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# NOVEL STRATEGY FOR IMPROVING BIOAVAILABILITY OF OCULAR DRUG DELIVERY USING COLLOIDAL NANOSUSPENSION

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**Keywords:**

Nanosuspensions, Ocular drug delivery, Bioavailability, Colloidal dispersion

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**ABSTRACT:** Nowadays, a very large proportion of new drug candidates arising from drug discovery programs are water-insoluble and, for that reason, poorly bioavailable. The trouble is even more complex for drugs that belong to the BCS Class II category. To overcome these problems, nanotechnology is used to enhance the solubility as well as bioavailability of poorly soluble drugs. In the ocular drug transport system, ocular infections are dealt with by various topical drug applications in the form of solutions, suspensions, and ointment. These conventional dosage forms go through from the problems of poor ocular bioavailability due to minimal ocular residence time because of various anatomical and pathophysiological barriers prevailing in the eye. Nanotechnology refers to the particle size range of 1–1000 nm. Nanosuspensions are a part of Nanotechnology. Nanosuspensions are defined as the submicron colloidal dispersions of pharmaceutically active ingredient particles in a liquid phase, the measurement under 1µm, without any matrix material, which is stabilized by surfactants and polymers. Major concerns with topical ocular delivery include poor drug absorption and low bioavailability. Thus nanosuspension is an efficient technology to enhance the bioavailability of the ocular drug delivery system. This review article ordinarily focuses on an overview of ocular obstacles to anterior section delivery, along with ways to overcome these barriers using nanocarrier systems. Nanosupension not solely solves the trouble of poor solubility and bioavailability however also alter the pharmacokinetics of the drug and thus improving protection and efficacy.

**INTRODUCTION:** Ophthalmic drug delivery is one of the most fascinating and challenging endeavors dealing with pharmaceutical scientists. The anatomy, physiology, and biochemistry of the eye render this organ exceptionally impervious to foreign substances. Drug delivery to the eye can be broadly categorized into anterior and posterior segments **Fig. 1**.

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Conventional systems like eye drops, suspensions, and ointments can't be considered most suitable in the cure of vision-threatening ocular diseases [1]. However, more than 90% of the marketed ophthalmic formulations are in the form of eye drops. These formulations mainly target the diseases in the anterior segment of the eye [2].

Topical ocular medications do not reach the posterior segment of the eye. The posterior segment (retina, vitreous, choroid) can be treated through a high drug dosage regimen given intravenously or by way of intravitreal administration or implants or by periocular injections. Currently, the posterior segment drug delivery is a rapidly growing interest area in ophthalmic drug delivery [3].

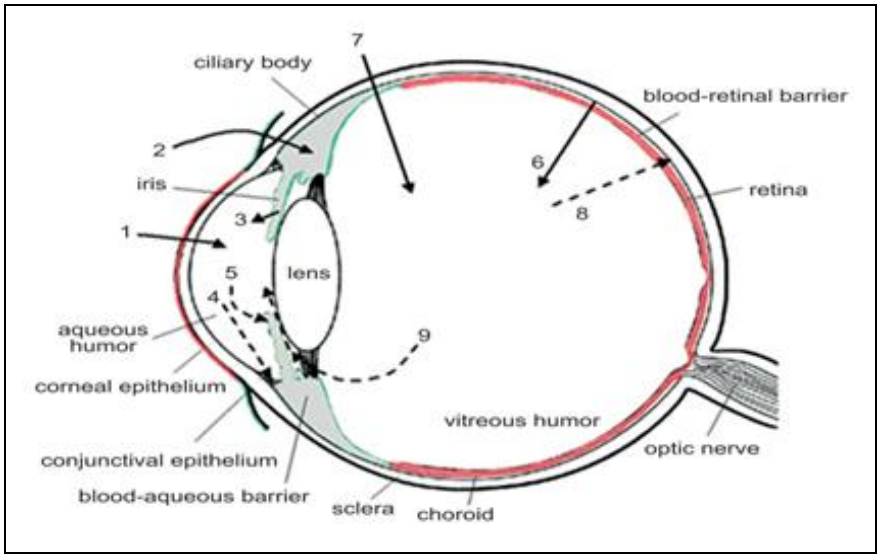


**FIG. 1: SCHEMATIC PRESENTATION OF THE OCULAR STRUCTURE WITH THE ROUTES OF DRUG KINETICS ILLUSTRATED** [4]

A suitable ocular formulation releases the drug overcoming the defensive barriers of the eye without causing permanent tissue damage. For anterior-segment drug delivery, frequent routes of administration are topical installation and subconjunctival injection, whereas, for posterior-segment drug delivery, common routes include systemic dosing, periocular and intravitreal injections, and topical dosing. The topical ocular administration of drugs has two different purposes: to treat superficial eye diseases, such as infections (*e.g.*, conjunctivitis, blepharitis, keratitis sicca) and to provide intraocular treatment through the cornea for illnesses such as glaucoma or uveitis.

