Review Article

Nanotechnology: Various methods used for preparation of Nanomaterials

Brahamdutt[1], Vipan Kumar Kamboj[1], Arun Kumar[1], Mangal Sain Hooda[2], Pradeep Sangwan[2*]

[1]*Department of Pharmaceutical Sciences, Maharishi Dayanand University, Rohtak, Haryana, Pin-124001, India*

[2]*Janta College of Pharmacy, Butana, Sonepat, Haryana, Pin-131302, India*

Received: 12 May 2018 Revised: 5 June 2018 Accepted: 17 June 2018

Abstract

In the modern system of drug delivery, even after several efforts by the scientists, the chief key issue remains the efficient and effective amount of drug delivery at particular site. Due to the low residence time of API's at the required site, leads to the poor bioavailability of drugs in the conventional drug delivery systems. At present nanotechnology is the emerging field for delivery of drugs at size of nano-scale and very effective in sustained and targeted delivery of medicines i.e. polyplexes (DNA/polycation complexes), block copolymer micelles and nano-gels etc. In the human trials, polymeric micelles have been found to be very convincing method for delivery of anticancer drugs. Selection of suitable method of preparation remain an important aspect as particulate systems like nanoparticles have been used as a physical approach to alter and improve the pharmacokinetic and pharmacodynamics properties of various types of drug molecules. Several methods to prepare polymeric nanoparticles have been developed and these techniques are classified according to whether the particle formation involves a polymerization reaction or nanoparticles form directly from a macromolecule or preformed polymer.

***Keywords**:* Nanotechnology, nanomaterials, solid lipid nanoparticles, liposomes, microparticles

Introduction

Nanotechnology helps to use the resources on an improbably tiny scale in order that they take on novel structure and properties in comparison to their bigger forms. Nanotechnology has the potential to remodel several of the attention merchandise that we have a tendency to use and a large vary of merchandise square measure already on the market as well as nanogels, ophthalmic preparations, metastatic tumor and nanoparticulate drug delivery system supported technology etc. nanotechnology in cosmetics is one space of specific interest as new varieties of merchandise may be created victimisation nano materials. Ultraviolet radiation filters employed in sunscreens made in nano type, as an example, become clear instead of white when put next to their bigger type. There has been a substantial analysis interest within the space of specific systems of drug delivery as carriers for little and enormous molecules. In nanosized materials like nanogels, the physicochemical properties of delivery system are being manipulated at smaller scale in comparison to the larger size range of assorted drug molecules. The reason of extensive research in the field of nanotechnology is because of their unleashed properties of controlled and sustained release as well as biocompatibility and lower toxicology to the body system. The classifications for various methods of preparation for nanoparticulates are based on polymerization reaction involvement and/or formation of nanomaterials from the bigger size material having same properties as the nanomaterial. However, still a lot of work is required to be done to know the extent of toxicity or harmfulness while using the nanomaterials based on polymerization. During this review, we'll discuss concerning varied methods for preparing nanosized particles or materials. However, there's uncertainty concerning whether or not, aboard the changes that bring shopper edges, a number of these nanomaterials might gift new risks. Materials may be additional unsafe and behave otherwise within the body in comparison to bigger forms (Nagavarma et al., 2012).

A lot of approaches that are tried to extend the bioavailability and therefore the period of the therapeutic action of assorted

Address for Corresponding Author:
Pradeep Sangwan
(Assistant Professor)
Janta College of Pharmacy, Butana, Sonepat, Haryana, Pin 131302, India
Email: bhardwaj.b007@gmail.com

DOI: https://doi.org/10.31024/ajpp.2018.4.4.2

medication may be alienated into 2 classes. The primary one relies on the employment of sustained drug delivery systems, which offer continues and controlled delivery of medicine whereas the secondary step includes increasing drug's absorption and lowering the loss of drug (Mundada et al., 2008). The drug delivery system should be ready to sustain the drug unleash. Consequently it's imperative to optimize drug delivery; one among the thanks to do thus is by addition of polymers of assorted grades, development of in situ gel or colloid (Wagh et al., 2008).

