RESEARCH PAPER

A Comprehensive Overview of Drug Nanocrystals and their Potential Applications in the Pharmaceutical Industry

[1]Neha Gallani[*], [2]Sachin Dighade and [3]S.D. Pande

[1]Department of Pharmaceutics, Institute of Pharmacy and Research, Badnera, Amravati, Maharashtra 444701
[2]Department of Pharmaceutical Chemistry, Institute of Pharmacy and Research, Badnera, Amravati, Maharashtra 444701
[3]Department of Pharmaceutics, Vidyabharti College of Pharmacy, Amravati, Maharashtra 444602
***Corresponding Author:** Neha Gallani, Department of Pharmaceutics, Institute of Pharmacy and Research, Badnera, Amravati, Maharashtra 444701*
E-mail: nehasgallani@gmail.com

Received: 24th April, 2026; Revised: 20th May 2026; Accepted: 24th August, 2026; Available Online: 30th August 2026

ABSTRACT
Drug nanocrystals have emerged as a highly promising strategy aimed at enhancing the solubility and dissolution rates of poorly water-soluble pharmaceuticals, a category that represents approximately 40% of newly developed drug compounds. Over the years, these microscopic particles have garnered significant attention due to their ability to enhance pharmaceutical performance by increasing the bioavailability and therapeutic effects of a variety of drugs. With their straightforward and easily scalable production techniques, nanocrystals have gained widespread acceptance in the pharmaceutical industry, leading to the successful commercialization of numerous products. This technology allows for the customization of various dosage form parameters, such as release kinetics, absorption profiles, and dosing requirements, thereby offering a versatile and adaptable solution for optimizing drug delivery systems. In essence, the versatility and efficacy of nanocrystal technology make it a highly promising tool for the design and development of advanced dosage forms tailored to meet the diverse needs and challenges of modern pharmaceutical formulations.

Keywords: Nanocrystals, Attractive approach, Novel Drug Delivery, Bioavailability, Advanced Dosage Forms

How to cite this article: Gallani N, Dighade S, Pande SD, A Comprehensive Overview of Drug Nanocrystals and their Potential Applications in the Pharmaceutical Industry. Int J Drug Deliv Technol. 2026;16(79s):774-779. DOI: 10.25258/ijddt.16.79s.141
Source of support: Nil.
Conflict of interest: None

INTRODUCTION

Nanotechnology, the "Defining Technology of the 21st century," is crucial in various scientific and engineering fields, including pharmaceuticals. It improves drug delivery, enhances effectiveness, and reduces drug size to nanometers. Nanomedicine, tissue engineering, and biosensors are among the applications of nanotechnology. Advancements in nanotechnology promise to improve drug delivery and expand the horizons of medicine and pharmacy in the future. Nanotechnology is a field focusing on creating and using nano-sized particles, measured in nanometers. Pharmaceutical Nanotechnology involves working with materials and devices with at least one dimension of extremely tiny size. Advancements in nano-based drug delivery systems, such as liposomes, carbon nanotubes, polymeric micelles, dendrimers, inorganic nanoparticles, nanocrystals, and quantum dots, are being studied to enhance drug targeting and delivery [1-3]. Drugs in the nanometer size range offer several -advantages in various dosage forms, including:

Larger surface areas enhance drug effectiveness, enhance solubility, facilitate faster dissolution, improve oral bioavailability, and lead to faster therapeutic effects. They require smaller doses and offer consistent performance with or without food [4].

**Author for Correspondence: nehasgallani@gmail.com*

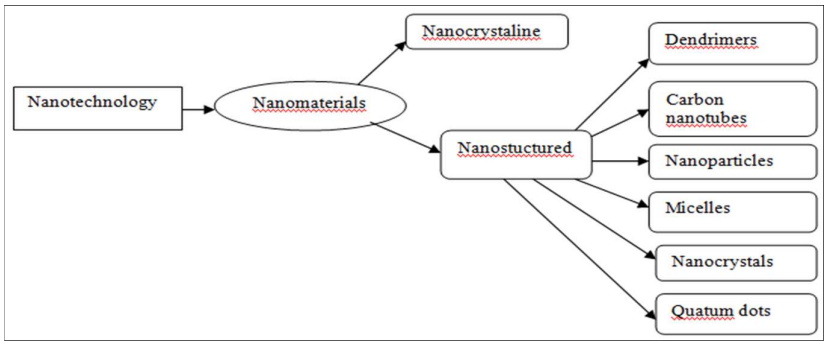

Figure 1: Schematic diagram of various types of Pharmaceutical Nanosystems

The field of drug development encounters significant obstacles when it comes to enhancing the solubility of therapeutic compounds, particularly those falling within the challenging BCS classes II or IV. To overcome this issue, nanonization has emerged as a cutting-edge technique that involves reducing the size of micronized particles to nanoparticles. One notable innovation within nanonization is the development of nanocrystals, which are crystalline nanoparticles typically ranging from 200 to 500 nm in size.