For their favorable price advantage, the higher simplicity of formulation improvement and production, and the good patient acceptability, 90% of the marketed ophthalmic formulations are in the form of eye drops for soluble drugs; yet these conventional systems cannot be considered most fulfilling in the treatment of vision-threatening ocular diseases, in that most of the drugs are washed off from the eye by various mechanisms (lacrimation, tear dilution and tear turnover). Moreover, the highly impermeable corneal barrier restricts the entry of foreign substances. As a result, less than 5% of administered drug penetrates the cornea and reaches intraocular tissues [5].

**Anatomy of Eye:** The eye consists of two parts,

- Anterior
- Posterior segments.

**Anatomy of Anterior Segment of the Eye:** For ailments of the eye, topical administration is generally preferred over systemic administration because before reaching the anatomical barrier of the cornea, any drug molecule administered by the ocular route has to cross the precorneal barriers. These are the first limitations that slow the penetration of an active ingredient into the eye and consist of the tear film and the conjunctiva. Poor bioavailability of pills from ocular dosage types is frequently due to the precorneal loss factors. Moreover, frequent instillations of eye drops are necessary to maintain a therapeutic drug level in the tear movie or at the site of action. But the regularly occurring use of especially concentrated options might also induce toxic side effects and cellular damage at the ocular surface [6].

**Anatomy of the Posterior Segment of the Eye:** The smaller anterior segment is the part of the eye that includes the cornea and the lens. These structures focus light onto the photoreceptor cells of the retina in the posterior segment. The posterior segment consists of three layers, the sclera, choroid, and retina, surrounding the vitreous cavity, which is filled through the vitreous body. The sclera is a tough outer coat composed largely of connective tissue. It has a protected characteristic and also, by resisting intraocular pressure, keeps the form of the eyeball. The choroid is a vascular layer that, in conjunction with a separate retinal blood grant, affords the blood supply that supports the retinal cells. The retina, which is separated from

the choroid through Bruch's membrane, is the sensory inner coat of the posterior segment of the eye [7].

**Topical Drug Delivery into the Eye:** After ocular instillation, aqueous eye-drops solutions and suspensions will mix with the tear fluid and be dispersed over the eye surface. However, a number of pre-corneal factors **Fig. 2** can restrict ocular absorption by shortening the corneal contacting time of applied drugs. The most important elements are the drainage of an instilled solution, noncorneal absorption, and induced lacrimation. These physiological and anatomical constraints will restrict the penetration of the topically administered ophthalmic drug. As a result, only a few percent amounts of the instilled drug is delivered into the intraocular tissues [8].

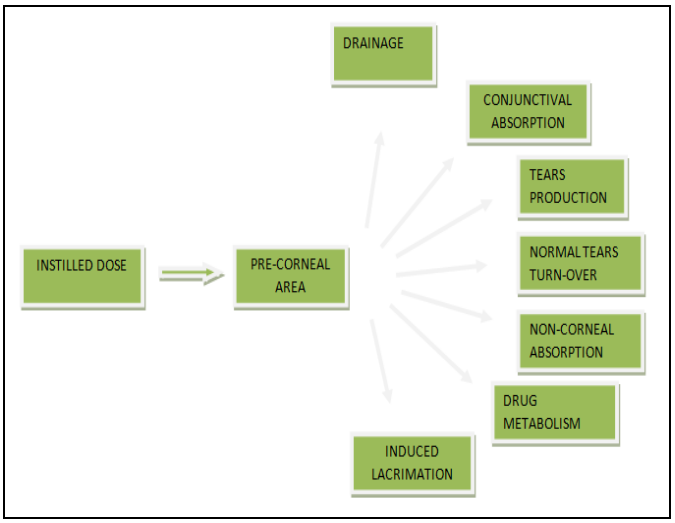


**FIG. 2: PRE-CORNEAL FACTORS LIMITING THE OCULAR ABSORPTION OF DRUGS**

For ailments of the eye, topical administration is commonly preferred over systemic administration because before reaching the anatomical barrier of the cornea, any drug molecule administered by the ocular route has to cross the precorneal barriers. These are the first barriers that slow the penetration of an active ingredient into the eye and consist of the tear movie and the conjunctiva. Poor bioavailability of tablets from ocular dosage forms is mostly due to the precorneal loss factors which are demonstrated in **Fig. 2**.