Various types of Nanomaterials used as Drug Delivery Systems

There are several new nanotechnology based drug delivery systems under investigation such as:

- Hydrogels
- Nanoparticles and Microparticles
- Liposomes
- Microemulsions
- Nanosuspensions
- Microneedles
- Gene therapy
- Ocular inserts/discs
- Dendrimers
- Trans-corneal iontophoresis

Different advantages of nanosized drug delivery system over conventional dosage forms

Using nanotechnology we obtained following advantages as compared to conventional dosage forms or drug delivery methods (Thassu et al., 2007; Nagavarma et al., 2012):

- Higher bioavailability for drugs having low solubility.
- Nanotechnology has various spectrum of application (I.V, Oral, Dermal etc.)
- The large scale production has an established method of preparation i.e high-pressure homogenization
- Increased bioavailability sustained and controlled release properties as well as drug molecule protection from environmental hazards.
- Good candidate for conveying the vaccines, anti-cancer API's and other biological products.
- Tissue engineering on nanoscale could be done with nanotechnology.

Various types of polymers used for preparation of Nanomaterials

The phenomena of mucoadhesion has become vital for its potential to localized drug delivery, by holding a dose kind at the location of action or general delivery, by holding a formulation up-to-date with the location of absorption (e.g. the oral cavity). Totally different studies are conducted on varied drug delivery systems victimization mucoadhesive polymers as well as principally polysaccharides. Polysaccharides are comparatively complicated carbohydrates. They supply excellent mechanical properties for applications as fibres, films, adhesives, physics modifiers, hydrogels, emulsifiers, and drug delivery agents. Some polysaccharides have proved to reinforce the contact between drug and human membrane because of their high mucoadhesive properties. Polysaccharides, such as xanthan gum, cellulose ethers, scleroglucan, locust bean gum, and gaur gum are some of the natural polysaccharide which has been evaluated in the hydrophilic matrix for drug delivery system (Shaikh et al., 2015).

Some of the synthetic polymers are also used for nanomaterials preparation such as Polylactides (PLA), Polyglycolides (PGA), Poly (lactide co-glycolides) (PLGA), Polyanhydrides, Polycyanoacrylates, Polycaprolactone, Poly glutamic acid, Poly malic acid, Poly (N-vinyl pyrrolidone), Poly (methyl methacrylate), Poly (vinyl alcohol), Poly (acrylic acid), Poly acrylamide, Poly (ethylene glycol), Poly (methacrylic acid) (Nagavarma et al., 2012).

Methods of preparation for nanoparticles

To achieve the required properties of interest in drug delivery systems, the mode of preparation plays a vital role. Thus, it is highly advantageous to have preparation techniques at hand to obtain PNPs with the desired properties for a particular application. So various techniques like ionic gelation, solvent evaporation etc are used for preparation of nanosized particulate materials (Nagavarma et al., 2012).

Different methods used for preparation for Nanomaterials

Ionic Gelation method

Ionic gelation technique, relies on the complexation of the positive or electric charge of the hydrophilic compound along a multivalent cationic (e.g. calcium chloride) or polyanionic (e.g. Na tripolyphosphate) to create extremely glutinous gel particle having a size range within the vary of a metric linear unit. The mechanism concerned within the construction of nanoparticles is that the static relations between charged amino teams gift in compound and charged ion. It is seen that within the ionic gelation technique, thanks to interaction the fabric undergoes

transition from liquid to gel part (Mudgil et al., 2012).

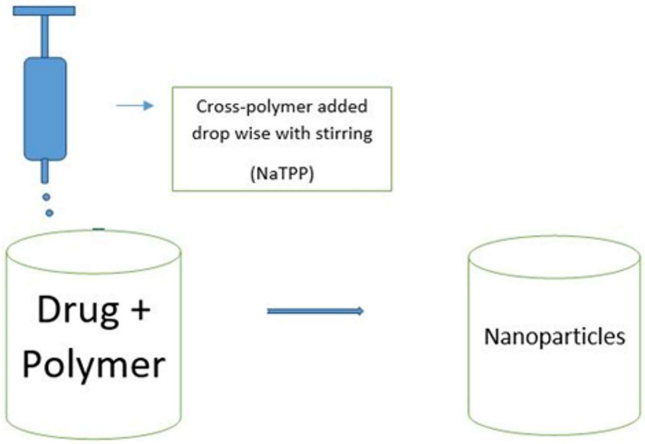

Figure 1. Ionic Gelation Method for nanoparticles preparation

Drug and polymer solution is prepared by dissolving them into distilled water and cross polymer (NaTPP or calcium chloride) solution in distilled water was being added drop-wise in the polymer drug solution under high speed stirring (3000 rpm) for a fixed time period. An opalescent suspension was being obtained. The obtained suspension was centrifuged to obtain the nanoparticles. The nanoparticles were freeze dried followed by lyophilisation using suitable cryoprotectant (Fathalla et al., 2015).

