Different Approaches for Producing the Nanoparticle: A Review

Rishika Chauhan
Lecturer, Pharmaceutical Science, Haridwar, Uttarakhand, 8077487875, Rishichauhan789@gmail.com

Abstract

Nanotechnology has shown a bridge to improve the pharmacokinetic and pharmacodynamics activity of the drug system. Because of their unique size reliant properties, it offers plausibility to grow new therapeutics. Nano delivery (NDS) systems a sort of new developing science where materials in the nanoscale extend has being utilised to serve as means of symptomatic tools in different manners. Recent decades, nanotechnology has been impressive research interest in particulate conveyance frameworks. Nanotechnology at present an attractive platform because of many reason there biosensor role, electrochemical sensor, agricultural development nanobots, stealth technology, high drug loading efficiency, thermal ablation of cancer cell by nanoshells, formulation by waste material and the single step procedure for biosynthesise of NP. Nanoparticle can be prepared by the chemical, physical, and biological method. It has a multiple benefits in treating diseases by site-specific, target-oriented delivery; various applications of nanotechnology applications are also discussed. This review focuses on nanoparticles synthesis methods using different techniques for obtaining Nano colloids, nanorods, metal nanoparticles, Silver, gold, nanoparticle also focus on solid lipid nanoparticles synthesis, classification of nanoparticles.

Key words: Nanoparticles, Preparation, solid lipid nanoparticle, classifications, Applications.

Introduction

Nanoparticle is Greek word denote dwarf or small.

Its indicate A/M=1 billiamiline of meter 10^9-------Understand by an example 100crore rupee=1rupee.

Various associations have a distinction in opinion in characterizing NMs According to the Environmental Protection Agency (EPA), "NMs can display unique properties dis comparable than the proportional synthetic compound in a larger dimension" [40] The US Food and Drug Administration(USFDA) refer to NMs as "materials that have at any rate one measurement in the scope of roughly 1 to 100 nm and show measurement subordinate marvels" Similarly, [42, 40] The International Organization for Standardization (ISO) has portrayed NMs as a "material with any outside nanoscale measurement or having inward nanoscale surface structure" Nanofibers, nanoplates, nanowires,quantum specks and other related terms have been characterized dependent on this ISO definition Likewise, the term

nanomaterials depicted as "a fabricated or common material that has unbound, amassed or agglomerated particles where outer measurements are between 1–100 nm size range", as indicated by the EU Commission. [49] As of late, the British Standards Institution proposed the accompanying definitions for the logical terms that have been utilized. The prefix "nano" has found in a decade ago an ever-expanding application to different fields of the information. Nanoscience, nanotechnology, nanomaterials or nanochemistry are just a few of the new nano-containing terms that happen every now and again in logical reports, in mainstream books as well as in papers and that have gotten comfortable to a wide open, even of non-specialists. [60] Along these lines, the nanosized world is regularly estimated nanometres (1nm comparing to 10-9 m) and it includes frameworks whose size is above molecular measurements and beneath naturally visible ones (for the most part > 1 nm and < 100 nm).

Nanotechnology is the study of the little; the extremely little. [7] It is the utilization and manipulation of matter at a modest scope. At this size, iotas and atoms work in an unexpected way, and give a variety of amazing and fascinating employments. Nanotechnology and Nanoscience examines have risen rapidly during the previous years in a wide scope of item spaces. It gives chances to the development of materials, including those for clinical applications, where ordinary techniques may arrive at their cut-off points. Nanotechnology ought not to be seen as a solitary method that only affects explicit territories. Albeit frequently alluded to as the 'modest science', [36] nanotechnology does not simply mean little structures and items. Nanoscale highlights are frequently fused into bulk materials and enormous surfaces. [55, 68, 72] Nanotechnology speaks to the plan, creation and application of materials at nuclear, atomic and macromolecular scales, so as to deliver new nanosized materials (Hahens et al., 2007). Pharmaceutical nanoparticles are characterized as solid, submicron-sized (under 100 nm in distance across) tranquilize transporter that might be biodegradable. The term nanoparticle is a joined name for both Nanosphere and nanocapsules. Nano spheres are framework in which medication is consistently scattered, while nanocapsules are the framework in 234which the medication is encompassed by a one of a kind polymeric membrane. Nanoparticles are light in weight, faster; easily get into smaller space, cheaper, more efficient, and having different properties at very small scale

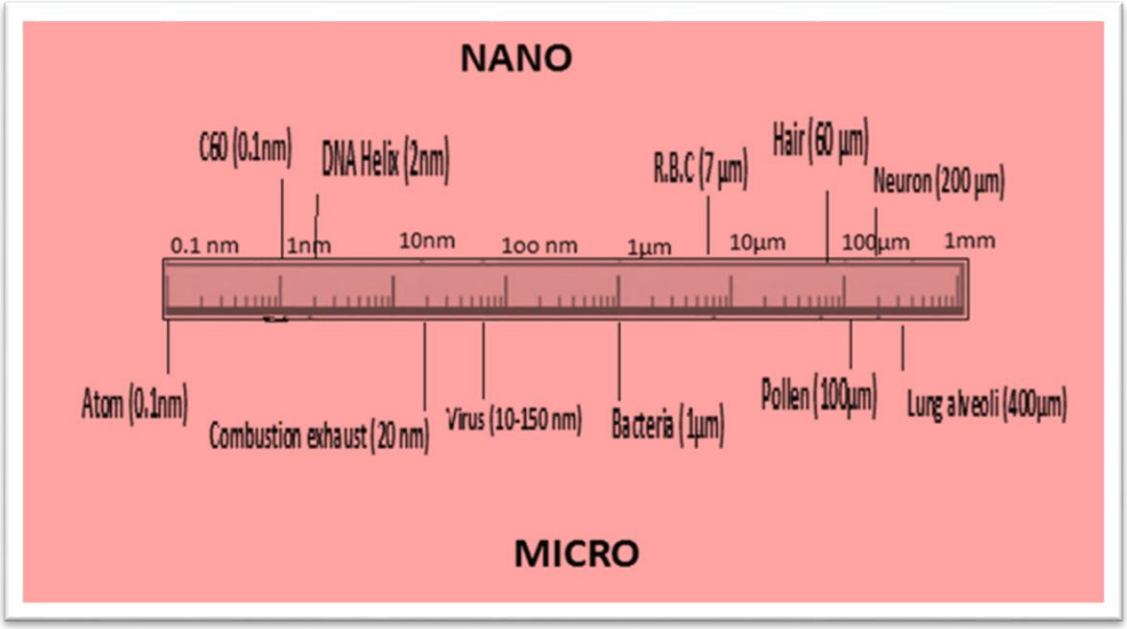


Fig:-1 Length scale showing definition of 'nano' and 'micro' size and compared to biological component

DRUG	**RANGE (nm)**
SLN	80-300
Carbon nanotube	1-5
Dendrimer	1-10
Antibody	10
Gold NP [47]	10
Quantum dots [92]	5-50
Liposomes	80-300

Table: - 1 Different drug measured in nanometre range [5, 9, 24, 49, and 76]

Properties:-

Larger surface area

Make material chemically reactive

Quantum effect

Size dependant

High strength

Optical properties

Category	**Synthesis method**	**Property**
Gold NP [47,53]	(P.B.C.M)	Optical, electric and magnetic properties

Silver NP [28, 90]	(P.B.C.M)	Unique optical, thermal, physical and chemical property and catalytic property
Quantum dots [24]	(P.B.C.M)	Electronic property and Unique luminescence characteristic
Qucertin NP [89]	Chemical and biological method	Cancer preventive property
MesoporousNP [10,23,38,94]	Conventional method	Unique adjustable property such as pore vol. High surface area etc.
ZNO NP [77]	(P.B.C.M)	Peculiar property
Chitosan NP [31, 95]	(P.B.C.M)	Mucoadhesive property

Table: - 2 Properties of different types of nanoparticle

Classification [12, 36, 40, 48, 49, 68, 78]

Nanoparticle are categorised by many ways on the basis of dimension, composition, morphology, uniformity, also on the physical and chemical characteristics and their origin.

Nanoparticles are categorised on the basis of their origin

a) Natural: - it produced by naturally either by biological species or anthropogenic activity.

b) Artificial or synthetic: - synthetic produced by mechanical grinding or synthetically way that was physical, chemical etc.