**Barriers to Ocular Drug Delivery:** The reason why it is difficult to achieve relevant therapeutic doses within the eye is primarily due to the presence of multiple barriers. When a dosage form is either administered topically or systemically, it faces multiple obstacles before reaching its site of action. As a result, ocular bioavailability from a topically administered drug is usually only 1%-7% of the applied dose. These barriers can be broadly classified as anatomical barriers and physiological barriers [9].

**Anatomical Barriers:** When a dosage form is topically administered, there are two routes of entry, either through the cornea or via the non-corneal route. The cornea is a very tight multilayered tissue that is mainly composed of five sections: epithelium, bowman's membrane, stroma, Descemet's membrane, and endothelium. Out of these, it's the epithelium, which acts as the principal barrier. These 5-6 layers of columnar epithelial cells with very tight junctions create high paracellular resistance of 12-16 kΩcm. It acts as a major barrier to hydrophilic drug transport through intercellular spaces. On the other hand, stroma, which consists of multiple layers of hexagonally arranged collagen fibers containing aqueous pores or channels, allows hydrophilic drugs to easily pass through, but it acts as a significant barrier for lipophilic drugs. Thus for a drug to have optimum bioavailability, it should have the right balance between lipophilicity and hydrophilicity. The remaining layers are leaky and do not act as significant barriers.

The non-corneal route bypasses the cornea and involves movement across the conjunctiva and sclera. This route is important especially for large and hydrophilic molecules such as peptides, proteins, and RNA [10]. The conjunctiva is more permeable than the cornea, especially for hydrophilic molecules, due to the much lower expression of tight junction proteins relative to the corneal epithelium. High vascularity of the limbal area renders this route not suitable for drug delivery as the blood vessels remove a large fraction of absorbed dose [11]. Only a small fraction of the dose reaches the vitreous.

**Physiological Barriers:** The eye's primary line of defense is its tear film. Bioavailability of topically administered drugs is further reduced by precorneal factors such as solution drainage, tear dilution, tear turnover, and increased lacrimation [12]. The lacrimal fluid is an isotonic aqueous solution containing a

mixture of proteins (such as lysozyme) as well as lipids. Following topical application, lacrimation is significantly increased, leading to dilution of an administered dose. This, in turn, lowers drug concentration leading to diminished drug absorption. Rapid clearance from the precorneal area by lacrimation and through nasolacrimal drainage and spillage further reduces the contact time between the tissue and drug molecules. This, in turn, lowers the exact time for absorption leading to reduced bioavailability. The average tear volume is 7-9 µL with a turnover rate of 16% per min [13]. Thus drugs administered as eye drops need to be isotonic and nonirritating to prevent significant precorneal loss.

**Barriers Avoiding Drug Delivery:** Topical administration is the most common route of ocular drug delivery. Despite its apparent easy accessibility, the eye is well protected from foreign materials and drugs by a number of very efficient mechanisms such as blinking, induced lacrimation, tear turnover, nasolacrimal drainage, which cause rapid removal of substances from the eye surface and by the cornea, which forms the physical-biological barrier **Fig. 3**. Consequently, these protective mechanisms and structural obstacles may cause subtherapeutic drug levels at the tissue target, particularly at the retinal level. Delivery of drugs to the posterior eye is challenging, and there is an increasing need for managing rapidly progressing posterior eye diseases, such as diabetic retinopathy, age-related macular degeneration, and optic neuropathy [14].

Currently, the intravitreal route is widely used to deliver therapeutic molecules to the retina. However, frequent administration of drugs via this route can lead to retinal detachment, endophthalmitis, and increased intraocular pressure. For this reason, ophthalmic drug delivery, particularly targeted to the posterior segment, is one of the most challenging endeavors facing ocular pharmacologists. The topical route represents a safer administration; therefore, a major challenge to the scientists is to overcome the ocular barriers and reach the tissue target. Systemic route (*e.g.*, oral, parenteral) is also used to reach the eye, though the drug transport across the ocular barriers (blood-aqueous barrier and blood-retinal barrier) is quite difficult [15].

