

# Exploring the dynamic of Nanoparticles, Preparation Techniques and Application

Sweta Thakur <sup>\*1</sup>, Abhishashi Sharma<sup>2</sup>, Kritika Sharma<sup>3</sup>, Mahendra Singh Ashawat<sup>4</sup>,  
Vinay Pandit<sup>5</sup>

<sup>1</sup>Research Scholar, Department of Pharmaceutics

<sup>2</sup>Research Scholar, Department of Pharmacology

<sup>3</sup>Research Scholar, Department of Pharmaceutics

<sup>4</sup>Director cum Principal of Laureate Institute of Pharmacy

<sup>5</sup>Professor and Head, Department of Pharmaceutics

Department of Pharmaceutics, Laureate Institute of Pharmacy, Kathog, H.P-176031

[Email<sup>4</sup>msaresearchg@gmail.com](mailto:Email<sup>4</sup>msaresearchg@gmail.com)

[Email<sup>5</sup>vinay2121@gmail.com](mailto:Email<sup>5</sup>vinay2121@gmail.com)

<sup>\*1</sup>Corresponding author: [shwetathakur8300@gmail.com](mailto:shwetathakur8300@gmail.com)

[Email<sup>2</sup>sharmaabhishashi@gmail.com](mailto:Email<sup>2</sup>sharmaabhishashi@gmail.com)

[Email<sup>3</sup>kritiksharma1582@gmail.com](mailto:Email<sup>3</sup>kritiksharma1582@gmail.com)

## Abstract

*Nanotechnology, the manipulation of matter at the atomic and molecular scale, has significantly transformed several scientific domains, notably nanomedicine. The development of nanoparticles—typically under 100 nm in size—has enabled the enhancement of drug properties such as bioavailability, solubility, pharmacokinetics, and targeted delivery, especially for poorly water-soluble drugs. These innovations allow for controlled and sustained release, reduced toxicity, and multifunctional drug systems capable of imaging and triggered release. Nanoparticles are also employed in various fields, including electronics, catalysis, cosmetics, food, environmental cleanup, construction, and renewable energy, owing to their high surface-to-volume ratio and tunable properties. Despite these advantages, nanoparticles face limitations such as aggregation, poor flowability, drug loading constraints, manufacturing challenges, and regulatory hurdles. Several methods exist for nanoparticle preparation, including solvent evaporation, solvent diffusion, polymerization, coacervation/ionic gelation, and supercritical fluid technology, each selected based on the desired characteristics of the nanoparticles and their application. These advancements indicate the vast potential and versatility of nanotechnology, making it a cornerstone of modern scientific innovation.*

**Keywords:** Nanotechnology, Drug delivery, Bioavailability, Controlled release, Pharmaceutical applications, Targeted therapy, Biomedical engineering.

## INTRODUCTION

Nanotechnology refers to the study and advancement of atomic, molecular, or macromolecular structures [1]. Over the past few decades, nanotechnology has advanced significantly in the field of nanomedicine. Nanomedicine, or the formulation of pharmaceuticals into nanoparticles, gives medications new characteristics including enhanced pharmacokinetics and bioavailability, less harmful side effects, controlled release, and the potential to increase dosage, among others. For instance, the water insoluble nature of many potent medicinal medications restricts their use in clinical settings [2-5]. The formation of hydrophobic drug-loaded nanomedicines reduces drug toxicity and increases therapeutic efficacy in addition to improving the drug's solubility, bioavailability, stability, biodistribution, pharmacokinetics, and pharmacodynamics [6-9]. To accomplish multifunctionality, nanomedicines can also combine additional features like imaging, triggered release, and tailored distribution [10].

Nanoparticles, which are defined as particles with at least one dimension of 100 nm, are thought to be the fundamental units of nanotechnology. For thousands of years, various businesses and humanity have employed particles in these size ranges; but, because to the ability to synthesis and manipulate such materials, there has been a recent comeback. Numerous fields, including electrical, magnetic and optoelectronic, biological, pharmaceutical, cosmetic, energy, environmental, catalytic, and materials applications, use nanoscale materials. Investments in nanotechnology research and development have increased globally due to the technology's potential [11]. The federal government will invest roughly \$1 billion in nanotechnology research in the United States, \$600 million in Western Europe, \$800 million in Japan, \$200 million in Korea, and roughly \$800 million in other nations in 2005. Since 1999, funding and research in nanotechnology have increased sevenfold. Sustainable development and wider societal advancements are also receiving a lot of attention [12]. The medication is encapsulated, dissolved, trapped, or bonded to a matrix of nanoparticles. Nanoparticles, nanospheres, or nanocapsules can be produced based on the preparation technique. Nanospheres are matrix systems where the drug is uniformly and physically distributed, whereas nanocapsules are systems where the medication is contained within a hollow encircled by a special polymer membrane. Biodegradable polymeric nanoparticles, especially those coated with hydrophilic polymers like poly(ethylene glycol) (PEG), also referred to as long-circulating particles, have been used as potential drug delivery devices in recent years due to their capacity to target a specific organ, circulate for an extended period of time, act as carriers of DNA in gene therapy, and deliver proteins, peptides, and genes [13-16].