These nanocrystals play a crucial role in boosting the oral bioavailability of drugs through various mechanisms. For starters, they effectively increase the saturation solubility of the drugs, thereby enhancing their overall dissolution rate. Additionally, nanocrystals have the potential to improve mucoadhesion, which can further enhance drug absorption and efficacy. One key advantage of using nanocrystals is that they eliminate the need for carrier molecules, simplifying the formulation process. Moreover, these innovative drug delivery systems can be seamlessly integrated with traditional dosage forms, offering a comprehensive approach to advancing drug therapy. Through the strategic application of nanocrystals, pharmaceutical researchers can unlock new possibilities for overcoming solubility challenges and improving the effectiveness of therapeutic compounds, especially those categorized under BCS classes II or IV. [5-7].

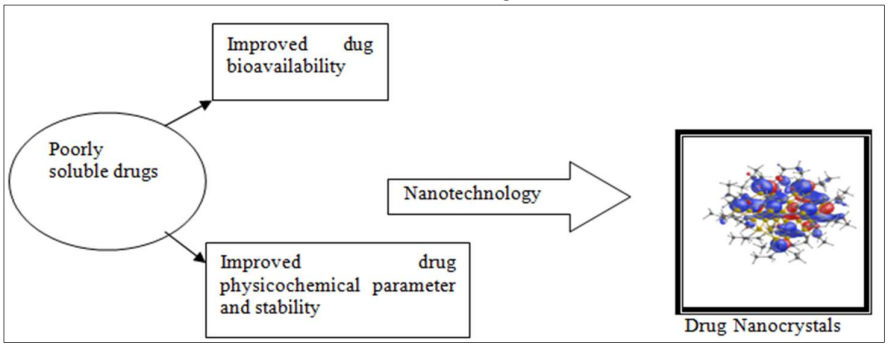

Figure 2: Nanocrystals of Poorly Soluble Drugs

The consideration in the scaling up process for nanocrystals drug products [8]:

1) Scaling nanocrystal drug products from academic to industrial scales is crucial for formulation development due to the gap between lab and industrial settings.
2) Maintaining batch-to-batch consistency is more challenging at larger industrial scales.
3) Addressing reproducibility challenges involves process characterization, equipment selection, robust formulation development, and stability studies. These considerations ensure consistency and quality in nanocrystal drug products.

Nanocrystals Based Formulations: The primary method for formulating poorly soluble drugs is through 'nanosuspensions,' offering versatile administration routes like oral, parenteral, and pulmonary, with a strong preference for intravenous (IV) use due to its safe profile without toxic chemicals and solvents [9-11].

Nanosuspension: Nanosuspensions are 200 nm drug particles for IV administration, prepared through precipitation and stabilizers. Stability is crucial due to crystal growth susceptibility, requiring stabilizers with high affinity, high diffusion velocity, and safety and acceptability for the body [9-11].

Tablet: Nanocrystals are incorporated into tablets through direct compression, resulting in various tablet types. Elan's Nano-Crystal® Technology simplifies medication disintegration, providing a convenient, water-free solution for patients[9-11].

Capsule: PEGs, available in liquid, semi-solid, and solid forms, are commonly used for capsule filling. Liquid PEG disperses drug powder, recrystallizes, and entraps

nanocrystals, while solid PEG fills hard gelatin capsules or solidified liquid suspensions [9-11].

Emulsion: Emulsions are preferred for parenteral formulations, but their complexity makes them unsuitable for large-scale production. Sol-Emuls technology offers a solvent-free alternative, using high-pressure homogenization to disperse liquid oil droplets with drug nanocrystals, efficiently localizing drugs with poor solubility in water and oils [9-11].

Powder for Inhalation: Nanocrystals are used for pulmonary drug delivery, especially for asthma. Techniques like milling and homogenization create nanosuspensions, which are spray-dried into inhalable powders. Carriers like lactose enhance flow[9-11].