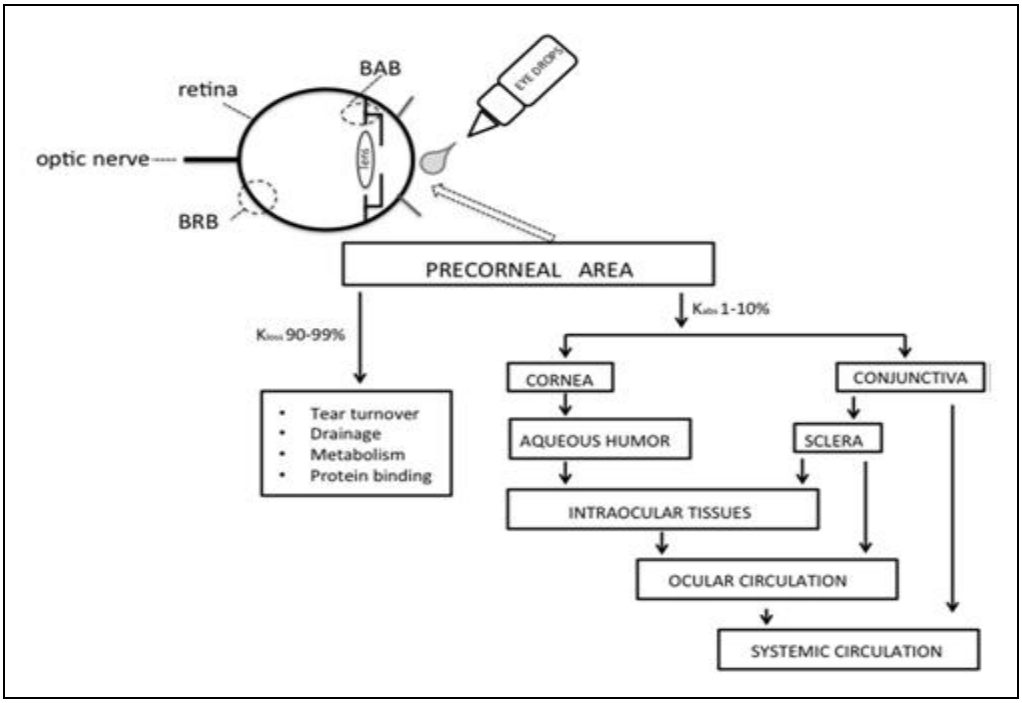


**FIG. 3: MODEL SHOWING THE MOVEMENT OF THE DRUG INTO THE EYE AFTER TOPICAL ADMINISTRATION. BAB, BLOOD-AQUEOUS BARRIER; BRB, BLOOD-RETINAL BARRIER**

**Novel Approach: Colloidal Nanosuspension:** An exciting challenge for developing suitable drug delivery systems targeted for ocular diseases is one of the major focuses of pharmaceutical scientists. There are several new ophthalmic drug delivery systems under investigation such as hydrogels [2],

microparticles [3] nanoparticles [4], liposomes [5], collagen shields [6], ocular inserts/discs [7], dendrimers [8], and transcorneal iontophoresis [9]. Polymeric nanoparticles are also able to target diseases in the posterior segment of the eye, such as age-related macular degeneration, cytomegalovirus retinitis, diabetic retinopathy, posterior uveitis, and retinitis pigmentosa [10]. Colloidal particles (nanoparticles) can be applied in the liquid form, just like eye drops and reduce discomfort caused by the application of semisolid ointments. They are patient-friendly due to less frequent applications, extended duration of retention in the extraocular portion without blurring vision [16].

Commercial ophthalmic suspension formulations were formulated with many problems such as non-homogeneity of dosage form, cake formation, settling of particles, aggregation of suspended particles. To overcome these problems, attempts have been made to prepare nanosuspensions for successful drug delivery. Nanosuspension not only improves the saturation solubility of a drug in media, but it is also an ideal approach for ophthalmic delivery of hydrophobic drugs in the eye. Nanosuspensions can also be used to achieve sustained release of the drug by incorporating or formulating with suitable hydrogel or muco-adhesive base or in ocular inserts [17]. Nanosuspensions are submicron colloidal dispersions of nanosized drug particles stabilized by suitable surfactants. Nanosuspensions are prepared using poorly water-soluble drugs without any matrix material suspended in dispersion. These can be used to enhance the solubility of drugs that are poorly soluble in water as well as lipid media. It also improves drug stability as well as bioavailability of poorly soluble drugs [18-25].