It i**s categorised on dimension based into 3 parts**

a) 1dimensions –it has only parameter either length or breadth or height (ex-very thin in surface coating) 1dimension<1000nm
b) 2 dimension:-it has only length and breadth ex;-nanowires, nanotubes 2dimension<100nm
c) 2 dimensions: - it has all parameter including length height, and breadth ex-Nano shell, nanoparticles, etc.

It is categorised on basis of **morphology 3 parts**

a) Highest aspect ratio: - nanoparticles include nanotubes and nanowires, with various shapes, such as helices, zigzags, belts, nanowires with diameter that varies with length.

b) Lowest aspect ratio: - it include spherical, oval, cubic, prism, helical, or pillar. Collections of many particles exist as suspension or colloids, powders.

It is categorised on **composition** based into 3 parts

a) Single material: - it consist a single constituent material or be a composite of several materials.

b) Composite: - it has multiphase NP one phase has based on dimension and either combines np with other another np example hybrid Nanofibers.

It can be categorised on **uniformity**

a) In homogeneous

b) Isometric

It is categorised on **physical and chemical character based** into 6 parts

a) Carbon-based nanomaterials: it contain carbon and it found morphologies such as sphere, tubes, example; - nanotubes, fullerenes etc.

b) Semiconductor nanomaterials: - it consist both properties b/w (between) non-metal and metal.it provide efficient in H2O splitting application.

c) Metallic based: - made of metal precursor it have a unique optoelectrical properties due to this property they have many application in research area.

d) Ceramic based: - are inorganic non-metallic solid used mainly in application like catalysis, photo degradation of dyes, photo catalysis. Examples are amorphous form dense form and crystalline forms etc.

e) Polymeric based: - are consisting mainly the polymer.

f) Lipid based NP: - It comprises ranging b/w 10- 1000 nm and consist lipid moieties.

Category name	**Sub divided**	**Example**
1. Based on morphology	a) Highest aspect ratio	Nanowire,tube,pillar, etc.
	b) Low aspect ratio	Nanowire, nanotube, nanohelics etc.
2.Based on dimension	a) 1dimensions	
	b) 2 dimension	Nano wire, nanotubes, etc.
	c) 2 dimension	Nanoshell , nanoparticles, etc.
3. Based on uniformity	a) In homogenous	Dispersed
	b) Isometric	Agglomerates
4. Based on composition	a) Single material	Compact hollow

	b) Composite	Coated ,encapsulated, etc.
5. Based on physical and chemical characters	a) Carbon based NP	Carbon nanotubes, fullerenes, etc.
	b) Metallic based NP	Cu. Ag, Au etc.
	c)Semiconductor	Both metal and non-metal
	d) Ceramics	Amorphous, dense, crystalline forms etc.
	e) Polymeric	Nanosphere, nanocapsules
	f) Lipid based NP	
6. Based on origin	a) Natural	Curcumin nanoparticle ,clove nanoparticle etc.
	b) Artificial	Zn, Ag, etc.

Table: - 3 Classification of nanoparticles

Limitations of nanotechnology

Little size and enormous surface area can prompt molecule – molecule aggregation, handling of nanoparticles in liquid and dry structures nd become difficult. These issues need to be over precede nanoparticles can be used clinically or made economically accessible. Polymeric NP (Nanoparticle) consist have a limited capacity of drug loading, it have slow bio degradable case systemic toxicity, on repeated administration toxic may be formed during the biotransformation of polymeric carrier. [55, 72]

A significant disadvantage is that the nanoparticles may be imperceptible subsequent to releasing them into nature, whereby can cause issue if remediation is required. In this way, investigative systems are should have been improved to identify nanoparticles in the environment. [93] Adequate data is required with respect to the relationship of surface area and science to the working and poisonous quality of nanoparticles. Additionally, novel nanoparticles inspire a danger of introduction during production or use. In this way, complete hazard appraisals must be thought about. [64] When there is a need to utilize the rare material for the elaboration of the nanoparticles, an effective procedure for reusing and recuperation is required. [15] Consequently, further examination is required to fill the wide information hole in the zone of Nano lethality as this will help to improve hazard appraisal.

Characterization of NP

by using Fourier transform infrared spectroscopy (FTIR), particle size distribution, powder X-ray diffraction (XRD),surface area, Dynamic Light Scattering (DLS), photon correlation

spectroscopy(PCS) using Zeta size Nano ZS, laser diffraction, Scanning electron microscopy (SEM) , saturation solubility, and Brunauer, Emmett and Teller (BET) . Determine the some method of characterization below: - [12, 49, 40]

UV-visible absorption spectroscopy: in this method light is passed through the sample solution and the amount of absorbed light is measured. if the particles aggregates the solution will be appear blue purple colour that means gold nanoparticle is dispersed and then black ppt to clear solution shown then it shows the agglomeration of nanoparticles. The peak is around 500-600nm.

Zeta potential: - the stability and size distribution both are the important criteria that should be measured by the help of zeta potential. Zeta potential of nanoparticle is the overall charge that particles require in a particular medium. It is measured in zeta meter, depend on the pH and electrolyte concentration, its value is ± 30 Mv or above shows the good stability property of a NP.

Dynamic light scattering (DLS): by using the same instrument we can also measure the DLS.By using this method is measured the direct particle size with in the solution. It measures the hydrodynamic dia. of particles, the range of measured is 0.6nm- 6micron.it give the exact particle size but not determine the shape of NP.

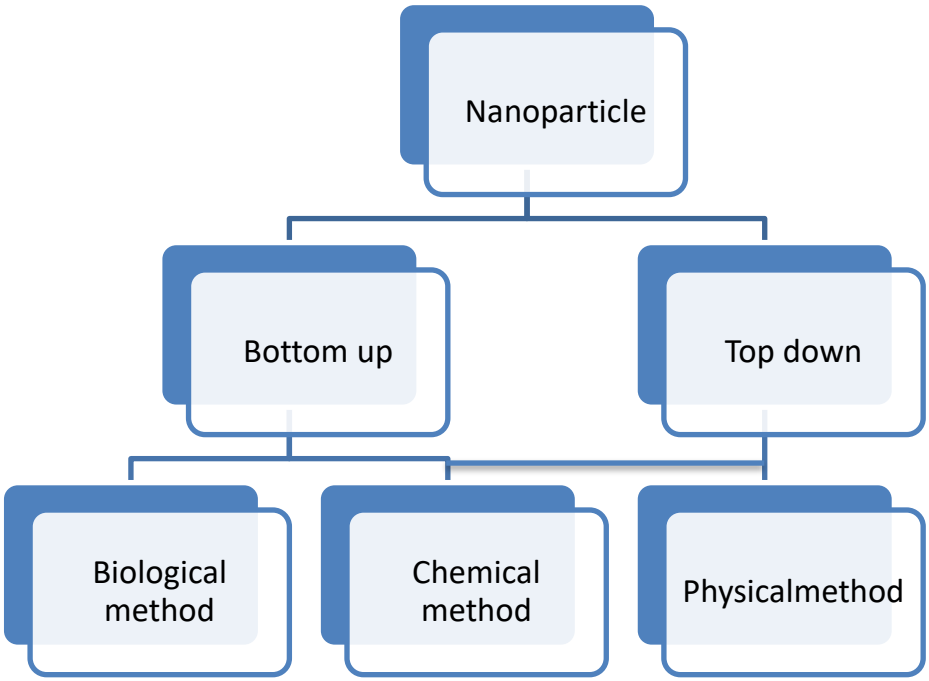
Microscopic techniques: - These techniques involve the SEM and TEM. Used for the morphological characters studied of NP.TEM (transmission electron microscopy) has a set of electromagnetic lenses that used to control the imaging electron that generate the structural details and recorded into a photographic film. A beam can pass through the specimen and give the detail about the size of nanoparticle, crystallography, and morphology as well as composition information or details. It has some major analysis method in a scientific fields, and biological sciences but it was a time consuming process. **(SEM) Scanning electron microscope:** another characterization method, this method of characterization is used electron beam instead of lenses and a series of coils; it gives high resolution images, it magnifying images up to 200.000times. It acts like optical microscope, it determine the morphology, topography, crystallography, elemental composition and orientation. Another improvisation microscopy technique is scanning tunnelling microscopy that was based on the tunnelling principle.

(**AFM) Atomic force microscopy:** It is an advanced microscopic technique. It provides a topographical map. It's have the ability to image non-conducting samples, most accurate method , measure the thickness of a crystal growth layer shows the real picture that will help to understand the function betterly.