## Applications

### Sunscreen and Cosmetics

1. When used for an extended period of time, the traditional UV protection sunscreen is unstable. The sunscreen that contains titanium dioxide nanoparticles has many benefits.

Because titanium oxide and zinc oxide nanoparticles are transparent to visible light and have the ability to both absorb and reflect UV rays, they have found usage in certain sunscreens due to their UV protection properties. Iron oxide nanoparticles are a pigment used in some lipsticks [17].

## **2. Electronics**

Nanoparticles are being utilized more often in display technology because of the increased need for large, brilliant screens that are used in televisions and computer monitors these days. For instance, light emitting diodes (LEDs) in contemporary displays use nanocrystalline lead telluride, cadmium sulfide, and zinc selenide and sulfide [18]. Compact, lightweight, and high capacity batteries are in increasing demand due to the advancement of portable consumer gadgets like laptop computers and cell phones. The best option for battery separator plates is nanoparticles. Because of their foam-like (aerogel) shape, they can store a significant amount more energy than conventional batteries. Because of their enormous surface area, batteries composed of nanocrystalline nickel and metal hydrides last longer and require less recharging [19]. Gases as NO<sub>2</sub> and NH<sub>3</sub> are detected using nanoparticles' increased electrical conductivity [20]. This results from the charge transfer from the nanoparticles to NO<sub>2</sub> as the gas molecules bind them together, increasing the pores of the nanoparticles and improving their gas sensor capabilities.

## **3.Catalysis**

The large surface area of nanoparticles provides greater catalytic activity. The nanoparticles incredibly high surface to volume ratio makes them effective catalysts in chemical synthesis [21]. One noteworthy application is the use of platinum nanoparticles in car catalytic converters, which considerably lower costs and improve performance by reducing the amount of platinum needed due to the nanoparticles' extremely high surface  $A = \pi r^2$ . Certain chemical reactions, such as the reduction of nickel oxide to nickel (Ni), are carried out with the aid of nanoparticles.

## **4.Drugs**

Through the use of nanoparticles in drug delivery, nanotechnology has advanced the medical industry. Nanoparticles can be used to deliver the medication to particular cells [22]. Placing the medicine in the appropriate location and amount greatly reduces both overall drug intake and negative effects. This approach lowers the price and adverse effects. Nanotechnology can be used to replicate and mend damaged tissue (a process known as tissue engineering). Tissue engineering can take the place of conventional therapies like organ transplants and artificial implants. Bone growth using carbon nanotube scaffolds is one such instance [23]. Gold has long been used in medicine. Gold is utilized in a number of procedures under the Indian medicinal system known as Ayurveda. Using gold to improve memory is one such recommendation. Some medicinal preparations use gold to improve a baby's mental capacity [24].

## 5. Food

The application of nanotechnology improves food production, processing, preservation, and packaging. In the food packaging process, for instance, a nanocomposite coating can directly incorporate antimicrobial materials onto the coated film surface [25].

## 6. Construction

Construction procedures are now safer, cheaper, and faster thanks to nanotechnology. Nanoparticles, for instance, can enhance the mechanical characteristics and durability of regular concrete when mixed with nanosilica ( $\text{SiO}_2$ ) [26]. Concrete becomes stronger when haematite ( $\text{Fe}_2\text{O}_3$ ) nanoparticles are added. The most accessible and often utilized material in the building sector is steel. Utilizing nanotechnology in steel can improve its qualities; for instance, utilizing nanosize steel in bridge construction results in stronger steel cables [26]. Glass is another essential building material. The use of nanotechnology in building glass is the subject of extensive investigation. Titanium dioxide ( $\text{TiO}_2$ ) nanoparticles are utilized to coat windows because of their anti-fouling and sterilizing qualities as well as their ability to catalyze a potent chemical reaction that breaks down organic contaminants and volatile organic compounds (VOV) [27].