Pellets: Nanocrystal pellets, similar to tablets and capsules, provide controlled-release oral dosages with high absorption and minimal side effects. Matrix pellets, produced through melt pelletization, offer simpler production methods [9-11].

Properties of Nanocrystals [12-15]:

Increased Dissolution Velocity: Surface area enlargement through size reduction improves drug dissolution, while micronization increases bioavailability. Nanonization increases surface area and dissolution velocity, reducing low solubility.

Increase in Saturation Solubility: Traditionally, saturation solubility (cs) is considered a constant dependent on the compound, dissolution medium, and temperature, valid for micrometer-sized or larger powders. However, for particles below 1-2 µm, saturation solubility becomes size-dependent, increasing with decreasing particle size (below 1000 nm).

Preparation of Nanocrystals: Nanocrystals are created through various methods, including the top-down method, which breaks down larger particles to nanoscale dimensions, the bottom-up method, which builds nanocrystals from smaller components or molecules, and the combination method, which combines elements of both methods to create nanocrystals using a hybrid approach. These techniques focus on producing nanosized crystals [16-20].

1) **Top down Methods:** High-pressure wet media milling is a method used to create nanosuspensions by dissolving a stabilizer in an aqueous medium, adding the drug, and milling the mixture with milling pearls under high pressure. Stabilizer concentrations can range from 10% to 80%. Top-down technology reduces large crystalline particles into smaller ones using techniques like milling and high-pressure homogenization. However, these methods may have limitations in achieving nanocrystals smaller than 100 nm, prompting the development of alternative methods.

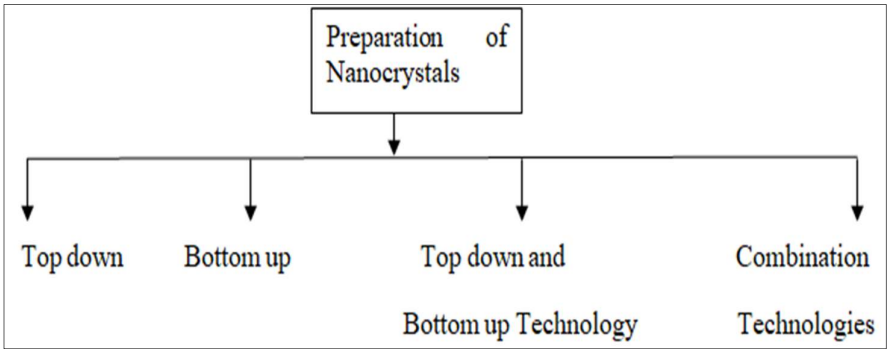

Figure 3: Preparation of Nanocrystals

Milling: Milling is a process used in pharmaceutical formulation to reduce particle size by applying mechanical energy. This process causes stress, strain, and deformation, leading to particle fracture. Crystalline materials are more prone to fracture due to their internal imperfections. Mills apply compression, shear, and impact stress types. Wet milling, specifically NanoCrystals® technology, uses bead or pearl mills to reduce particle size using impact-driven shear forces. This low-energy technique can face challenges like erosion and product adherence. To address these, coating the beads and using agitator-equipped mills or container movement for larger batches is used. Milling time varies based on factors like surfactant content, drug hardness, and media size.

High-Pressure Homogenization: High-pressure homogenization: Microfluidizer Technology (IDD-PTM) creates small particles by collision of two fluid streams under pressures up to 1700 bar. This method is used in technologies like Insoluble Drug Delivery-Particles and Triglide®. Dissocubes® Technology uses piston-gap homogenizers to force a drug through a gap at high pressure, reducing particle size. Nanopure® Technology uses a piston-gap homogenizer with non-aqueous dispersion media and optional low-temperature homogenization, reducing particle size with shear forces and particle collisions.

Bottom Technology: Bottom-up methods for producing nanocrystals in pharmaceutical formulations involve precipitation and evaporation methods, such as cryogenic

solvent evaporation, high gravity controlled precipitation, and supercritical fluid technology. Solvent-antisolvent precipitation is a cost-efficient and straightforward option when combined with high-speed homogenization or sonication. Low-temperature evaporation processes like spray drying or fluid bed drying can also be cost-effective alternatives for solidification. The bottom-up method, also known as the Precipitation method, is one of the earliest techniques for producing drug nanocrystals, where the drug is dissolved in a solvent system miscible with the anti-solvent, typically using water.