Electron diffraction:- this method is used to determine the nature of drug .it determine easily the material is exhibit in which form whether crystalline ,amorphous or poly crystalline in case of amorphous material it shows the images in diffused rays while in crystalline form material it will shows the spotted.

Differential scanning calorimetry (DSC):- is used to determine the nature of crystallinity within nanoparticles by measuring the glass transition temperature, melting point and their associated enthalpies. This method along with XRPD is used in determination of the extent of which multiple phases exists in the interior and their interaction with the drug.

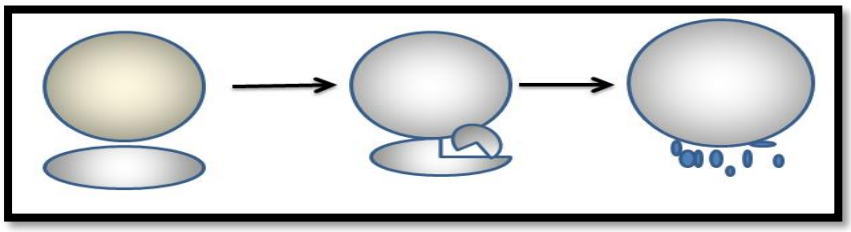
Methods of preparation of nanoparticle:-



Physical method:-

Mechanical milling: - it is a kind of top down process. Top down process phenomena is based on the Bulk material is break into small particles. [62] Nanoparticle produced by mechanical attrition. Nanoparticle formed in this method by using a mill in which energy is imparted a course- grained material to effect a reduction in particle size .with the help of metallic ball going to break the bulkmatreial into nanosized particle. Its principle is based on the size reduction in mechanical attrition device lies in the energy imparted to the sample

during impacts between the milling media. When the moment of collision during which particles [48] (between) b/w two colloiding balls formed the nanosized powder particle.



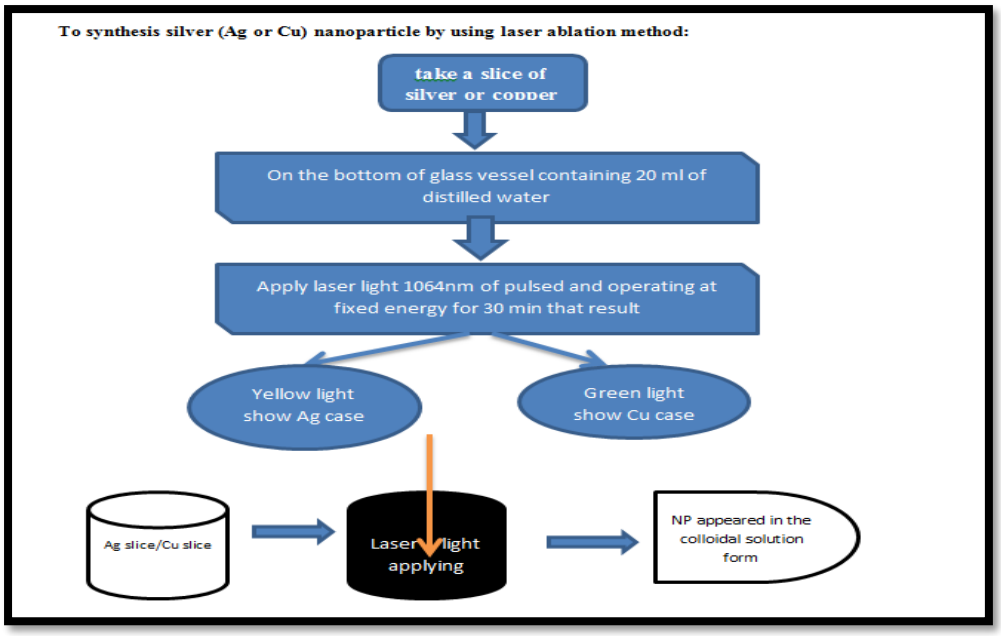
To synthesis silver (Ag or Cu) nanoparticle by using laser ablation method:-

Laser ablation: - using laser (light amplification by stimulated emission of radiation) light to vaporize material. Nanoparticle by laser ablation a solid target that lies liquid or gaseous state and collection of NP [3] in the form of power or colloidal solutions.

Advantages:-

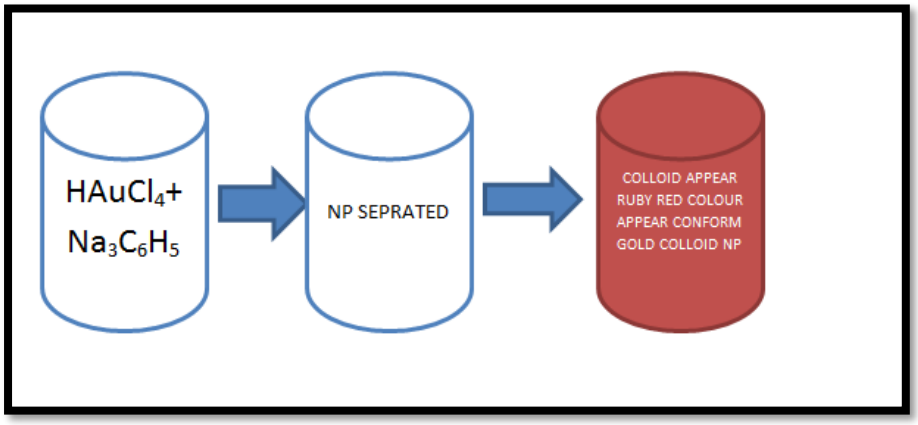
- Fast, cheap, straight formed for nanoparticles as compared to other
- Not required any kind of long reaction
- Don't use any kind of toxic, hazardous, materials.
- Does not require multistep
- It has ecofreindly method also one of the methods that have been used for biological application by using this techniques collection of nanoparticles in the form of colloidal solution
- It functionalised as ligand of choice
- Simplest experimental techniques

To synthesis by laser ablation of silver or copper nanoparticle require high purity of silver or copper. [52, 75]



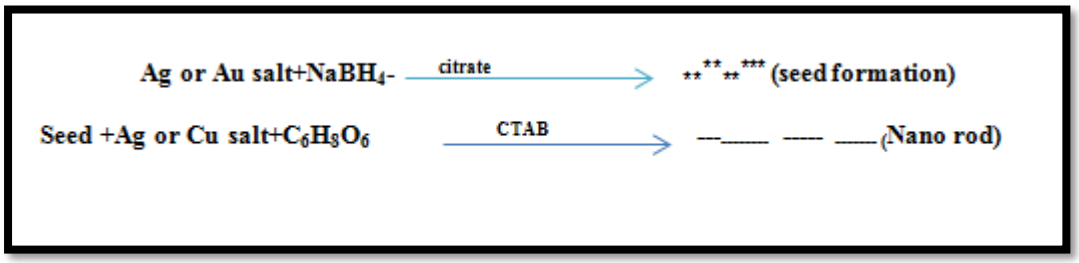
Chemical method of synthesis:-

Synthesis of gold colloid: - the synthesis method of gold colloid is simple, convenient procedure also done in laboratory scale. In this synthesis method firstly in water starting from solution of using hydrogen tetrachloroaurate [69] + solution of ($Na_3C_6H_5$) trisodioum citrate for achieving size 10-20nm [25]. In this method of synthesise citrate act as weak reducing agent or as a stabilizer or both. Then a layer of citrate anions adsorbs around each nanoparticle and prevent aggregating the anions electrostatic repulsion keep the nanoparticle separated as a result ruby red appearance in colloid conform the gold nanoparticle. [20, 47]

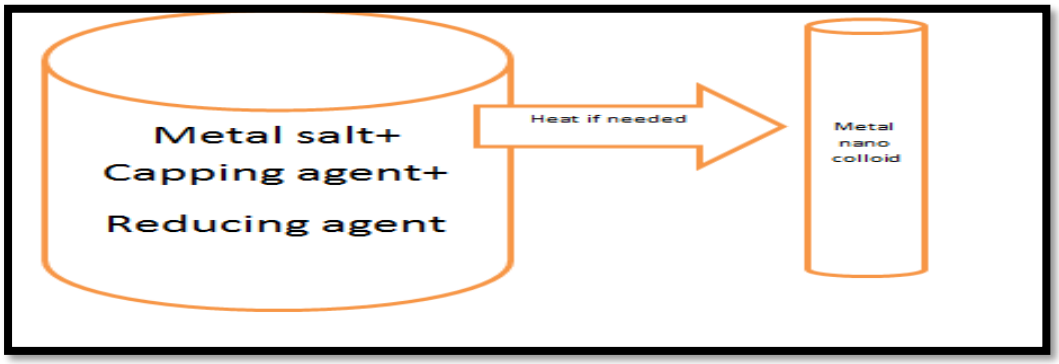


Synthesis of gold Nano rods:-sodium borate hydrate will reduce gold or silver salt into very small size particle and get the seed form and [80] citrate act like stabilising agent /capping agent that will inhibit particle growth so next step use in this that seed add the gold or silver metal salt and weak reducing agent such as ascorbic acid, [84] weak reducing agent favour the growth and using cetyltrimethylammoniumbromide stabilizer provide the rod shaped like