Brahamdutt et al., (2016) prepared sustained release tropicamide loaded chitosan nanoparticles through ionic gelation method. The goal of research was to enhance the residence time of drug in eye, enhancing bioavailability and reducing dosing frequency. Nanoparticles were formulated by ionic gelation method using chitosan as polymer and sodium TPP as cross-polymer. Nanoparticles were optimized using (2^2) factorial design and characterized by their particle size analysis, drug entrapment efficiency and percentage yield. Nanoparticles formed were spherical in shape and size ranged between 402.4 nm to 604.5 nm. Drug entrapment efficiency, percentage drug release of optimized formulation was found to be 54.9% and 30.44% respectively. The study of drug release pattern revealed its sustained release properties (Brahamdutt et al., 2016).

Kaur et al., (2011) studied Tropicamide-loaded carboxymethyl tamarind kernel polysaccharide nanoparticles and evaluated for ocular delivery. Nanoparticles were prepared by ionic gelation technique and optimized by employing three-levels, two-factor central composite design. Concentration of polymer and cross linker had significant synergistic effect on particle size and percent encapsulation efficiency. The optimal calculated parameters were concentrations of carboxymethyl tamarind kernel polysaccharide 0.10% (w/v) and calcium chloride 0.11% (w/v). The optimized tropicamide-loaded carboxymethyl tamarind kernel polysaccharide formulation showed ex vivo corneal permeation of tropicamide across isolated goat cornea comparable to its aqueous solution. Further, the mucoadhesive and non-irritant nature of nanoparticles indicate their suitability as ocular delivery system (Kaur et al., 2011).

Ries et al., (2006) studied the fundamental method concerned within the development of nanoparticles is that the static connections between charged amino teams gift in chemical compound and charged ion. In alternative language it will be seen that within the ionic gelation methodology, thanks to interaction involving the material undergoes alteration from fluidic to gellic section. The prepared nanoparticles of chitosan usually square measure of tiny size within limit of 200-500nm (Ries et al., 2006).

Ahuja and Yadav (2010) used the ionic gelation methodology to arrange gum Cordia laden fluconazole nanoparticles. The analysis of particulates size, encapsulation efficiency and zeta potential was performed using design expert software. The result of permeation study revealed a higher %age of encapsulation efficiency of nanoparticles loaded with fluconazole as compared to the formulation available in the market (Ahuja and Yadav., 2010).

Campos et al. (2004) studied the effect of chitosan nanoparticles within the eye through checking their interactions with mucosal layers and to check their toxicity with conjunctival cell lines In-Vivo. The soundness of the particles within the presence of enzyme was investigated by determinant the scale and their interaction with glycoprotein, by measurement the consistence of the glycoprotein dispersion. The in vivo interaction of CS-fl nanoparticles with the rabbit tissue layer and mucous membrane was analyzed by spectrofluorimetry and confocal research. Their potential toxicity was assessed during a human mucosa cell line by determinant cell survival and viability (Campos et al., 2004).

Mahmoud et al. (2011) prepared chitosan nanoparticles loaded with econazole with sulfobutylether-β-cyclodextrin metal as cross-linking agent by ionic gelation method for sustained ocular drug delivery. In vitro unleash of econazole from nanoparticulates was ready to controlled five hundredth of the first quantity free from nanoparticles up to eight hours. The in vivo studies counsel that, the Econazole laden chitosan Econazole nitrate nanoparticles give higher antifungal activity in comparison to solution of Econazole nitrate. So the results conclude that chitosan/ sulfobutylether-β-CD nanoparticles were established a good applicant for ophthalmic drug release (Mahmoud et al., 2011).

Nanoprecipitation Method

In this method, the polymer is going to be precipitated from the organic solvent and the organic solvent diffuses in the hydrophilic medium with or without the help of a surfactant. Water-miscible solvent is generally used to dissolve the polymer leading to the nanosized particle formation via precipitation of polymer. Now this phase is introduced into the hydrophilic medium having a stabilizer i.e surfactant with stirring. With the help of quick diffusion process, the deposition of polymer on the interface between organic and aqueous solvent take place and this phenomena leads to the formation of nanosized materials. Nanoparticulates formation can be enhanced on the first stage of this method; a completely miscible solvent system is used for the phase separation. Nanocapsules could also be prepared with this technique by introducing a little amount of nontoxic oil in the organic phase. The use of this technique is limited to water-miscible solvents, in which the diffusion rate is enough to produce spontaneous emulsification (Nagavarma et al., 2012).