\An increase in the dissolution rate and bioavailability is observed in the reduction of drug particles into the sub-micron range. The vapor pressure effect leads to an increase in the solution velocity and saturation solubility of the nanosized particles. Also, an increased concentration gradient is observed due to decreased diffusional distance on the surface of drug nanoparticles; thereby increasing saturation solubility is also observed [26]. Various physicochemical parameters such as ionic strength, pH, monomer concentration, particle size, and molecular weight as well as surface charge are important for drug delivery [27]. Nanosuspensions had a quicker onset of action and enhanced dose proportionality. Nanosuspensions also alter the pharmacokinetic parameters, improves the safety and efficacy of the drugs [28].

**Advantages of Nanosuspension in Ophthalmology:** [29] Colloidal delivery systems have become a focus of attention in the field of biomedicine due to the potential benefits in providing wide improvements in drug delivery and targeting. They have been successfully used to:

- ✓ Enhance the solubility and bioavailability of drugs.
- ✓ Suitable for hydrophilic drugs.
- ✓ Higher drug loading can be achieved.
- ✓ Dose reduction is possible.
- ✓ Enhance the physical and chemical stability of drugs.
- ✓ Provides passive drug targeting.

**Formulation Consideration:** [30-32]

**Stabilizer:** The main function of a stabilizer is to wet the drug particles thoroughly and to prevent ostwald's ripening and agglomeration of nano-suspensions in order to yield a physically stable formulation by providing a steric or ionic barrier. The type and amount of stabilizing have a pronounced effect on the physical stability and *in-vivo* behavior of nanosuspension. Stabilizers that have been used so far are poloxomers, polysorbate, cellulosic, povidones, and lecithins [30].

**Organic Solvent:** Organic solvents are used in the formulation of nanosuspension if emulsions or microemulsions are used as a template. The pharmaceutically acceptable is less hazardous water-miscible solvent, such as methanol, ethanol, chloroform, ispropanol, and partially water-miscible solvents ethyl acetate, ethyl formate, butyl lactate, triacetin, propylene carbonate, benzyl alcohol, are preferent in the formulation over the conventional hazardous solvents, such as dichloromethane [31].

**Co-Surfactants:** The choice of co-surfactant is critical when using microemulsions to formulate nanosuspensions. Since cosurfactants can greatly influence phase behavior, the effect of co-surfactant on uptake of the internal phase for selected micro emulsion composition and on drug

loading should be investigated. Various solubilizers, such as Transcutol, glycofurol, ethanol, and isopropanol, can be safely used as co-surfactants in the formulation of microemulsions [32].

**Other Additives:** Nanosuspensions may contain additives such as buffers, salts, polyols, osmogent and cryoprotectant [32].

**Preparation of Nanosuspension:** For the preparation of nanosuspensions, mostly two methods, namely "Bottom-up technology" and "Top-down technology," are used, as shown (in **Fig. 4**) [33]. Bottom-up technology is an assembling method to form nanoparticles like precipitation, microemulsion, melt emulsification method and top-down technology involves the disintegration of larger particles into nanoparticles, examples of which are high-pressure homogenization and milling methods.