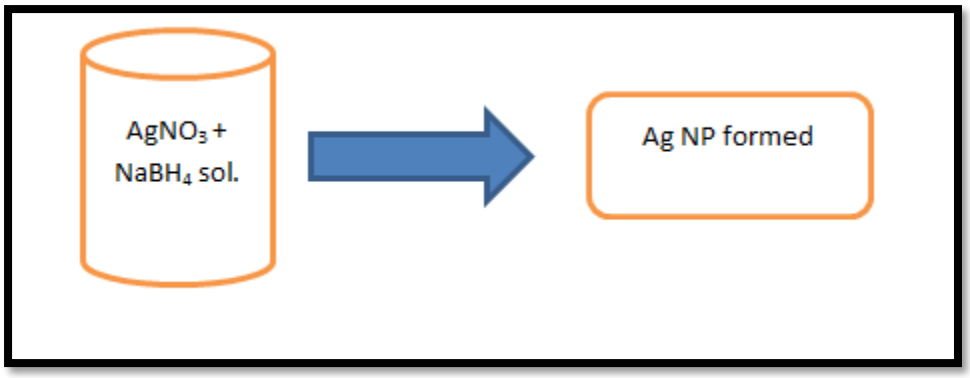
template [69] (by using weak reducing agent rod shaped NP obtained and by using strong reducing agent synthesis the seed)



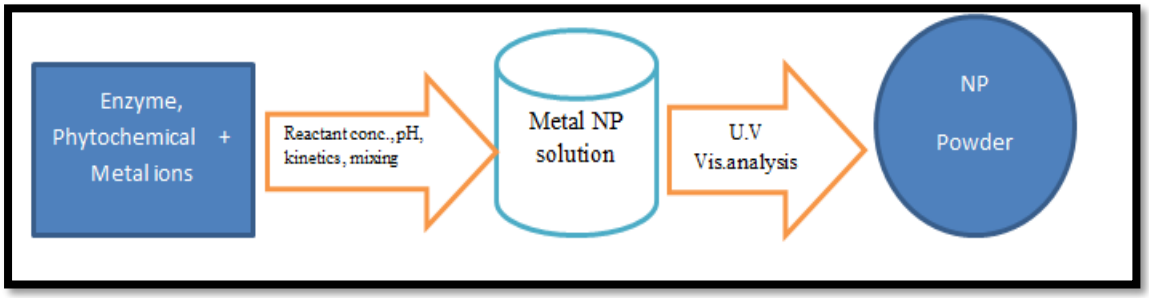
Synthesis of metal nanoparticles: - For production of metal NP required capping agent, reducing agent and metal salt it is type of chemical method .In this method the synthesis of metal NP are produced by using the reducing agent such as sodium citrate, ascorbic acid etc. [44] that reducing agent will reduce metal salt into metal nanoparticle. But these metals NP are highly unstable; that metal NP can make an effort to conjugate formed an agglomeration/aggregation form, for avoiding the problem in the synthesis addition of capping agent or stabilising agent such as thiol citrate polymer, PVP that will prevent the aggregation or Agglomeration reaction in the synthesis process.



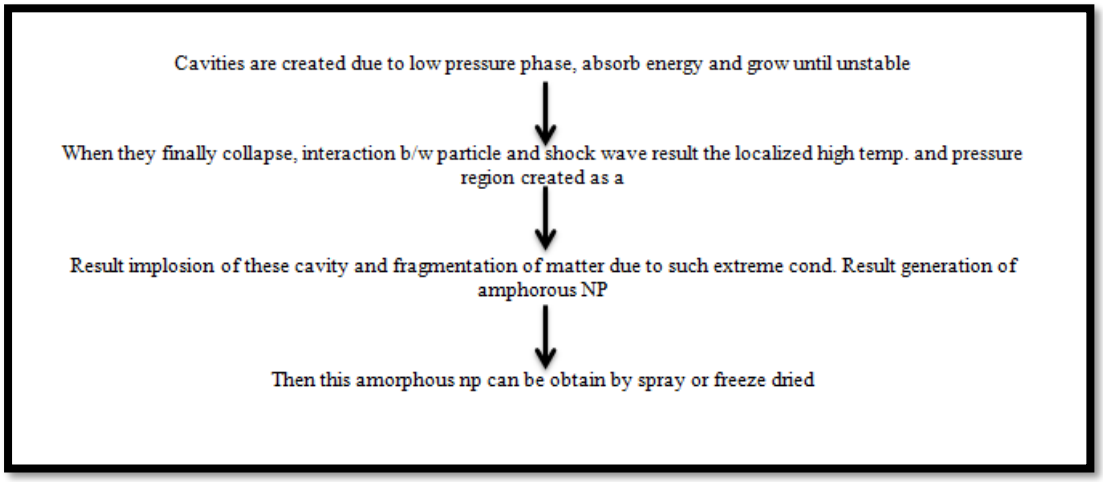
Synthesis of silver nanoparticles: - By using this method silver nanoparticle can be formed in laboratory. [57, 75] By using deionized water in micro centrifuge tube and some appropriate amount of silver nitrate ($AgNO_3$) in the tube then immediately add of some amount of freshly prepared sodium borohydride solution and SDS sol. The solution agitates the micro centrifuge tube containing all compounds vigorously. If yellow colour appears in the tube so it indicates the presence of silver nanoparticle.



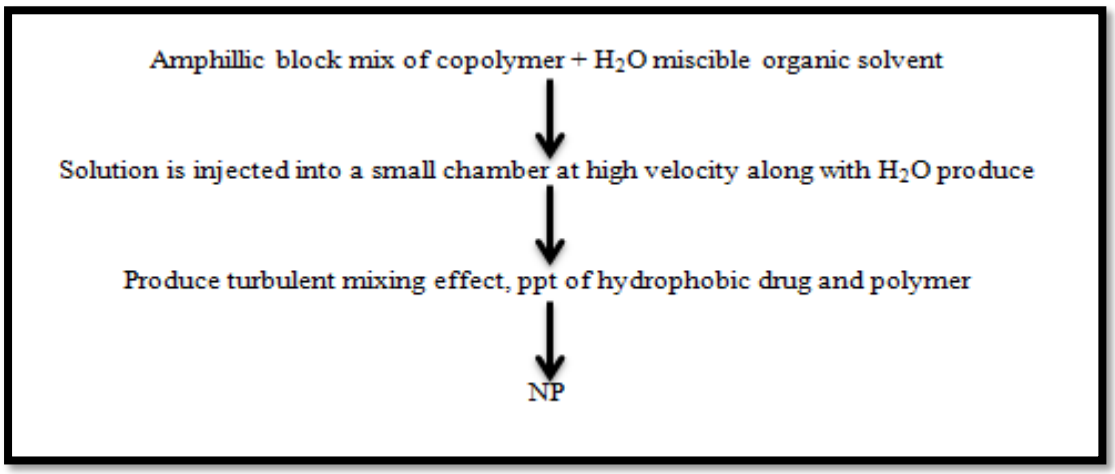
Synthesis by Biological method: - Cheap, convenient, economic, suitable, one single step procedure, By using of enzyme (bacteria, yeast, fungi, microorganism) or phytochemical (such as leaves, roots, flower, plant tissue) the enzyme present microorganism will act as reducing agent/stabilizer both and in phytochemical plant tissue act like a reducing agent and capping agent. [84] This method helped has several advantages it reduce toxic chemical conc., ecofreindly, fast by modifying culture, ph, temp., and nutrient media. Using bacteria can be synthesised the gold, silver, Pd, lead, Cd Ex:-neem using synthesized the Ag/Au NP etc. [25, 33]