The preparation process comprises the following steps: The process of creating a drug solution involves dissolving the drug in an organic solvent, which is chosen based on the drug's solubility. The solution is then added to water containing polymeric stabilizers, causing particles to precipitate from the anti-solvent, forming a milk-like suspension. This suspension is then filtered and dried using a tray dryer set at 40°C. Methods like Rapid Expansion of Supercritical Solutions (RESS), Supercritical Anti-Solvent (SAS) techniques, and Enhanced Precipitation by the Anti-Solvent (EPAS) technique have been used to develop products like Hydrosols and Nanomorph™.

Nanoprecipitation: Precipitation methods involve dissolving active drug substance in an organic solvent and adding it to a nonsolvent, causing nanocrystals to precipitate. Stabilizers are needed to prevent nanocrystal growth. This simple, cost-effective, and scalable method requires control of parameters like stirring rate, temperature, and solvent type. However, it's limited for insoluble drugs. Some drugs create an O/W two-phase system, resulting in carotenoid nanocrystals.

Supercritical Fluid Technology: Supercritical fluid technology, a cutting-edge method, is utilized to produce solid nanoparticles by dissolving pharmaceutical drugs in carbon dioxide, a natural and widely available compound, and then exposing them to vacuum atomization, a crucial step in the process that aids in the formation of uniform particles with enhanced properties. The supercritical anti-solvent technique, recognized for its environmental friendliness, plays a pivotal role in the pharmaceutical industry by generating highly pure particles that meet strict quality standards, thereby contributing to the development of advanced drug delivery systems. Additionally, supercritical fluid crystallization, characterized by its reliance on high temperatures and pressures, stands out as a preferred method due to its unique ability to utilize carbon dioxide as a solvent, offering a safe and cost-effective alternative in comparison to traditional solvents. Furthermore, Rapid Expansion of Supercritical Solutions (RESS), a technique specifically designed for active pharmaceutical ingredients (APIs) with high solubility in supercritical carbon dioxide, showcases superior efficiency in producing fine particles that are vital for improving drug bioavailability and efficacy. Lastly, the solvent evaporation method known as spray drying, while effective in creating dry powders from liquid solutions, poses certain limitations such as potential thermal degradation of sensitive drugs, underscoring the importance of selecting the most suitable technique based on the specific characteristics of the pharmaceutical compound being processed.

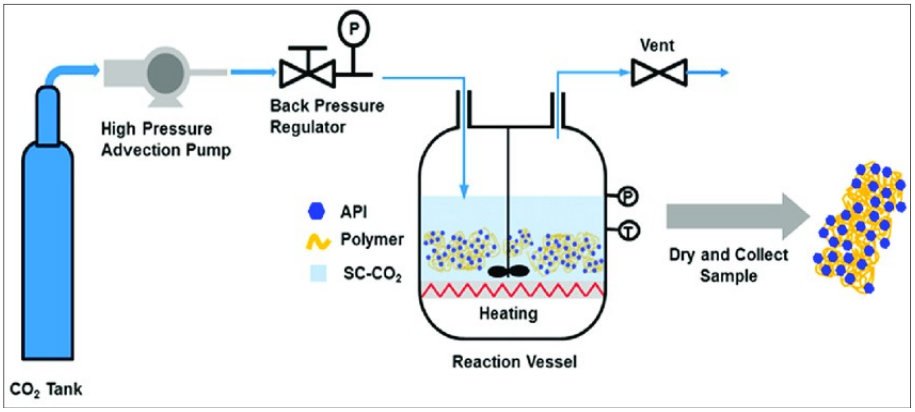

Figure 4: Supercritical Technology

Top Down and Bottom up Technology: Top-down and bottom-up technology, including Nano-Edge® and spray drying, is used for nanocrystal preparation. Nano-Edge Technology involves homogenization, micro-precipitation, and lipid emulsions to create small particles for poorly water-soluble drugs. Spray drying, which involves spraying solution droplets in a cyclone, enhances dissolution rate and bioavailability of drugs.

Combination Technologies:

Nanoedge® Technology (Microprecipitation™ and High Shear Forces (NANOEDGE™): Baxter's Nanoedge® Technology uses precipitation and high-energy shear forces to prevent particle growth during precipitation. This process, known as the annealing process, converts amorphous or partially amorphous particles into crystalline material, making it suitable for drugs with low toxicity and low toxicity, such as N-methyl-2-pyrrolidinone [21].

Nanopure® XP Technology: Nanopure® XP technology offers scalability and large-scale production under conventional conditions. PharmaSol uses pre-treatment and homogenization to create nanocrystals smaller than 100 nm, producing translucent nanosuspensions.