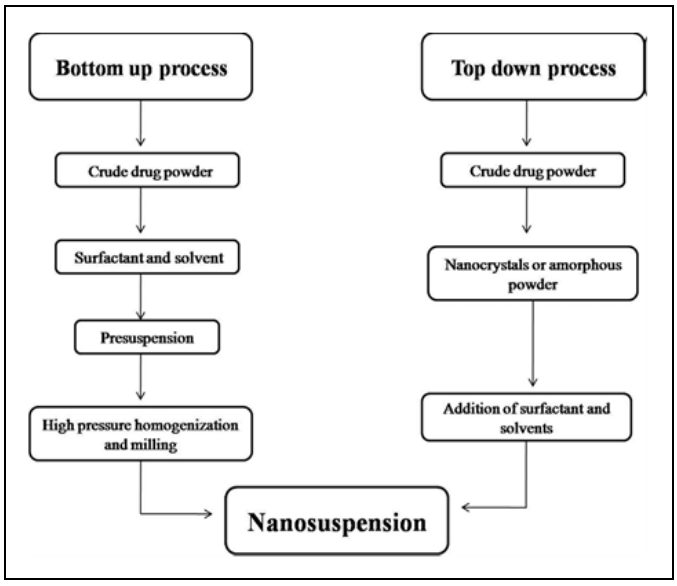


**FIG. 4: APPROACHES FOR THE PREPARATION OF NANOSUSPENSION**

**1. Milling Techniques:**

**Media Milling:** This method was first developed and reported by Liversidge (1992) [34]. The nanosuspensions by this method are prepared by a high shear media mill. The milling chamber was charged with the milling media, water, drug, and stabilizer and rotated at a very high shear rate under controlled temperature at least 2-7 days [35]. The milling medium is composed of glass, Zirconium oxide or highly cross-linked polystyrene resin. The high energy shear forces are formed as a result of the impaction of milling media with the drug, which results in the breaking of drug microparticles to nanosized particles. This technique is simple, inexpensive, and easily scalable. The only drawback associated with this technology is the contamination related to the beading material. That aside, several products have successfully reached the commercial level using this technology. Djordje Medarevic *et al.* formulated carvedilol nanosuspension by using wet media milling with help of hydroxyl propyl cellulose SL and sodium lauryl sulphate as stabilizers that resulted in stabilized formulation with enhanced dissolution rate [36].

Ligang Guo *et al*., used wet media milling to prepare andrographolide nanosuspension with non-ionic and ionic stabilizers resulted in nanosuspension having a particle size of about 300 nm with no chemical degradation [37]. Chengying Shen *et al*., has prepared nitrofurazone nanosuspension by using wet media milling has shown better bioavailability *via* dermal route when compared to nitrofurazone marketed gel [38]. Song Huang *et al*., used wet milling to formulate nanosuspensions of efonidipine hydrochloride resulted in enhanced bioavailability [39].

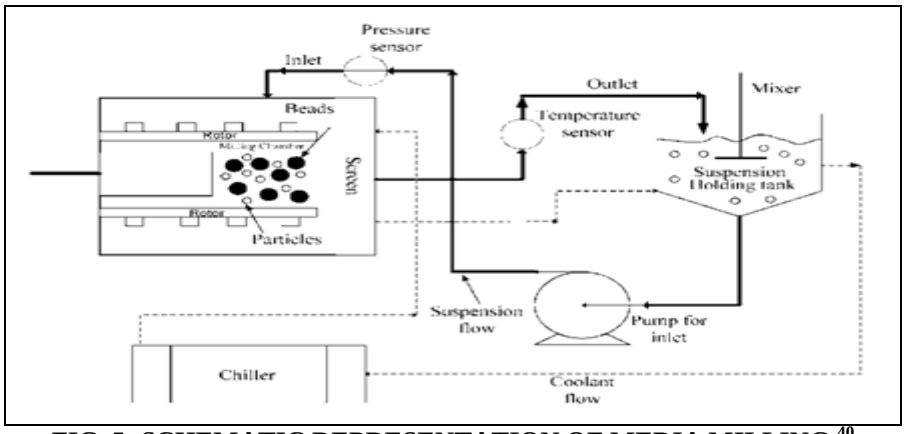


**FIG. 5: SCHEMATIC REPRESENTATION OF MEDIA MILLING [40]**

**Advantages:** [35]

- Very dilute as well as highly concentrated nanosuspensions can be prepared by handling 1 mg/ml to 400 mg/ml drug quantity.
- Nanosized distribution of a final nanosized product.

**Disadvantages:** [35]

- The media milling technique is time-consuming.
- Some fractions of particles are in the micrometer range.
- Scale-up is not easy due to mill size and weight.

**2. High-Pressure Homogenization:** This technique involve the following three steps: First, drug powders are dispersed in a stabilizer solution to form presuspension; after that, presuspension is homogenized by high-pressure homogenizer at a low pressure sometimes for pre-milling; and finally homogenized at high pressure for 10 to 25 cycles until the nanosuspensions are formed with desired size [41]. Alptug Karakucuk *et al*., have prepared Ritonavir nanosuspension *via* high-pressure homogenization using microfluidizer with HPMC 3 cps and sodium dodecyl sulfate as stabilizers resulted in improved oral bioavailability in fed state [42]. Emine Tashan *et al*., formulated the nanosuspension of ziprasidone by using a microfluidizer resulted in increased aqueous solubility compared to a coarse powder and physical mixtures of drug [43]. Sumathi R *et al*., prepared polymeric nanosuspension of naringenin by utilizing high-pressure homogenization led in elevated dissolution rate and better stability [44].