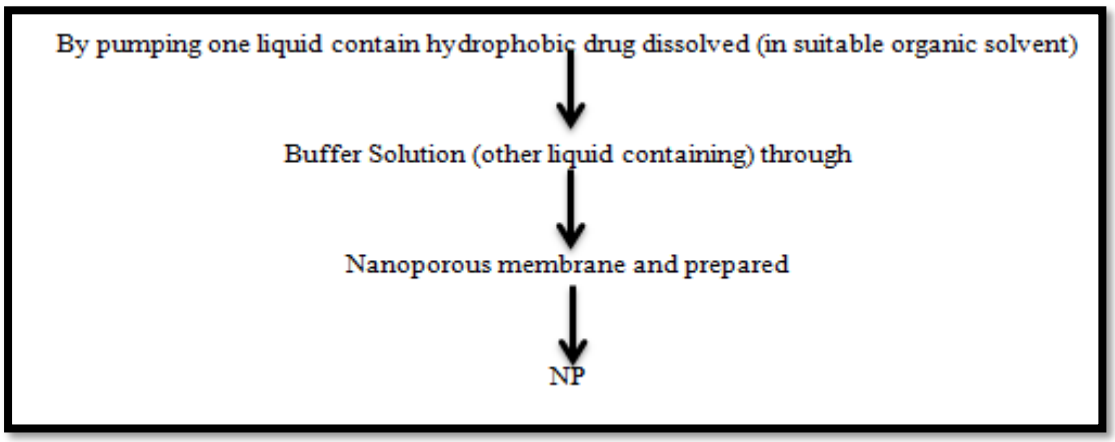
Synthesis of amphorous nanoparticle by ultra sonication using spray or freeze dried: - schematic representation [34, 44]



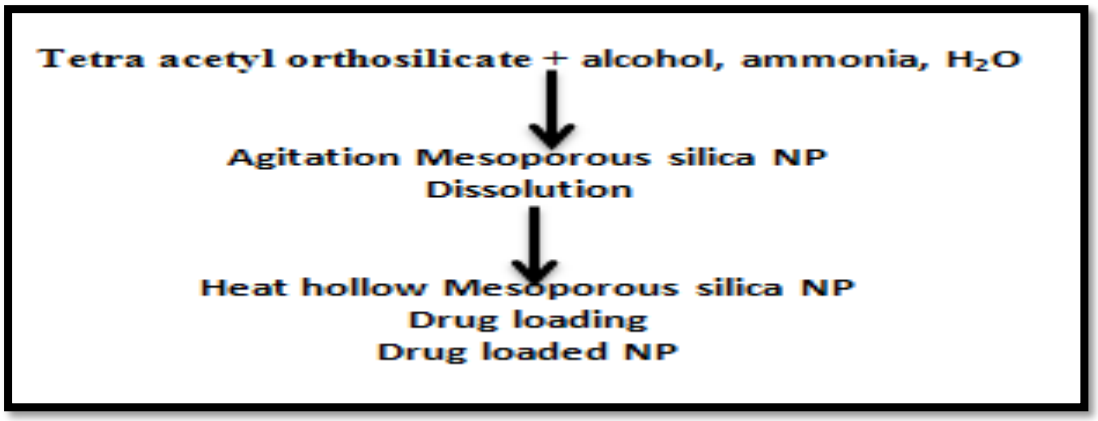
Synthesis of nanoparticle by flash ppt: - schematic representation [48 ,58,82]



Synthesis of nanoparticle by membrane extrusion:-schematic representation [12, 49, 36]



Synthesis of Mesoporous nanoparticle: - schematic representation [10, 23, 63, 66, 94]



Synthesis of nanoparticles of solid lipid nanoparticles by different methods: - [2]

1. Solvent evaporation method

2. Solvent emulsification-diffusion method

3. High pressure homogenization

A. Hot homogenization

B. Cold homogenization

4. Microemulsion based method

5. Ultra sonication/high speed homogenization

A. Probe ultra sonication

B. Bath ultra sonication

6. Supercritical fluid method

7. Spray drying method

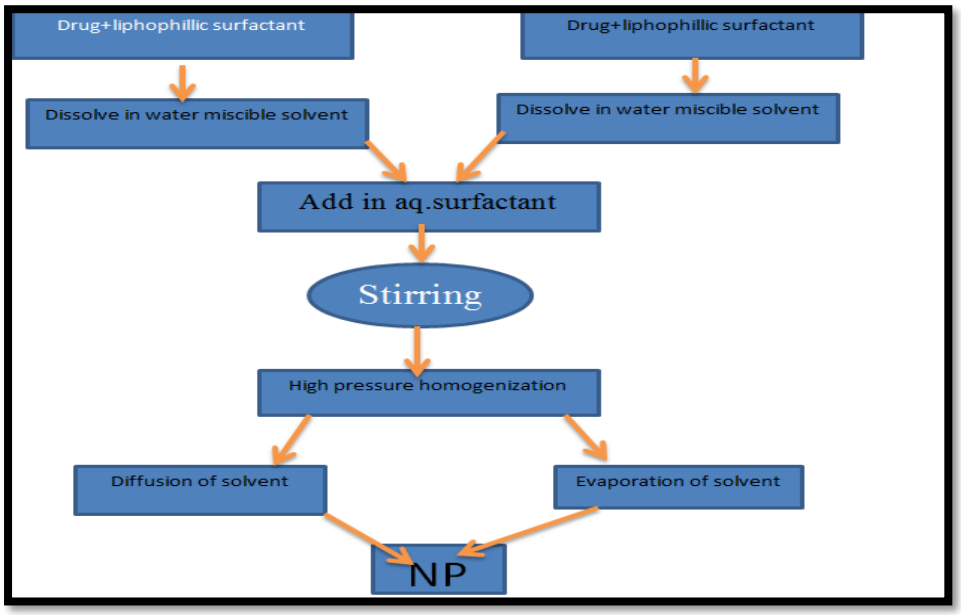
8. Double emulsion method

9. Precipitation technique

10. Film-ultrasound dispersion

11. Ionic gelation method

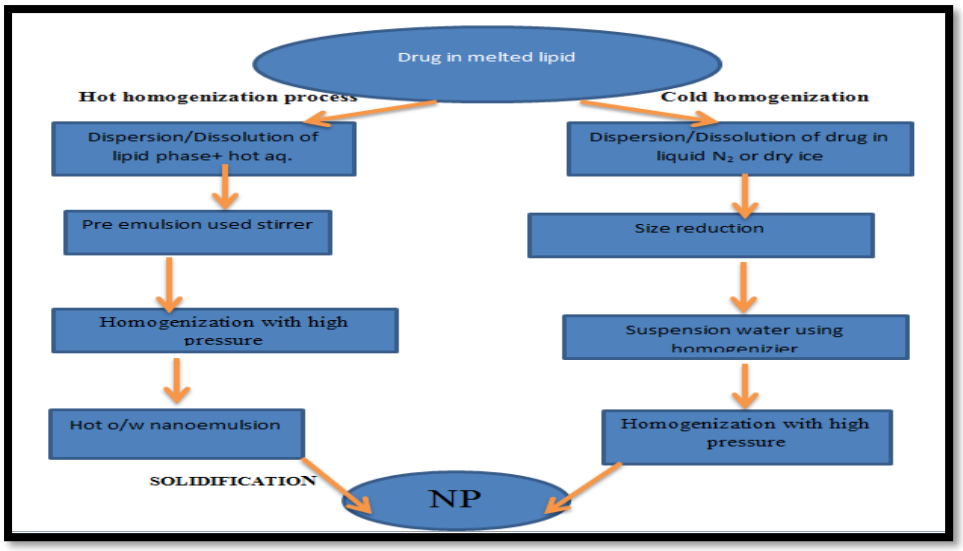
1+2=Synthesis of nanoparticles by emulsification solvent-diffusion method and emulsification-solvent evaporation method [15, 36, 74, 78]



Example of drug used in making np for this method

Formulation	Category	Method
Irbesartan:	Anti-hypertensive	solvent emulsification
Rifampicin, isoniazid	Anti-tubercular chemotherapy	By using the emulsion solvent diffusion