## 7. Environmental cleanup and renewable energy

Because of their distinct physical and chemical characteristics, nanoparticles are currently a great option for environmental cleanup and for improving the performance of the renewable energy industry [28]. Some of the nanoparticles that are found in nature have been shown to have environmental healing properties. For more than ten years, air, water, and soil have been effectively treated or decontaminated through environmental remediation employing nanoparticles, also known as nano remediation. [29]

### Advantages of Nanoparticles [30-31]

- a) It is simple to control the size and surface properties of nanoparticles to accomplish both passive and active medication targeting following parenteral injection.
- b) They regulate and maintain drug release during transit and at the localization site, changing the medication's organ distribution and subsequent clearance to improve therapeutic efficacy and minimize adverse effects.
- c) By using magnetic guidance or attaching targeting ligands to the particle surface, site-specific targeting can be accomplished.
- d) The selection of matrix ingredients allows for easy modulation of controlled release and particle degrading characteristics. An essential component of maintaining drug activity is the comparatively high drug loading and the ability to incorporate medicines into systems without causing any chemical reactions.
- e) The system can be administered via a number of methods, such as parenteral, intraocular, nasal, and oral.

## Limitations of Nanoparticles [30,32]

- Pronounced **aggregation** due to high surface energy and small size, complicating handling in both liquid and powder forms.
- Poor **flowability** and sticking in containers, leading to handling difficulties and dose inconsistency.
- Unstable **dispersions**, with a tendency for agglomeration over time unless stabilized.
- Limited **drug-loading capacity**, often <10–20 wt%, restricting the therapeutic payload.
- Burst **release** phenomenon from surface-bound drug, resulting in initial dose spikes.
- Poor **control over sustained release**, leading to suboptimal pharmacokinetics.
- Encapsulation **inefficiency**, where hydrophobic or crystalline matrices expel drug over time.
- Low **yields in manufacturing**, particularly with stickiness and aggregation .
- **Scale-up challenges**, as lab-scale stabilization techniques often fail at industrial volumes.
- Batch **variability**, leading to inconsistent drug loading and release properties.
- Complex **stabilization needs**, requiring surfactants or polymer coatings that add cost and complexity.
- Regulatory **challenges**, including undefined safety and environmental guidelines.
- High **production costs**, often due to specialized equipment and multi-step processes.
- Environmental **persistence**, especially for non-biodegradable materials accumulating in organs or ecosystems.
- Limited or **unpredictable biodistribution**, complicating targeted delivery.
- Design **complexity**, where achieving high loading, stability, and functionality simultaneously is difficult.

## Methods and Preparation of Nanoparticles

Nanoparticles can be prepared using physical, chemical, and biological methods. Each method has its own advantages depending on the desired properties of the nanoparticles, such as size, shape, surface charge, and application. The goal is to create nanoparticles from a range of substances, including proteins, polysaccharides, and synthetic polymers. Numerous factors influence the selection criteria for matrix materials, including: (a) the necessary size of the nanoparticles; (b) the drug's inherent properties, such as stability and solubility in water; (c) surface characteristics, such as charge and permeability; (d) the degree of toxicity, biodegradability, and biocompatibility; (e) the desired drug release profile; and (f) the final product's antigenicity. First, preformed polymers are dispersed; second, monomers are polymerized; and third, hydrophilic polymers are ionic gelated or coacervated to create nanoparticles. However, additional techniques for producing nanoparticles have also been reported in the literature, including particle replication in non-wetting templates and supercritical fluid technologies. In order to produce nanoparticles, the literature has also described particle replication in non-wetting templates. It was asserted that the latter may provide a model for the industrial mass production of nanoparticles in the future since it had complete control over particle size, shape, and content. In order to produce nanoparticles, the literature has also described particle replication in non-wetting templates. It was asserted that

the latter may provide a model for the industrial mass production of nanoparticles in the future since it had complete control over particle size, shape, and content[33].

### **Preformed polymer dispersion**

A popular method for creating biodegradable nanoparticles from poly (lactic acid) (PLA), poly (D,L-glycolide), PLG, poly (D,L-lactide-coglycolide) (PLGA), and poly(cyanoacrylate) (PCA) is the dispersion of premade polymers[34,35].