**Homogenization in Aqueous Media (Dissocubes):** Dissocubes technology was developed by Muller in 1999. The instrument can be operated at pressure varying from100 to 1500 bars (2 800 - 21 300 psi) and up to 2 000 bars with a volume capacity of 40 ml (for laboratory scale). For the preparation of nanosuspension, it is essential to prepare a presuspension of the micronized drug in a surfactant solution using a high-speed stirrer. According to Bernoulli's Law, the flow volume of liquid in a closed system per cross-section is constant. The reduction in diameter from 3 cm to 25 μm leads to an increase in dynamic pressure and a decrease of static pressure below the boiling point of water at room temperature. Due to this, water starts boiling at room temperature and forms gas bubbles, which implode when the suspension leaves the gap (called cavitation), and normal air pressure is reached. The size of the drug nanocrystals that can be achieved mainly depends on factors like temperature, number of homogenization cycles, and power density of homogenizer, and homogenization pressure. Preprocessing like micronization of drugs and high-cost instruments increases the overall cost of the dosage form. Various drugs like Amphotericin B, Ordinon, Thiomerasol, Fenofibrate, Melarsoprol, Buparvaquone, Prednisolone, Carbamazepine, and Dexamethasone were prepared as nanosuspensions using this method [45].

**Homogenization in Nonaqueous Media (Nanopure):** Nanopure is suspension homogenized in a water-free medium. It is a "deep-freeze" homogenization where the drug suspensions in a nonaqueous medium are homogenized at 0 °C or sometimes below the freezing point. Because of the very high boiling point and low vapor pressure of water, oils, and fatty acids, the drop of static pressure is not enough to begin cavitation in nanopore technology [46].

**3. Ionic Gelation:** In the ionic gelation method, the positive or negative charge of the hydrophilic polymer is complexed with a multivalent cationic (*e.g.* calcium chloride) or polyanionic (*e.g.* sodium tripolyphosphate) to form highly viscous gel particles with a size in the range of a nanometer. Ionic gelation method was developed by Calvo and Coworkers for the preparation of chitosan nanoparticles. In this method, polymer solutions and polyanion solutions are mixed to form nanoparticles. The basic mechanism involved in the formation of nanoparticles is the electrostatic interactions between positively charged amino groups present in polymer and negatively charged anion. In other words, it can be seen that in the ionic gelation method, due to interaction, the material undergoes the transition from liquid to the gel phase. The obtained chitosan nanoparticles generally are of small size in the range of 200-500 nm [47].

The study design was done using the design expert software for the statistical data presentation for analyzing the effect of % encapsulation efficiency, particle size, and zeta potential. The permeation study concluded that the optimized formulation of fluconazole showed higher permeation (%) compared to the marketed formulation of fluconazole [48].

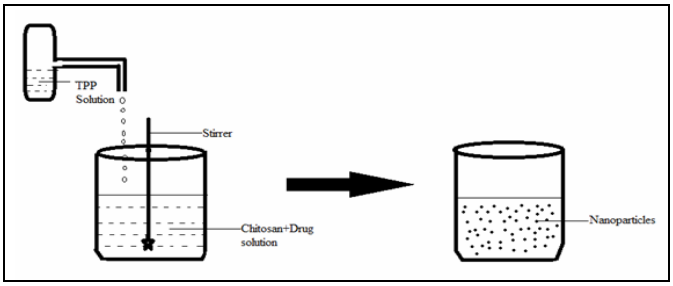


**FIG. 6: IONIC GELATION TECHNIQUE**

**4. Precipitation:** Within the last decade, precipitation has been applied to prepare submicron particles, especially for poorly soluble drugs [49]. The drug is first dissolved in a solvent; then this solution is mixed with a miscible antisolvent in the presence of surfactants. Rapid addition of a drug solution to the antisolvent leads to sudden supersaturation of drug and formation of ultrafine crystalline or amorphous drug solids [50].