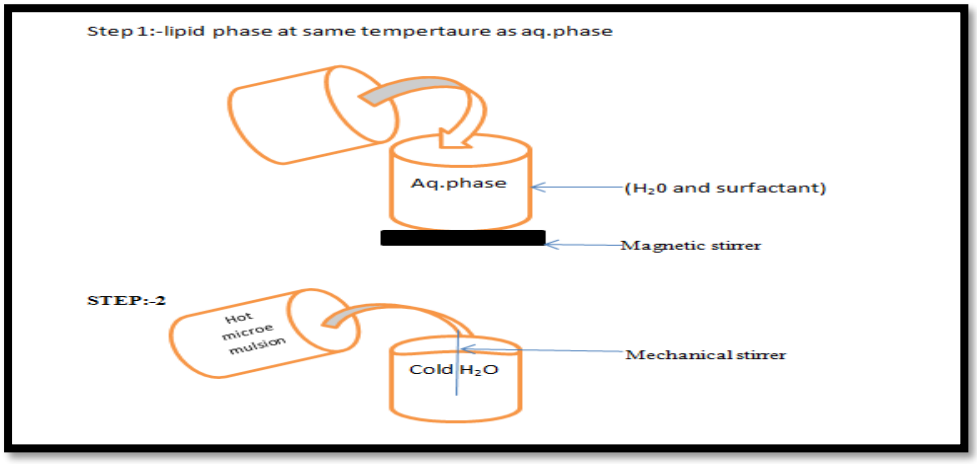
3) Synthesis of nanoparticles by hot and cold high pressure homogenization method [18, 27, 36, 65]



Example of drug used in making np for this method

Formulation	Category	Method
Didanosin	antiretroviral drug	hot and cold high pressure homogenization
Ezetimibe	Cholesterol drug	Homogenization method
Ramipril	Anti-hypertensive	Homogenization method
Raloxifene HCL	Antineoplastic	Homogenization method
Meloxicam	NSAIDS	Homogenization method

4) Synthesis of microemulsion nanoparticle:-

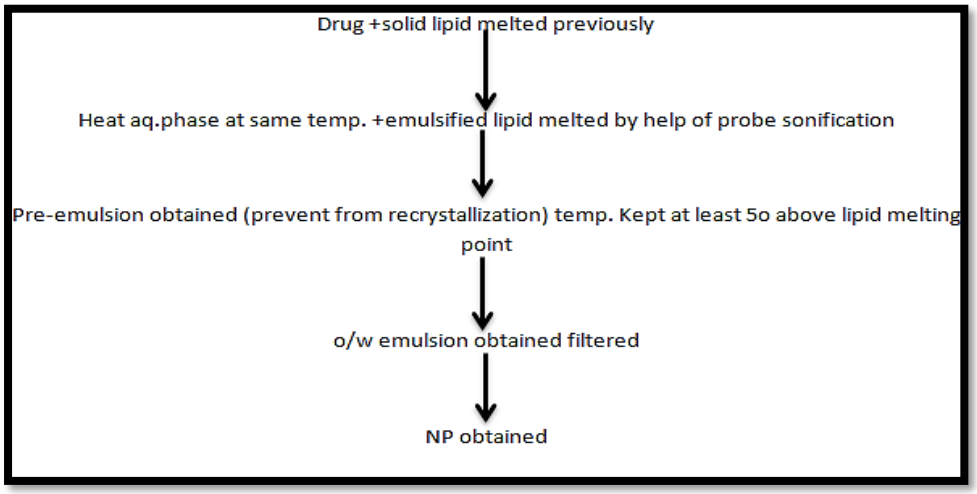


Example of drug used in making np for this method

Formulation	Category	Method
Breviscapine	Anti-hypertensive	Micro emulsion method

Grisofulvin	Anti-fungal	Micro emulsion method
Mitotane	Adrenal Cortex	Micro emulsion method
Ibuprofen	NSAIDS	Micro emulsion method

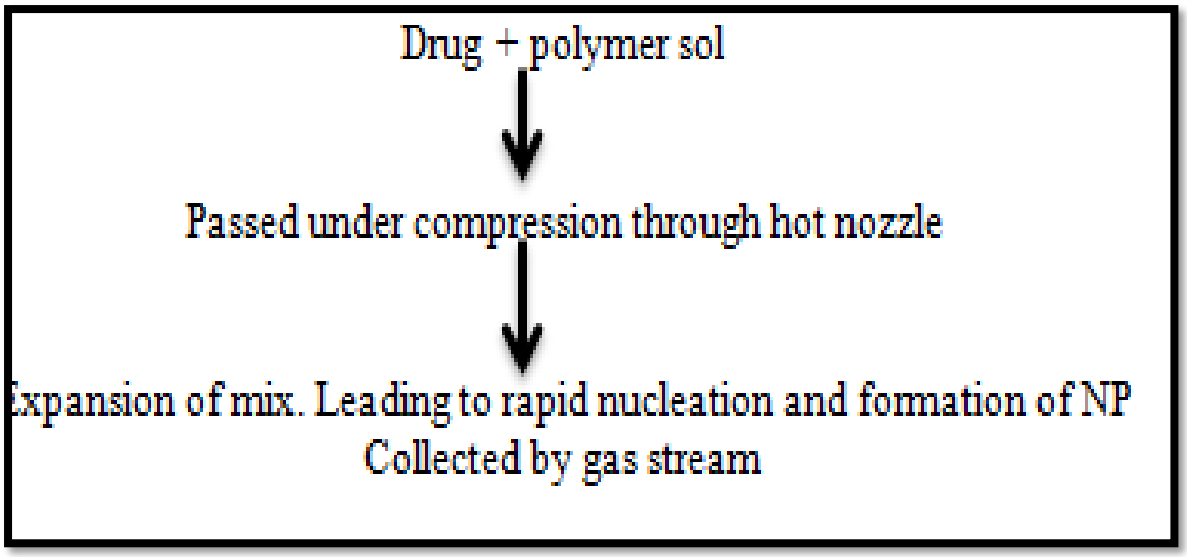
5) Synthesis of nanoparticles by method Ultra sonication/high speed homogenization:- [2, 9, 65, 50, 83]



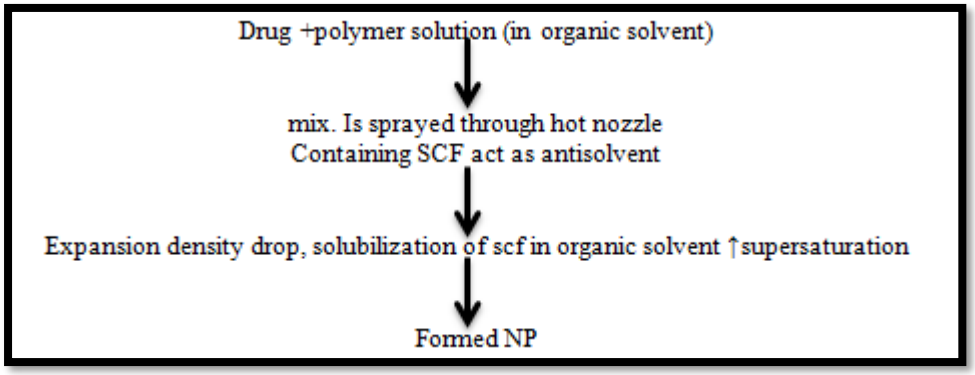
Example of drug used in making NP for this method

Formulation	Category	Method
Ramipril	Anti-hypertensive	Ultra Sonification
Atovaquone	Anti-malarial	High pressure homogenization
Azithromycin	antibiotic	High pressure homogenisation
Budesonide	Asthma	High pressure homogenization
Bupravaquone	Antibiotic	High pressure homogenization
Clofazamine	Antimycobacterials	High pressure homogenization
Fenofibrate	Lipid lowering	High pressure homogenization
Glucocorticoid	corticoid	High pressure homogenization

6. Synthesis of nanoparticles by method Supercritical fluid method:-it involve two methods super critical fluid antisolvent and gas anti-solvent [2, 7, 23, 44, 78]



a) Scf antisolvent:-

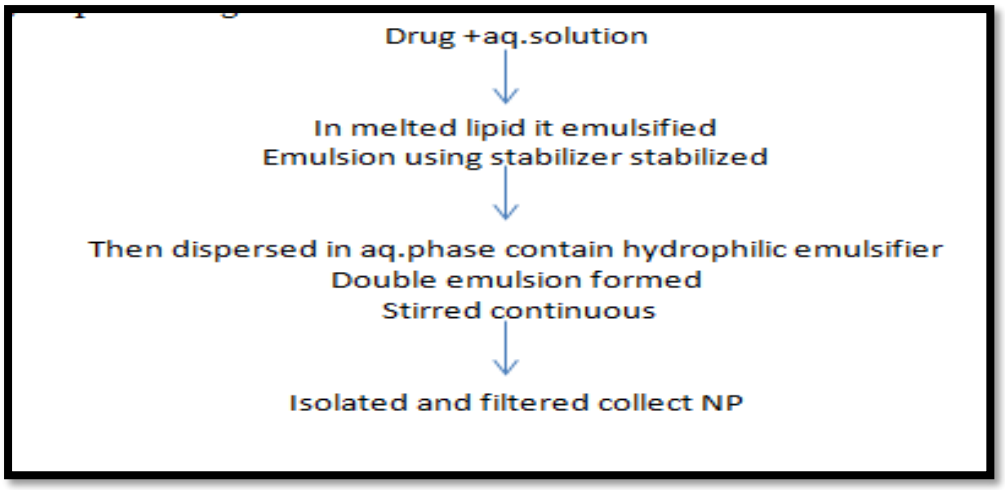


7. Synthesis of nanoparticles by method Spray drying method: - Nanoparticles by Spray-Drying and Their Use for Efficient Pulmonary Drug Delivery [27, 37, 45, 85]