This method can be applied in a number of ways, as explained below:

#### **❖ Solvent Evaporation Method**

This procedure involves dissolving the polymer in an organic solvent, such as ethyl acetate, dichloromethane, or chloroform, which is also used to dissolve the hydrophobic medication. To create an oil in water (o/w) emulsion, the polymer and drug solution mixture is then emulsified in an aqueous solution that contains a surfactant or emulsifying agent. The organic solvent is evaporated either by lowering the pressure or by constant stirring once a stable emulsion has formed. It was discovered that the kind and amounts of stabilizer, the speed of the homogenizer, and the concentration of the polymer all affected particle size. High-speed homogenization or ultrasonication are frequently used to create tiny particle sizes[36].

#### **❖ Solvent diffusion method or spontaneous emulsification**

The solvent evaporation process has been updated. The water miscible solvent and a tiny quantity of the water immiscible organic solvent are utilized in this procedure, as stated by Small particles arise as a result of the interfacial turbulence produced between the two phases by the spontaneous diffusion of solvents. The size of the particle can be reduced as the watermiscible solvent concentration rises. For medications that are hydrophilic or hydrophobic, both solvent diffusion and solvent evaporation techniques can be applied [37].

#### **❖ Polymerization Method**

This process creates nanoparticles in an aqueous solution by polymerizing monomers. The drug is integrated either by dissolving in the polymerization liquid or by adhering to the nanoparticles following the completion of polymerization. By using ultracentrifugation and re-suspending the particles in an isotonic surfactant-free solution, the nanoparticle suspension is further filtered to exclude different stabilizers and surfactants used for polymerization. There have been reports of using this method to create polybutylcyanoacrylate or poly (alkylcyanoacrylate) nanoparticles[38-40].

### ❖ **Coacervation or ionic gelation method**

Chitosan, gelatin, and sodium alginate are examples of biodegradable hydrophilic polymers that are used in the creation of nanoparticles. creating an ionic gelation process to produce hydrophilic chitosannanoparticles. This technique creates coacervates with a size in the nanometer range by interacting the positively charged amino group of chitosan with the negatively charged tripolyphosphate[40]

### ❖ **Supercritical fluid technology**

Traditional techniques include solvent extraction-evaporation, solvent diffusion, and organic phase separation call for the use of organic solvents, which are harmful to both human systems and the environment. Due to the environmental safety of supercritical fluids, this technology has been studied as a substitute for creating biodegradable micro- and nanoparticles. A solvent at a temperature higher than its critical temperature, when it maintains its single phase under all pressures, is referred to as a supercritical fluid. Rapid expansion of critical solution (RESS) and supercritical antisolvent (SAS) are the two most often used processing methods employing supercritical fluids. In SAS, the solute to be micronized is dissolved using a liquid solvent, such as methanol, which is perfectly miscible with the supercritical fluid (SC CO<sub>2</sub>). Under process conditions, the solute is insoluble in the supercritical fluid, so the extraction of the liquid solvent by the supercritical fluid causes the solute to precipitate instantly, forming nanoparticles.

### **Conclusion**

Nanotechnology has revolutionized science and medicine by introducing nanoscale materials that exhibit unique physicochemical properties. In Nanomedicine, nanoparticles offer solutions to long-standing drug delivery issues, including poor solubility, rapid degradation, and systemic toxicity. Their ability to encapsulate, protect, and deliver therapeutic agents to specific sites significantly improves treatment outcomes. Additionally, the multifunctionality of nanoparticles enables integration with diagnostic agents, site-specific targeting Ligands, and responsive release mechanisms. Beyond medicine, nanoparticles have found widespread applications in electronics, catalysis, cosmetics, energy storage, environmental remediation, construction, and the food industry. However, their widespread application is still challenged by issues such as particle aggregation, limited drug-loading capacity, manufacturing scalability, regulatory uncertainty, and high production costs. The choice of nanoparticle preparation technique—whether by physical, chemical, or biological means—is guided by factors like the intended application, material compatibility, and drug properties. Techniques such as solvent evaporation, solvent diffusion, polymerization, ionic gelation, and supercritical fluid processing offer versatility in tailoring nanoparticle attributes. Continued research is essential to overcome current limitations, improve scalability, and address safety concerns. As nanotechnology matures its integration into clinical, industrial, and environmental frameworks promises to unlock unprecedented capabilities in science, healthcare, and sustainable development.