Characterization of Drug Nanocrystals [22-24]:

- Particale size and size distribution:
- Shape and Morphology
- Particle Surface Charge:
- Crystalline State
- Sedimentation/Creaming
- Dissolution Velocity & Saturation Solubility

Key Characteristics of Drug Nanocrystals [25]:

- Increased Saturation Velocity: Nanocrystals exhibit an enhanced saturation velocity, allowing drugs to reach their maximum solubility more rapidly.
- Increased Dissolution Velocity: The dissolution rate of drugs in nanocrystal form is accelerated, leading to faster and more effective absorption.
- Increased Adhesiveness: Nanocrystals adhere better to surfaces and cell membranes, which can enhance their interaction with biological systems.

CONCLUSION

Nanocrystals are a valuable solution for poorly soluble drugs, enhancing their solubility and bioavailability by reducing particle size. Nanosuspensions offer a cost-effective method to address these issues. Large-scale production employs high-pressure homogenization and media milling. Nanosuspensions exhibit advantages like faster dissolution, improved solubility, bioadhesion, surface modification flexibility, and simplified post-production processing, making them versatile for various administration routes. The poor solubility of drugs presents a significant challenge for oral delivery, prompting the use of innovative formulation technologies. Drug nanocrystals offer a versatile approach to enhance drug performance across different administration routes, including oral, parenteral, dermal, ophthalmic, nasal, vaginal, and pulmonary. This technology is emerging as a successful solution for improving drug delivery in various applications.

REFERENCES

1) Yellanki SK, Singh J, Nerella NK, Deb SK, Goranti S. Nanotechnology for Poorly Soluble Drugs. Research Journal of Pharmacy and Technology. 2010;3(3):688-93.
2) Chauhan NN, Patel NV, Suthar SJ, Patel JK, Patel MP. Micronization of BCS Class–II Drugs by Various Approaches for Solubility Enhancement–A Review. Research Journal of Pharmacy and Technology. 2012;5(8):999-1005.
3) Vyas A, Gidwani B. Technologies to counter poor solubility issues: a review. Research Journal of Pharmacy and Technology. 2013;6(11):1258-70.
4) Birajdar GO, Kadam VS, Chintale AG, Halle PD, Nabde MK, Maske KS. A Comprehensive review on nanotechnology. Research Journal of Pharmacy and Technology. 2013;6(5):486-95.
5) Kalimuthu S, Yadav AV. Nanobased Drug Delivery System: A Review. Research Journal of Pharmacy and Technology. 2009;2(1):21-7.
6) Shinde V, Amsa P, Tamizharasi S, Karthikeyan D, Sivakumar T, Kosalge A. Nanosuspensions: a promising drug delivery strategy. Research Journal of Pharmacy and Technology. 2010;3(1):39-44.
7) Babu VR, Aleem MA, Nikhat SR, Aslam S, Khan M. Nanosuspension Technology for Poorly Water Soluble Drugs: An Overview. Research Journal of Pharmacy and Technology. 2011;4(4):515-20.
8) Patel N, Parmar J, Gupta A, Choudhary R. Aquasome: A Self Assembling Nanoparticulate Drug Carrier System. Research Journal of Pharmacy and Technology. 2012 Nov 1;5(11):3.
9) Gadhvi V, Brijesh K, Gupta A, Roopchandani K, Patel N. Nanoparticles for brain targeting. Research Journal of Pharmacy and Technology. 2013;6(5):454-8.
10) Sharma S, Issarani R, Nagori BP. Development of Aceclofenac Nanosuspension Stabilized by Poly vinyl alcohol and Sodium dodecyl sulphate. Research Journal of Pharmacy and Technology. 2015;8(3):235-41. DOI: 10.5958/0974-360X.2015.00027.X
11) Malviya V, Manekar S. Design, development and evaluation of aceclofenac and curcumin agglomerates by Crystallo Co-Agglomeration technique. Research Journal of Pharmacy and Technology. 2021;14(3):1535-41. DOI: 10.5958/0974-360X.2021.00272.9
12) Shen D, Jin T, Xiao Y, Zhu X, Hua Y. Preparation of pazopanib-fumarate disodium glycyrrhizinate nanocrystalline micelles by liquid-assisted ball milling. European Journal of Pharmaceutical Sciences. 2023 Sep 1;188:106530. https://doi.org/10.1016/j.ejps.2023.106530
13) Fathi-Karkan S, Ramsheh NA, Arkaban H, Narooie-Noori F, Sargazi S, Mirinejad S, Roostaee M, Sargazi S, Barani M, Shadman SM, Althomali RH. Nanosuspensions in ophthalmology: Overcoming challenges and enhancing drug delivery for eye diseases. International Journal of Pharmaceutics. 2024 Jun 10;658:124226. DOI: 10.1016/j.ijpharm.2024.124226
14) Parveen N, Abourehab MA, Thanikachalam PV, Khar RK, Kesharwani P. Nanocrystals as an emerging