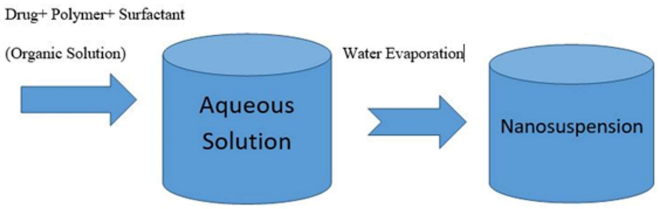

Figure 2. Nanoprecipitation method for nanomaterial preparation

Gadad et al. (2012) studied the effect of Moxifloxacin loaded poly (lactic-co-glycolic acid) nanoparticle on ocular retention time. Nanoprecipitation method was utilised for nanoparticles preparation and then particulate size, zeta potential, %age encapsulation efficiency and drug release pattern was evaluated. Uniformly spherical particulates (>202.5 nm) with a negative zeta potential (-25.45 mV) were obtained. The % encapsulation efficiency was 83.1% having controlled and sustained release pattern of drug to exclude out the frequent dosing requirements (Gadad et al., 2012).

Aksungur et al. (2011) compared cyclosporine containing nanoparticles of poly lactide co-glycolic acid (PLGA) and Eudragit RL-100 in mixture or PLGA coated with carbopol for severe dry eye syndrome treatment. Nanoparticles prepared with Eudragit RL provide smallest size. The particulate size reduces with increasing the concentration of Eudragit RL due to its physicochemical properties while effect of freeze drying leads the increment in particulates size range (Aksungur et al., 2011).

Liu et al. (2008) prepared alginate microspheres loaded with bovine serum albumin and then introduced them into a collagen hydrated hydrogel for ocular application. This hydrogel having microspheres retained the optical clarity in better ways than the hydrogel without microspheres. For 11 days period, the hydrogel exhibited a controlled and sustained drug release pattern in neutral phosphate buffer. The hydrogel having microsphere shows a good biocompatibility and mechanical strength with corneal epithelial cell growth of human eye (Liu et al., 2008).

Solvent Evaporation Technique

In this technique, the volatile solvents are used to prepare polymeric solutions through emulsification. In the past, mostly chloroform and Dichloromethane were used for preparation of polymer solutions but currently ethyl acetate is used due to its better toxicological profile. Through solvent evaporation, this emulsion leads to formation of nanoparticulates via polymeric diffusion into the continuous phase of emulsion. Solvent evaporation is followed by high speed homogenization by constant magnetic stirring or under decreased pressure. To collect the nanomaterials ultracentrifugation technique is used followed by washing with distilled water and lyophilisation (Nagavarma et al., 2012).

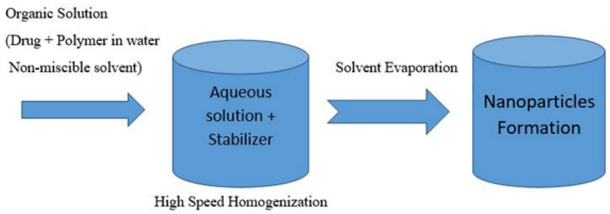

Figure 3. Solvent Evaporation Technique

Mandal et al. (2010) used solvent *Evaporation* procedure to frame Eudragit RL-100 containing sulfacetamide nanoparticles for ocular delivery. Nanoparticle were formulated by taking pluronic F-109 (1% w/v) as stabilizer and acetone. Drug and polymer ratios were varied for formulation optimization. The outcomes of study revealed that nanoparticles could be used for drug delivery in treatment of ophthalmic bacterial treatments (Mandal et al., 2010).

Agnihotri et al. (2009) formulated biopolymeric nanosuspension loaded with diclofenac with two polymers poly(lactide-co-glycolide) (PLGA) and polymers poly[Lac(Glc-Leu)] via emulsification and solvent evaporation techniques. The outcomes revealed improved stability and corneal mucoadhesion of nanoformulation. To treat the inflammatory diseases of eyes could be treat effectively by using nanosuspensions (Agnihotri et al., 2009).

Pignatello et al. (2006) checked the increment in stability and bioavailability of cloricromene in ocular drug delivery

via nanoparticulates formulation using solvent displacement method. Mean particle size and positive superficial charges presence made these nanoparticles a suitable drug carrier in ocular drug delivery. A higher degree of heterogeneity in particulates sizes were exhibited due to High polydispersity index. Nanoparticles of ester drugs formulated in saline solution with small or negligible amount of tween exhibited high degree of chemical stability (Pignatello et al., 2006).