Example of drug used in making np for this method

Formulation	Category	Method
Etravirine	Anti-retro viral	Spray drying method
Everolimus	Antineoplastic	Spray drying method
Ivacaftor	Cystic fibrosis	Spray drying method
Teleprevir	Anti-viral	Spray drying method

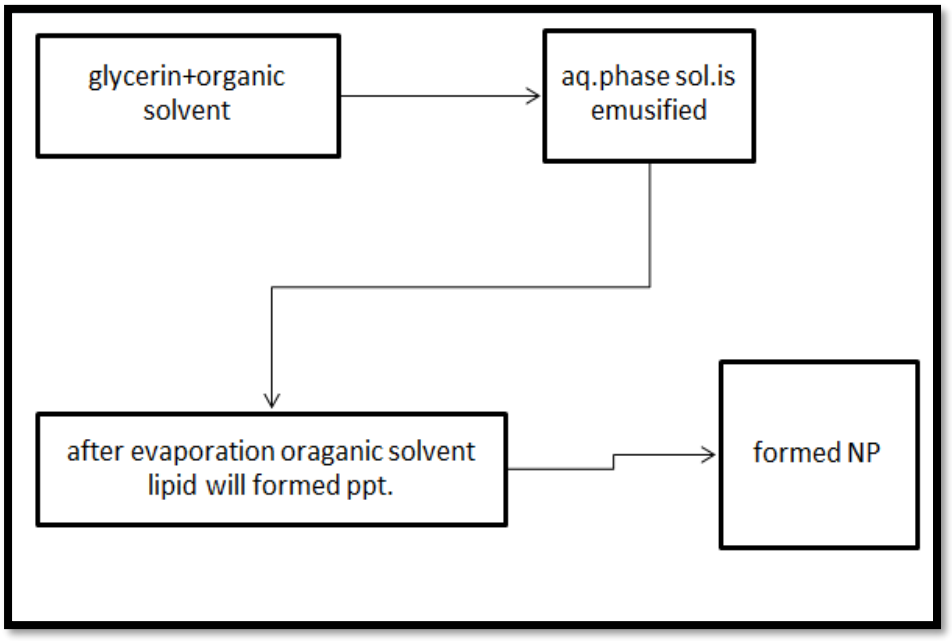
8. Synthesis of nanoparticles by method Double emulsion method:-mainly used for encapsulated hydrophilic drug [27, 45, 60, 76, 85]



Example of Drug used in making NP for this method

Formulation	Category	Method
Ixabepilone	Breast cancer	Double emulsion method
Metformin	Type 2diabeties	Double emulsion method
Zidovudine	Anti-retroviral	Double emulsion method

9. Synthesis of nanoparticles by method Precipitation technique: - [3, 13, 15, 16, 27]

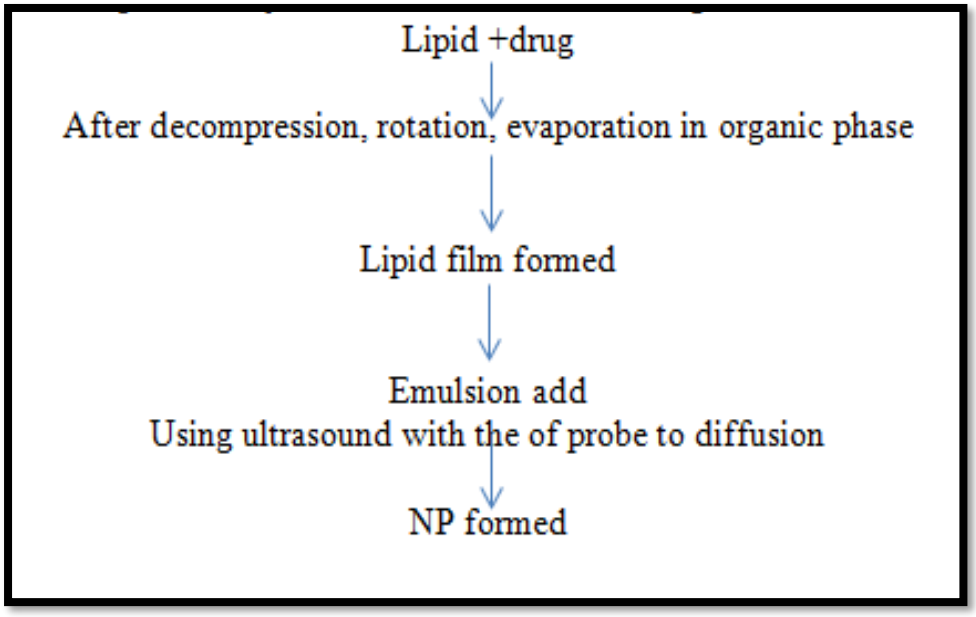


Example of drug used in making np for this method

Formulation	Category	Method
Carbamazepine	Anti convulsant	Precipitation method
Cyclosporine	Immunosuppressant	Precipitation method

Grisofulvin	Anti-fungal	Precipitation method
Retinoic acid	Anti-cancer	Precipitation method

10. Synthesis of nanoparticles by method Film-ultrasound dispersion:

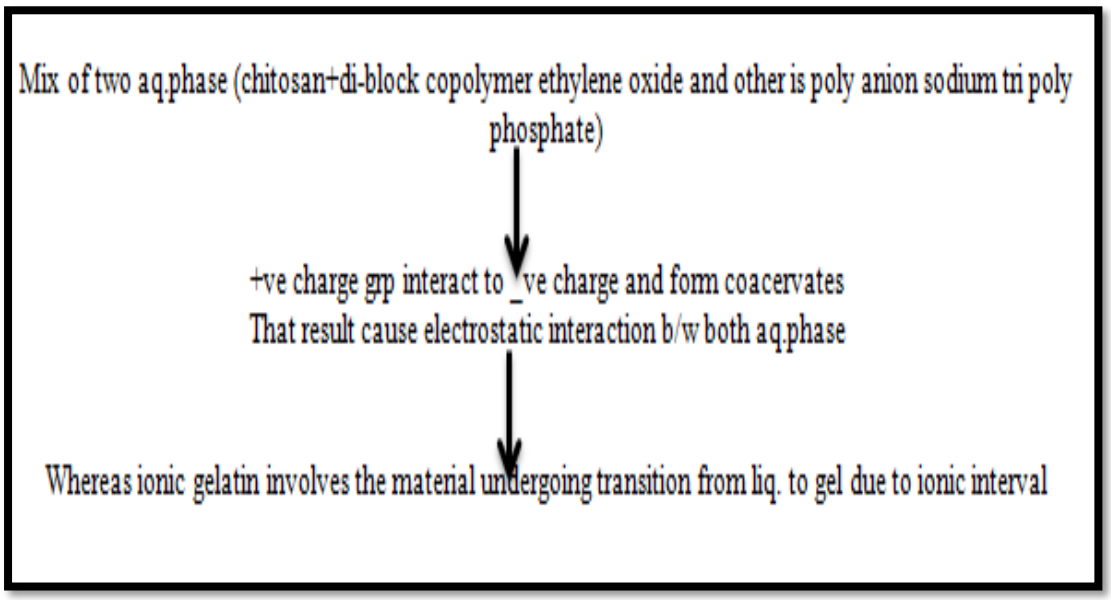


Schematic procedure of Film-ultrasound dispersion technique

Example of Drug used in making NP for this method

Formulation	Category	Method
Zinc oxide	Anti-bacterial	Film-ultrasound dispersion
Silver	Anti-microbial	Film-ultrasound dispersion