nanocarrier for the management of dermatological diseases. Colloids and Surfaces B: Biointerfaces. 2023 May 1;225:113231. DOI: 10.1016/j.colsurfb.2023.113231

15) Liu Y, Zhao J, Chen J, Miao X. Nanocrystals in cosmetics and cosmeceuticals by topical delivery. Colloids and Surfaces B: Biointerfaces. 2023 Jul 1;227:113385. https://doi.org/10.1016/j.colsurfb.2023.113385

16) Karimian A, Parsian H, Majidinia M, Rahimi M, Mir SM, Kafil HS, Shafiei-Irannejad V, Kheyrollah M, Ostadi H, Yousefi B. Nanocrystalline cellulose: Preparation, physicochemical properties, and applications in drug delivery systems. International journal of biological macromolecules. 2019 Jul 15;133:850-9. DOI: 10.1016/j.ijbiomac.2019.04.117

17) Raghav N, Vashisth C, Mor N, Arya P, Sharma MR, Kaur R, Bhatti SP, Kennedy JF. Recent advances in cellulose, pectin, carrageenan and alginate-based oral drug delivery systems. International Journal of Biological Macromolecules. 2023 Jul 31;244:125357. DOI: 10.1016/j.ijbiomac.2023.125357

18) Safitri N, Rauf N, Tahir D. Enhancing drug loading and release with hydroxyapatite nanoparticles for efficient drug delivery: a review synthesis methods, surface ion effects, and clinical prospects. Journal of Drug Delivery Science and Technology. 2023 Oct 21:105092. DOI:10.1016/j.jddst.2023.105092

19) Malehmir S, Abedini A, Sobhani-Nasab A, Eshraghi R, Akbari M, Atapour A, Hasan-Abad AM. A review of biogenic routes for the manufacture of manganese oxide nanostructures and its anti-cancer, drug delivery, anti-bacterial, and bioimaging potentialsmanrathanami. Inorganic Chemistry Communications. 2023 Aug 26:111306. https://doi.org/10.1016/j.inoche.2023.111306

20) Nagdiya D, Kumar M, Arora S, Bajaj T, Kujur S, Rana P, Kumar A, Singh A, Singh C. Drug delivery systems of gefitinib for improved cancer therapy: A review. OpenNano. 2023 Aug 19:100183. https://doi.org/10.1016/j.onano.2023.100183

21) Geng F, Fan X, Liu Y, Lu W, Wei G. Recent advances in nanocrystal-based technologies applied for ocular drug delivery. Expert Opinion on Drug Delivery. 2024 Feb 1;21(2):211-27. DOI: 10.1080/17425247.2024.2311119

22) Lhaglham P, Jiramonai L, Jia Y, Huang B, Huang Y, Gao X, Zhang J, Liang XJ, Zhu M. Drug nanocrystals: Surface engineering and its applications in targeted delivery. iScience. 2024 Oct 16. DOI: 10.1016/j.isci.2024.111185

23) Ghodrati AD, Turk CT. Nanocrystals and their applications in pharmaceutical technology: An up-to-date overview. Journal of Research in Pharmacy. 2024 Nov 1;28(6). http://dx.doi.org/10.29228/jrp.865

24) Malviya V, Burange P, Thakur Y, Tawar M. Enhancement of solubility and dissolution rate of atazanavir sulfate by nanocrystallization. Indian Journal of Pharmaceutical Education and Research. 2021 Jul 1;55(3):S672-80. DOI: 10.5530/ijper.55.3s.17

25) Castillo Henríquez L, Bahloul B, Alhareth K, Oyoun F, Frejková M, Kostka L, Etrych T, Kalshoven L, Guillaume A, Mignet N, Corvis Y. Step-By-Step Standardization of the Bottom-Up Semi-Automated Nanocrystallization of Pharmaceuticals: A Quality By Design and Design of Experiments Joint Approach. Small. 2024 Feb 1:2306054. https://doi.org/10.1002/smll.202306054