Kumar et al. (2014) studied the formulation and evaluation of Artemisinin HCl nanoparticles to minimalize frequency of dosing, tang cloaking and noxiousness and to increase therapeutic effectiveness through articulating artemisinin HCl nanoparticulates. Solvent displacement technique was employed for nanoparticles formulation via using poly(ε-caprolactone) polymer. Characterizations of nanoparticles were performed through particles size determination, %age entrapment efficiency and pattern of drug release. The particulates size fall between 100-240 nm having >99% of %age entrapment efficiency. The results of drug release pattern exhibited a controlled and sustained release of drug up to 24 hrs (Kumar et al., 2014).

Nimbalkar et al. (2011) Formulated and optimize SLN's of cefpodoxime proxetil with use of box-behnken design. Precirol was used as lipid carrier in SLN's via solvent evaporation technique. Variables like concentration of lipids, span 60 and speed of stirring were used in box-behnken design. Optimized formulation was selected based on surface response plots. The optimized preparation revealed the advantages of using SLN's as drug carrier as compared to marketed formulations (Nimbalkar et al., 2011).

Salting Out Technique

In this method, we use salting out effect to remove the water miscible solvent system from hydrophilic solution. Here the API and polymers get incorporated into an organic solvent and this solution is then emulsion with aqueous solution having salting out agent i.e calcium chloride, magnesium chloride etc. and some stabilizers like hydroxyethylcellulose and polyvinyl pyrrolidone etc. the diffusion of organic solvent is enhanced by adding adequate amount of aqueous solution into the emulsion leading to formation of nanosheres. The encapsulation efficiency depends upon the salting out agent, so utmost care should be taken to choose the suitable salting out agent (Nagavarma et al., 2012).

Pardeike et al. (2009) prepared nanosuspension of PX-18 and PX-13 (phospholipase A2 inhibitors) via homogenization at high pressure. On PX-18 and PX-13 substance and 5% w/w PX-18 and PX-13 nanosuspensions, ocular irritation experiments as well as pre-clinical dermal testing were performed with EPISKIN and HET-CAM test to expand proposal for efficient and safe human trials. The prepared formulation was found to be efficient and safe for ophthalmic and dermal use (Pardeike et al., 2009).

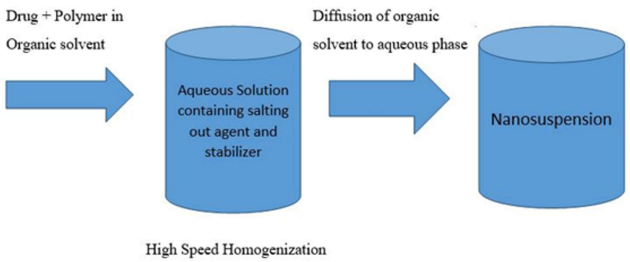

Figure 4. Salting Out technique

Konat et al. (2011) synthesized polyanions loaded gelatine nanoparticulates for expression of MUC5AC in ocular surface epithelial cells whose reduced production leads to dry eye syndrome. The particulate size, zeta potential and entrapment efficiency was found to be <200nm, +20/+30 mV and >95% respectively. Higher amount of MUC5AC expression in the conjunctiva was found after in vivo instillation of the nanoparticles compared to untreated control (Konat et al. 2011).

Dialysis method

In this method, dialysis tube is used with suitable molecular weight cut off and organic solvent carrying polymer is placed. With the help of this technique, narrowly distributed and smaller sized nanoparticles could be prepared. Here the solvent within the tube is displaced is followed by aggregation of polymers because of loss of its solubility leading to the formulation of nanosuspension (Nagavarma et al., 2012).

Chronopoulou et al. (2009) prepared numerous synthetic and natural polymeric nanoparticles based on dialysis method. The method of preparation was based on physiological barrier, particularly the dialysis or semi-permeable membrane through which the solvents have to pass via passive diffusion, which allow the mixing of non-solvent with polymer solutions. The membrane contains the polymeric solutions (Chronopoulou et al., 2009).

Emulsification/ solvent diffusion

This technique is the amended form of solvent evaporation technique. Here the polymer is mixed with partially hydrophilic solvents *viz*. propylene carbonate and sufficient amount of water was added to make both liquids at their thermodynamic equilibrium. Polymer precipitation followed by nanoparticulates formation take place by promoting the diffusion of the solvent of the dispersed phase by dilution with an additional amount of water where the organic solvent is partly miscible with water or with another organic solvent in the opposite case. This aqueous polymer solution is

emulsified with hydrophilic solution having stabilizers causing diffusion of solvent towards the outer phase and leading to nanomaterials formation as per the oil: polymer ratio. At last stage of process solvent is evaporated or filtered according to their boiling points. Advantages gained by using this technique are higher encapsulation efficiencies, easy scale-up, no requirements of homogenization and robustness (Nagavarma et al., 2012).