**REFERENCE**

1. National Nanotechnology Initiative. Available at <http://www.nano.gov/html/facts/EHS.htm> (accessed 2004).
2. H. Van Ngo, P. K. Nguyen, T. Van Vo, W. Duan, V.-T. Tran, P. H.-L. Tran, T. T.-D. Tran, *Int. J. Pharm.* 2016, 513, 148-152.
3. T. T.-D. Tran, P. H.-L. Tran, J. Lim, J. B. Park, S.-K. Choi, B.-J. Lee, *Ther. Delivery* 2010, 1, 51-62.
4. T. N. G. Nguyen, V. T. Tran, W. Duan, P. H. L. Tran, T. T. D. Tran, *Curr. Drug Metab.* 2017, 18, 1000-1015.
5. A. Fahr, X. Liu, *Expert Opin. Drug Delivery* 2007, 4, 403-416.
6. J. Hrkach, D. Von Hoff, M. M. Ali, E. Andrianova, J. Auer, T. Campbell, D. De Witt, M. Figa, M. Figueiredo, A. Horhota, *Sci. Transl. Med.* 2012, 4, 128ra139-128ra139;
7. Y. Lu, Z. Yue, J. Xie, W. Wang, H. Zhu, E. Zhang, Z. Cao, *Nat. Biomed. Eng.* 2018, 2, 318;
8. E. P. Thi, C. E. Mire, A. C. Lee, J. B. Geisbert, J. Z. Zhou, K. N. Agans, N. M. Snead, D. J. Deer, T. R. Barnard, K. A. Fenton, *Nature* 2015, 521, 362;
9. J. Bhattacharyya, J. J. Bellucci, I. Weitzhandler, J. R. McDaniel, I. Spasojevic, X. Li, C.-C. Lin, J.-T. A. Chi, A. Chilkoti, *Nat. Commun.* 2015, 6, 7939.
10. Y. Hui, D. Wibowo, Y. Liu, R. Ran, H.-F. Wang, A. Seth, A. P. Middelberg, C.-X. Zhao, *ACS Nano* 2018, 12, 2846-2857.
11. Roco, M.C. *Broader Societal Issues of Nanotechnology*; *J. Nanopart. Res.* 2003, 5, 181-189.
12. Choi, M.; Biswas, P.; Fissan, H.; Pui, D. Y. H. *Special Issue on Nanoparticles: Technology and Sustainable Development*; *J. Nanopart. Res.* 2003.
13. Langer R. *Biomaterials in drug delivery and tissue engineering: one laboratory's experience.* *Acc Chem Res* 2000; 33: 94-101.
14. Bhadra D, Bhadra S, Jain P, Jain NK. *Pegnology: a review of PEG-ylated systems.* *Pharmazie* 2002; 57: 5-29.
15. Kommareddy S, Tiwari SB, Amiji MM. *Long-circulating polymeric nanovectors for tumor-selective gene delivery.* *Technol Cancer Res Treat* 2005; 7: 615-25.
16. Lee M, Kim SW. *Polyethylene glycol-conjugated copolymers for plasmid DNA delivery.* *Pharm Res* 2005; 22: 1-10.
17. Wiechers J W and Musee N 2010 *Engineered Inorganic Nanoparticles and Cosmetics : Facts , Issues , Knowledge Gaps and Challenges* 6.
18. Teng W, Jeng S, Kuo C, Lin Y, Liao C and Chin W 2008 *liquid crystal displays* 33 1663-5.
19. Published A, Link C and Terms D 2016 *Platinum-Gold Nanoparticles : A Highly Active Bifunctional Electrocatalyst for Rechargeable Lithium-Air Batteries* The MIT Faculty has made this article openly available . Please share Citation and may be subject to US copyright law . Please refer to the P.
20. Liu X, Zhang J, Wang L, Yang T, Guo X, Wu S and Wang S 2011 *3D hierarchically porous ZnO structures and their functionalization by Au nanoparticles for gas sensors* 349-56.