**Advantages:**

- Simple process.
- Ease of scale-up.
- Economic production.

**Disadvantages:**

- Growing of crystals needs to be limit by surfactant addition.
- The drug must be soluble at least in one solvent.

**5. Supercritical Fluid Method:** Supercritical Fluid Method Supercritical fluid technology can be used to produce nanoparticles from drug solutions. The various methods attempted are the rapid expansion of the supercritical solution process (RESS), supercritical anti-solvent process, and precipitation with the compressed anti-solvent process (PCA). The RESS involves the expansion of the drug solution in supercritical fluid through a nozzle, which leads to loss of solvent power of the supercritical fluid resulting in precipitation of the drug as fine particles. Young et al. prepared cyclosporine nanoparticles in size range of 400-700 nm using this process. In the PCA method, the drug solution is atomized into a chamber containing compressed $CO_2$. As the solvent is removed, the solution gets supersaturated and thus precipitates as fine crystals. The supercritical antisolvent process uses a supercritical fluid in which a drug is poorly soluble and a solvent for the drug that is also miscible with the supercritical fluid. The drug solution is injected into the supercritical fluid and the solvent gets extracted by the supercritical fluid and the drug solution gets supersaturated. The drug is then precipitated as fine crystals [51-56].

**TABLE 1: SUMMARY OF METHODS USED FOR PREPARATION OF POLYMERIC NANOPARTICLES FOR OCULAR DELIVERY [57-59]**

| Method | Drug | Category | Polymer | Stablizer |
|---|---|---|---|---|
| Solvent | Carvedilol | Non-selective beta blocker | Eudragit E100 | Poloxamer 407 |
| displacement | Levofloxacin | Antibiotic | PLGA | PVA |
| Method | Diclofenac | NSAID | Eudragit S100 | Poloxamer 188 |
| Homogenization | Prednisolone | Antiinflamatory | Hydroxy ethyl | PLuronic F68 |
| | Dexamethasone | | cellulose | |
| Ionic Gelation | Fluconazole | Triazole antifungal | Gum cordial | Di octyl sodium sulfosuccinate |
| | Indomethacin | NSAID | Chitosan | - |
| Milling | Cyclosporine A | Immunosuppressant | PVA | - |

**Future Perspectives and Challenges:** In recent years, the nanosuspension approach has been complementarily utilized to solve the grievances developed due to poorly soluble drugs. The nanosuspensions having better solubility or redispersibility in the aqueous medium have attracted the attention of formulators due to their unique properties. Nanosuspension of poorly soluble drugs can be fabricated through a variety of methodologies, including media milling, ultra-sonication, high-pressure homogenization, precipitation, *etc*., as these techniques are observed to be quite fruitful and productive for obtaining nanosuspension. However, the nanosuspension obtained through

such techniques may be subjected to some kinds of stability problems like crystals growth, Ostwald ripening, *etc*. hence suitable stabilizers/polymers are imparted into nano-suspension to make them stable. The selection of stabilizers is very complicated and challenging as it takes too much time and efforts [60].

The future prospects of nano-suspension are encouraging since they can contribute as a valuable tool for product development scientists to overcome various formulation and drug delivery challenges, particularly with intractable drugs. Regardless of the several published research in the area of nanosuspension, the critical aspects of stability issue pertaining to nanosuspension is still unresolved. The stabilization capability of the electrostatic and steric stabilizers and its relationship with the properties APIs, attainable maximum particle size and resulting physical stability are the critical factors need to be further investigated. Future development of enabling technologies like nanosuspension will provide technical solutions to many formulation challenges currently faced by protein and peptide-based drugs [61].

**CONCLUSION:** Effective treatment of ocular diseases is a formidable challenge because of the nature of diseases and the presence of ocular barriers, especially in posterior ocular segments. Attempts have been made to improve ocular bioavailability through manipulation of product formulation such that Ocular drug delivery systems provide local as well as systemic delivery of the drugs. The novel advanced delivery systems offer more protective and effective means of therapy for the nearly inaccessible diseases or syndromes of eyes. Nanosuspension technique opens new vista for agents having poor bioavailability and instability that are related with the delivery of hydrophobic drugs, including those that are poorly soluble in aqueous as well as organic media. Nanosuspension techniques have proved to be an efficient delivery system in improving the bioavailability of ocular formulations.

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**CONFLICTS OF INTEREST:** None

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