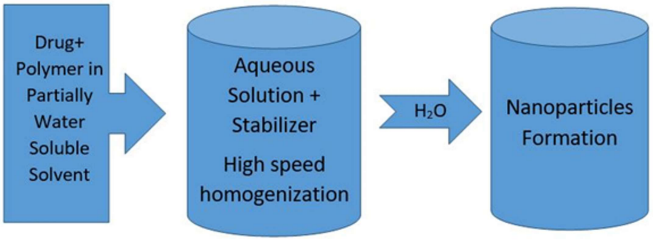

Figure 5. Emulsification/ Solvent Diffusion Technique

Sharma et al. (2015) formulated Eudragit RS 100 and Eudragit RL 100 laden Amikacin sulphate nanoparticles via w/o/w emulsification solvent evaporation with homogenization by varying the drug: polymers ratio. Evaluations of formulations were performed on the basis of particulates size range, zeta potential value, encapsulating efficiency and antimicrobial activity against *Staphylococcus aureus*. *In-vivo* testing included ocular retention, irritancy and drug release pattern. The results of study showed promising results in the favour of nanomaterials prepared via the said method (Sharma et al., 2015).

Javadzadeh et al. (2010) used mono-emulsion technique for preparation of poly (lactic-co-glycolic acid) nanoparticles having naproxen as API. Optimization parameters were taken into consideration i.e drug: polymer ratio, homogenizer's speed and volume of aqueous phase to obtain the optimized batch. The results of study revealed that nanoparticulates drug delivery of naproxen give better anti-inflammatory action in ocular or intra-joint administration (Javadzadeh et al., 2010).

Wadhwa et al. (2010) prepared Hyaluronic acid or modified chitosan nanoparticles loaded with dorzolamide hydrochloride or timolol maleate for the treatment of glaucoma. Both Hyaluronic acid and chitosan provide controlled and sustained delivery of drugs via mucoadhesion phenomena in ophthalmic site. A significant lowering of intraocular pressure was noted by instillation of nanosuspension compared to the solution form of drugs. On the basis of study it was concluded that mucoadhesion of chitosan nanoparticles was significantly improved by hyaluronic acid (Wadhwa et al., 2010).

Kumari et al. (2010) formulated PLGA nanoparticles via this method and concluded a negligible toxicity profile associated with PLGA as drug delivery carrier. The study also concluded the biocompatibility of these nanoparticles with cells and tissues. These nanomaterials converts into biodegradable materials via interactions with body fluids and hydrolysis (Kumari et al., 2010).

Supercritical Fluid Technology

Supercritical fluids are environmentally safe. Supercritical anti-solvent (SAS), rapid expansion of supercritical solution (RESS) and precipitation with compressed anti-solvent process (PCS) are commonly used methods using supercritical fluids. In SAS technique, two completely miscible solvents involved, one is supercritical liquid and another fluid solvent. While the solutes are insoluble in supercritical liquid, nanoparticulates formation occur due to immediate precipitation of solutes formed via extraction of fluid solvent by supercritical fluid. In case of RESS technique, the solutes get dissolved into the supercritical liquid leads to the loss of solvent power significantly and thus solutes gets precipitated due to rapid extension of solutes via small nozzle into the area of decreased pressure. This is the basic difference between SAS and RESS techniques (Mudgil et al., 2012).

Meziani et al. (2004) prepared nanoparticles of Poly (heptadecafluorodecyl acrylate) via supercritical fluid technique with a size of (>50nm). Although, there is no requirement of organic solvents in RESS technique for nanoparticle preparation, but the major drawback of this technique is that the product obtained at primary stage are microscaled rather than nanoscaled. But currently a newer supercritical fluid technology named RESOLV comes into action in which fluid solvent suppresses the growth of particulates in the expansion jet nozzle, leading to formation of nanoscaled particulates at their primary stages (Meziani et al., 2004).