21. Lugscheider E, Bärwulf S, Barimani C, Riester M and Hilgers H 1998 Magnetron-sputtered hard material coatings on thermoplastic polymers for clean room applications *Surf. Coatings Technol.* 108-109 398–402.
22. Marsalek R 2014 Particle Size and Zeta Potential of ZnO APCBEE *Procedia* 9 13–7.
23. Sharma V and Rao L J M 2014 An overview on chemical composition, bioactivity and processing of leaves of *Cinnamomum tamala*. *Crit. Rev. Food Sci. Nutr.* 54 433–48.
24. Bzdek B R, Zordan C A, Iii G W L, Murray V, Bzdek B R, Zordan C A, Iii G W L, Murray V, Bzdek B R, Zordan C A, Iii G W L and Johnston M V 2016 Nanoparticle Chemical Composition During New Particle Formation *Formation* 6826.
25. Hodoroaba V, Rades S and Unger W E S 2014 Inspection of morphology and elemental imaging of single nanoparticles by high- resolution SEM / EDX in transmission mode.
26. Yano F, Hiraoka A, Itoga T, Kojima H, Kanehori K and Mitsui Y 1996 Influence of ion implantation on native oxidation of Si in a clean-room atmosphere *Appl. Surf. Sci.* 100-101 138–42.
27. Wiechers J W and Musee N 2010 *Engineered Inorganic Nanoparticles and Cosmetics : Facts , Issues , Knowledge Gaps and Challenges* 6.
28. Liu W 2006 *Nanoparticles and Their Biological and Environmental Applications* 102 1–7.
29. Assessment R 2007 *Nanoparticles in the Environment*.
30. Langer R. *Biomaterials in drug delivery and tissue engineering; one laboratory's experience.* *Acc ChemRes.*2000;33:94-101.
31. Welch, C. M., & Compton, R. G. (2006). The use of nanoparticles in electroanalysis: a review. *Analytical and bioanalytical chemistry*, 384(3), 601-619.
32. Bhadia D, Bhadra S, Jain P and Jain NK. *Pegnology; a review of PEGylated systems; Pharmazin.* 2002;57:5 20.
33. Reverchon E and Adami R. *Nanomaterial and supercritical fluids.* 2006;37:1-22.
34. Rolland JP, Maynor BW, Eullis LE, Exner AE, Denison GM and Desimonal JM. *Direct fabrication and harvesting of monodispersed shape specific nanobiomaterial.* *J Am Chem Soc.* 2005;127:10096-10100.
35. KompellaUB, Bandi N, Ayalasomayajula SP. *Poly(lactic acid) nanoparticles for sustained release of budesonide.* *Drug deliv Technol.* 2001;1:1-7.
36. Li YP, Pei YY, Zhou ZH, Zhang XY, GuZH and Ding J. *Nanoparticles as tumornecrosis factor-[alpha] carriers.* *J control release.* 2001;71:287-296.
37. Boudad H, Legrand P, Lebas G, CheronM, Duchene D and Ponchel G. *Combined Hydroxypropyl-[beta]- cyclodextrins ;nanoparticles intended for oral administration of sequinarvir.* *Ind J Pharm.* 2001;218:113-124.
38. Puglisi G, Fresta M, Gimmona G and Ventura CA. *Influence of the prepration condition on poly(ethylcyanoacrylate)* *IJRPC* 2012, 2(3) PrabhjotKaur et al ISSN: 2231-2781761nanocapsules formation. *Ind JPharm.* 1995;125:283-287. 12. Calvo P, RemunanLopez C, Vila-JatoJL and Alonso MJ. *Novel hydrophilic chitosan –polyethylene oxide nanoparticles as protein carrier.**J Appl Polymer Sci.* 1997;63:125-132
39. Kroil RA, Pagel MA, Muldoon LL, Roman-Golstein S, Flamengo SA and Neuwet EA. *Improving drug delivery tiintracerabletumor and surrounding brain in a rodent*

*model;comparision of osmatic and bradyknin modification of blood tumor barrier. Neurological 1998;43:879-886.*

40. Kreuter J, Ramage PV, Hamm S, Gelpenia SE, Engeltatdt B and AlyantdinRyvonBriesen H. Direct evidence that polysorbate -80 coated poly (butylcyanocrylate) nanoparticles deliver drugs to the CNS via specific mechanisms required prior binding of drug to the nanoparticles. *PhrmRes.2003;20:409-16.*

41. Kreuter J, Ramage PV, Hamm S, Gelpenia SE, Engeltatdt B and AlyantdinRyvonBriesen H. Direct evidence that polysorbate -80 coated poly (butylcyanocrylate) nanoparticles deliver drugs to the CNS via specific mechanisms required prior binding of drug to the nanoparticles. *PhrmRes.2003;20:409-16.*

42. Puglisi G, FrestaM ,Giammona G and Ventura CA. Influence of the preparation conditions on poly(etyhycyanoacrylate) nanocapsules formation. *Ind J Pharm.1995;125:283-287.*