availability ocular disorders due to its high residence time, more drug absorption rate, more bio and adverse nano particles are more specific drug targeted delivery system with reduced toxicity and effects with maintaining the therapeutic safety and bio compatibility .some nano particles are anti oxidative agents which inhibit the free radicals thus increasing the anti oxidative enzyme and reduces the oxidative stress of degenerative disorders.

REFERENCES

1. Andreas Zimmer and Jorg Kreuler. Microspheres and nano particles used in ocular delivery system ; Advanced drug delivery reviews. 1995;16:61-73.
2. Rathore KS and Nema RK . An insight in to ophthalmic drug delivery system; International journal of pharmaceutical sciences and drug research 2009;1(1):1-15.
3. Xiang Li , shu-fang Nie and Jun Kong. A controlled release ocular delivery system for Ibuprofen based on nano structured lipid carriers ; International journal of pharmaceuticals. 2008; 363:177-182.
4. Angela M De campos, Volando , Dibold, Edison LS and carvalho. Chitosan nano particles are new ocular drug delivery system : In vitro stability , In vivo fate and cellular toxicity, pharmaceutical research. 2004;21(5):803-810.
5. Walter L Zielinski and Timothy R Sullivan. Ophthalmic drug therapy – challenges & advances in front of eye delivery. Touch Briefings. 2007;44-45.
6. Reeta rani thakur and Mridul Kashiv. Modern delivery system for ocular drug formulations ; comparative over view W.R.T conventional dosage form. International journal of research in pharmaceutical & bio-medical sciences. 2011; 2(1):9-19.
7. Patel Vishal and Agrawal YK. Current status & advanced approaches in ocular drug delivery system; Journal of global trends in pharmaceutical sciences. 2(21): 131-148.
8. Venkata Ratnam, Madhavi G, Rajesh S. Ocular drug delivery : An update review ; International journal of pharmacy & biological

- sciences , IJPBS. 2011;1(4):437-446.
9. Shashi K Murth., Nano particles in modern medicine: state of the Art & future challenges , International journal of nano medicine. 2007;2(2):129-141.
 10. Jitendra, Sharma PK and Banik A. A New trend : ocular drug delivery system ,pharma science Monitor. 2011;2(3):1-25.
 11. Patel PB, Shastri DH and Shelat PK. ophthalmic drug system :challenges & approaches delivery, invited review. 1(2):113-120.
 12. Zoe Diana and Draclos MD. Nano particles , skin care & sunscreens ,Plastic surgery practice, Issue stories . 2011;1-2.
 13. Amir Nazem G and Ali Mansoor. Nano technology for Alzheimer's disease detection &treatment ;In sciences journal. 2011;1(4):169-193.
 14. Wang, May D, Shin and Dong M. Nano technology for targeted cancer therapy , Expert review of anti cancer therapy. 2007;7(5):833-837.
 15. Selvaraj Barath Manikanth, Kalimuthu kalish waralal and Ram kumar pandian. Anti oxidant effect of gold nano particles restrains hyperglycemic conditions in diabetic mice ,JCPDS. 2010;01-1174 , 1477-3155:8-16.
 16. Bomboywala MA, Hajare RA and Bakde BV. Nano technology in HIV/AIDS Therapy. International journal of pharma research and development. 2006;5(2):269-286.
 17. Lallemand F ,Daul P and Benita S. Successfully improving ocular drug delivery using the cationic nano emulsion Novasorb, journal of drug delivery. 2011;1-54.