Milling method

Milling methods includes pearl mills or high shear media mills, which are currently used for preparation of nanomaterials or nanosuspensions. These mills are generally having a milling shaft, milling chamber and recirculation chamber. Due to mechanism of impaction and shearing generated by these mills leading to the reduction of microsized drug materials to nanosized materials. The milling media or balls are generally composed of zirconium oxide or ceramic-sintered aluminium oxide or cross-linked polystyrene resin having highly scratch resistance. Planetary ball mills could produce near about less than 0.1µm sized particles. The milling media, drug, stabilizer with suitable buffer or water is filled within the milling chamber. The milling media produce high impact and shear stress within the chamber (Mudgil et al., 2012).

Sapkota and Mishra (2013) studied a simple ball milling method for preparation of p-CuO/n-ZnO Nano composite

photo catalyst with high photo catalytic activity. The structural, optical and surface properties were studied using XRD, TEM, UV Spectroscopy and zeta potential analyser. The photocatalytic activity was studied using photocatalytic oxidation of methylene blue in the presence of UV light (Sapkota and Mishra, 2013).

Kar et al. (2013) prepared Lithium Niobate Nanoparticles by high energy ball milling and then characterise them using XRD, SEM, TEM and DLS techniques. The UV- Visible transmission shows the blue shift in cutoff, which reveals nearly stoichiometric composition of prepared material. It also reveals that with increasing the milling speed and time the size of particles decreases (Kar et al., 2013).

Conclusion

With the use of nanotechnology, there are numerous factors which could be overcome *viz*. poor drug absorption, uncontrolled and untargeted delivery of drugs, frequent dosing requirements, higher toxicity profile of drugs etc. Nanomaterials provide a better control over these shortcomings in pharmaceutical scenario of drug delivery. Numerous newer techniques are present which could be used for bulk production of nanomaterials at industrial level. According to the literature it is clear that nanotechnology is reported to enhance more than one pharmaceutical characteristic at the same time. Till date total marketed formulations of nanomaterials are very less, therefore this is a recent and emerging field. Very less is done and very much is required to be done in this direction.

Acknowledgement

We wish to acknowledge the staff of Janta College of Pharmacy, Butana, Sonepat, Haryana and Maharishi Dayanand University, Rohtak, Haryana for providing us the required facilities and resources.

Conflict of interest

There is no conflict of interest for this work or manuscript.

References

Agnihotri S, Vavia P. 2009. Diclofenac-loaded biopolymeric nanosuspensions for ophthalmic application. Nanomedicine, 5(1):90-5.

Aksungur P, Demirbilek M, Denkbas E, Vandervoort J, Ludwig A, Unlu N. 2011. Development and characterization of cyclosporine A loaded nanoparticles for ocular drug delivery: cellular toxicity, uptake, and kinetic studies. International Journal, 151(3):286-94.

Brahamdutt, Choudhary M, Kumar S, Bhatia M, Budhwar V. 2016. Formulation and In-Vitro Evaluation of Sustained Release Tropicamide Loaded Chitosan Nanoparticles for Ocular Drug Delivery. International Research Journal of Pharmacy, 7(10):27.

Campose A, Diebold Y, Alonso M. 2004. Chitosan nanoparticles as new ocular drug delivery systems: in vitro stability, in vivo fate, and cellular toxicity. Pharmaceutical Research, 21(5):807-809.

Chronopoulou L, Fratoddi I, Palocci S, Venditti I, Russom V. 2009. Osmosis Based Method Drives the Self-assembly of Polymeric Chain upto Micro and Nanostructures, Langmuir, 25:119406.

Fathalla Z, Khaled A, Hussein A, Alany R, Vangala A. 2015. Formulation and corneal permeation of ketorolac-tromethamine loaded chitosan nanoparticles. Journal of Drug Development and Industrial Pharmacy, 1:2-9.

Gadad A, Chandra P, Dandagi P, Mastiholimath V. 2012. Moxifloxacin loaded polymeric nanoparticles for sustain ocular drug delivery. Journal of Pharmaceutical Sciences and Nanotechnology, 5(2):1727-1731.

Javadzadeh Y, Ahadi F, Davaran S, Mohammadi G, Sabzevari A, Adibkia K. 2010. Preparation and physicochemical characterization of naproxen PLGA nanoparticles. International Journal, 81(2):498-502.

Kar S, Logd S, Om P, Debnath C, Verma S, Kumar S. 2013. Preparation of Lithium Niobate Nanoparticles by High Energy Ball Milling and their Characterization. Universal Journal of Material Science, 1(2):18-24.

Kaur H, Ahuja M, Kumar S, Dilbaghi N. 2011. Carboxymethyl tamarind kernel polysaccharide nanoparticles for ophthalmic drug delivery. International Journal of Biological Macromolecules, 1:833-837.

Konat Z, Contreras-Ruiz L, Loopez G, Romero B, Diebold Y, Seijo B, Saanchez A. 2011. Expression of MUC5AC in ocular surface epithelial cells using cationized gelatin nanoparticles. Molecular Pharma, 8(5): 1783-1788.

Kumar G, Rajdan B, Bajpai M. 2014. Formulation and evaluation of nanoparticles containing artemisinin HCL, International Journal of Research and Development in Pharmacy and Life Sciences, 3(2):925-932.

Liu W, Griffith M, Fangfu L. 2008. Alginate microsphere-collagen composite hydrogel for ocular drug delivery and implantation. Journal of Master Science, 19:3365-3369.

Mahmoud A, Feky G, Kamel R, Awad G. 2011. Chitosan/sulfobutylether-b-cyclodextrin nanoparticles as a potential approach for ocular drug delivery. International Journal of Pharmacy, 413(1-2):229-236.

Mandal B, Alexander K, Riga A. 2010. Sulfacetamide loaded Eudragit RL100 nanosuspension with potential for ocular delivery. Journal of Pharmaceutical Sciences, 13(4):510–523.

Meziani M, Pathak P, Hurezeanu R, This M, Enick R, Sun Y. 2004. Supercritical Fluid Processing Technique for Nanoscale Polymer Particles. Angewandte Chemie International Edition, 43:7047.

Mudgil M, Gupta N, Nagpal M, Pawar P. 2012. Nanotechnology: A new approach for ocular drug delivery system. International Journal of Pharmacy and Pharmaceutical Sciences, 4(2):105-110.

Mundada A, Avari J, Mehta S, Pandit S. 2008. Recent Advances in Ophthalmic drug delivery system. Pharmaceutical Review, 6(1):481.

Nagavarma B. Yadav H. Ayaz A. Vasudha L. Kumar S. 2012. Different techniques for preparation of polymeric nanoparticles. Asian Journal of Pharmaceutical and Clinical Research, 5(3):16-20.

Nimbalkar U, Dhoka M, Sonawane P. 2011. Formulation and optimization of cefpodoximeproxetil loaded solid lipid nanoparticles by box-behnkin design. International Journal of Research in Ayurveda and Pharmacy, 2(6):1779-1782.

Pardeike J, Muller R. 2009. Dermal and ocular safety of the new phospholipase A2 inhibitors PX-18 and PX-13 formulated as drug nanosuspension. Journal of Biomed Nanotechnology, 5(4):437-444.

Pignatello R, Ricupero N, Bucolo C, Maugeri F, Maltese A, Puglisi G. 2006. Preparation and characterization of Eudragit retard nanosuspensions for ocular delivery of cloricromene. AAPS PharmaSciTech, 7(1):27.

Ries C, Neufeld R, Ribeiro A, Veiga F, 2006, Nanoencapsulation: Method for preparation of drug loaded polymeric nanoparticles. Nanomedicine, 2:8-21.

Sapkota B, Mishra S. 2013. A Simple Ball Milling Method for the Preparation of P-Cuo/Zno Nanocomposite Photocatalysts with High Photocatalytic Activity. Journal of Nanoscience and Nanotechnology, 13(10):6588.

Shaikh S, Shivsharan K, Pawar R, Missal N, Mene H, More B. 2015. Tamarind Seed Polysaccharide: A Versatile Pharmaceutical Excipient And Its Modification, International Journal of Pharmaceutical Science Review and Research, 33(1):108.

Sharma U, Verma A, Kumar S, Pandey H, Pandey A. 2015. In vitro, in vivo and pharmacokinetic assessment of amikacin sulphate laden polymeric nanoparticles meant for controlled ocular drug delivery. Springer, 5:143-152.

Thassu D, Deeleers M, Pathak Y. 2007. Handbook of Nanoparticulate Drug Delivery System, Informa Healthcare USA, Inc. New York, 166 pp 6-8.

Wadhwa S, Paliwal R, Paliwal S, Vyas S. 2010. Hyaluronic acid modified chitosan nanoparticles for effective management of glaucoma: development, characterization, and evaluation. Journal of Drug Target, 18(4):292-302.

Wagh V, Inamdar B, Samanta M. 2008. Polymer Used in Ocular Dosage Form and Drug Delivery System. Asian Journal of Pharmaceutics, 2(1):12.

Yadav M, Ahuja M. 2010. Preparation and evaluation of gum cordia, an anionic polysaccharide for ophthalmic delivery. Carbohydrate Polymers, 81(4):871-877.