11**. Synthesis of nanoparticles by method Ionic gelation method**:-



Schematic procedure of Ionic gelation technique

Example of Drug used in making NP for this method

Formulation	Category	Method
Narigen	Cold	Ionic gelation method
Pravastatin	Cholesterol drug	Ionic gelation method
Ciprofloxacin	Antibiotic	Ionic gelation method

CONCLUSIONS

Development of new pharmaceutical formulations faces some problem and certain difficulties, including the achievement of sussed bioavailability for poorly (H_20) Water soluble drugs. There are so many techniques in improving the solubility problem. Nanotechnology is now one of the important tools for the pharmaceutical industry, they have quite effective in improving dissolution, solubility, and bioavailability of drugs. Proper selection of carrier materials and excipients is also important measures to achieving the successful nanomaterial. However some aspects still need to improvement, such as related to the nucleation growth and agglomeration type problem create the difficulty, but that difficulty can be improve by selecting the appropriate material, focusing the manufacturing process have been studied that's can achieved to overcome such limitations, which may increase the bioavailabity thus products demand based on the market also improved . Finally, that the main focus of this work has been studied the different kinds synthesis method that can help to the immediate-release of drug. Several techniques of synthesis of

nanoparticle including biological, physical and chemical methods can all of them is suitable for achieving the bioavailabity and solubility. These all three method have the different method of origin of nanoparticle and all have different function and application. These approaches has obtain sustained-release drug delivery systems, targeting the drug less expensive, more accurate, ease scale up etc. this review article focused only the different methods of formulation development owever there are some limitation but still needed to be addressed in depth to achieved the succeed result from this technology.

References

1. Ahmed, T., 2016. Preparation of finasteride capsules-loaded drug nanoparticles: formulation, optimization, in vitro, and pharmacokinetic evaluation. International Journal of Nanomedicine, p.515.
2. Akash, C., Sudheer, P. and Sogali, B.S. (2017). Solid Lipid Nanoparticles- An Innovative approach for Improving the Solubility and Bioavailability. Journal of Pharmaceutical Research, 16(2), p.148.
3. Aldana, J., Wang, Y.A. & Peng, X.G. Photochemical instability of CdSe nanocrystals coated by hydrophilic thiols. Journal of the American Chemical Society 123, 8844-8850 (2001).
4. Amoabediny, G.H., Naderi, A., Malakootikhah, J., Koohi, M.K., Mortazavi, S.A., Naderi, M. and Rashedi, H. (2009). Guidelines for safe handling, use and disposal of nanoparticles. Journal of Physics: Conference Series, 170, p.012037.
5. Artuso, R.D. and Bryant, G.W. (2013). Quantum dot–quantum dot interactions mediated by a metal nanoparticle: Towards a fully quantum model. Physical Review B, 87(12).
6. Attaalmanan, E., Mohammed-Ahmed, H., Hussein, S., Farag, M., Eltayeb, M. and Fragoon, A., 2020. The Biostability of Gold Nanoparticles for Cancer Treatment. Journal of Clinical Engineering, 45(1), pp.66-71.
7. Baoshan Xing, Vecitis, C.D. and N Senesi (2016). Engineered nanoparticles and the environment : biophysicochemical processes and toxicity. Hoboken, New Jersey: Wileypp.37
8. Başpinar, Y., Akbaba, H. and BAyraktar, O., 2019. Encapsulation of paclitaxel in electrosprayed chitosan nanoparticles. Journal of Research in Pharmacy, 23(5), pp.886-896.

9. Bhalekar, M., Upadhaya, P. and Madgulkar, A., 2017. Formulation and characterization of solid lipid nanoparticles for an anti-retroviral drug darunavir. Applied Nanoscience, 7(1-2), pp.47-57.
10. Bharti, C., Gulati, N., Nagaich, U. and Pal, A., 2015. Mesoporous silica nanoparticles in target drug delivery system: A review. International Journal of Pharmaceutical Investigation, 5(3), p.124.
11. Bhatjire, G., 2017. Hot melt extrusion technique for solid oral dosage form - a review. World Journal of Pharmaceutical Research, pp.249-263.
12. Bhatjire, G.S. (2017). Hot melt extrusion technique for solid oral dosage form - a review. World Journal of Pharmaceutical Research, pp.249–263.
13. Bhosale, R.R., Osmani, R.A., Ghodake, P.P., Shaikh, S.M. and Chavan, S.R. (2014). Nanoemulsion: A Review on Novel Profusion in Advanced Drug Delivery. Indian Journal of Pharmaceutical and Biological Research, 2(01).
14. Bruchez, M., Jr., Moronne, M., Gin, P., Weiss, S. & Alivisatos, A.P. Semiconductor nanocrystals as fluorescent biological labels. Science 281, 2013-2016 (1998).
15. Bunjes, H., 2010. Lipid nanoparticles for the delivery of poorly water-soluble drugs. Journal of Pharmacy and Pharmacology, 62(11), pp.1637-1645.
16. C.Nagarwal, R., Kumar, R., Dhanawat, M., Das, N. and K. Pandit, J. (2011). Nanocrystal Technology in the Delivery of Poorly Soluble Drugs: An Overview. Current Drug Delivery, 8(4), pp.398–406.
17. Chandra, A., Sharma, U., Jain, S. and Soni, R., 2013. Nanosuspension: an overview. Journal of Drug Delivery and Therapeutics, 3(6).
18. Chen, Q., Chasiotis, I., Chen, C. and Roy, A. (2008). Nanoscale and effective mechanical behavior and fracture of silica nanocomposites. Composites Science and Technology, 68(15–16), pp.3137–3144.
19. Cho, S.J. et al. Long-term exposure to CdTe quantum dots causes functional impairments in live cells. Langmuir 23, 1974-1980 (2007).
20. D.G. Rickerby and M. Morrison (2007) “Nanotechnology and the environment: A European perspective”, Science and Technology ofAdvanced Materials 8(1-2): 19-24.
21. DeFrates, K., Markiewicz, T., Gallo, P., Rack, A., Weyhmiller, A., Jarmusik, B. and Hu, X. (2018). Protein Polymer-Based Nanoparticles: Fabrication and Medical Applications. International Journal of Molecular Sciences, 19(6), p.1717.

22. Ditzinger, F., Dejoie, C., Sisak Jung, D. and Kuentz, M., 2019. Polyelectrolytes in Hot Melt Extrusion: A Combined Solvent-Based and Interacting Additive Technique for Solid Dispersions. Pharmaceutics, 11(4), p.174.
23. Dogra, P., Adolphi, N.L., Wang, Z., Lin, Y.-S., Butler, K.S., Durfee, P.N., Croissant, J.G., Noureddine, A., Coker, E.N., Bearer, E.L., Cristini, V. and Brinker, C.J. (2018). Establishing the effects of mesoporous silica nanoparticle properties on in vivo disposition using imaging-based pharmacokinetics. Nature Communications, 9(1).
24. Dr.bohlavova, J., Adam, V., Kizek, R. and Hubalek, J., 2009. Quantum Dots — Characterization, Preparation and Usage in Biological Systems. International Journal of Molecular Sciences, 10(2), pp.656-673.
25. Dutta, S. and Ghosh, A., 2018. Green approaches for preparation and comparative analysis of three different molecular sizes of multifunctional sericin nanoparticles. New Biotechnology, 44, pp.S11-S12.
26. E.Priyanka, Dr. P. Tripura Sundari (2018). formulation and evaluation of simvastatin loaded gelatin nanoparticles internayional Journal of Current Pharma Research, vol 51(2), pp.754–753
27. Ekambaram, P. and Abdul Hasan Sathali, A., 2011. Formulation and Evaluation of Solid Lipid Nanoparticles of Ramipril. Journal of Young Pharmacists, 3(3), pp.216-220.
28. Elzey, S. and Grassian, V.H. (2009). Agglomeration, isolation and dissolution of commercially manufactured silver nanoparticles in aqueous environments. Journal of Nanoparticle Research, 12(5), pp.1945–1958.
29. FM, M. (2014). Quercetin- A Mini Review. Modern Concepts & Developments in Agronomy, 1(2).Chinese journal of analytical chemistry (Chinese version), 40(8), pp.1169-1174.
30. Gan, Q. and Wang, T., 2007. Chitosan nanoparticle as protein delivery carrier—Systematic examination of fabrication conditions for efficient loading and release. Colloids and Surfaces B: Biointerfaces, 59(1), pp.24-34.
31. Gonçalves, M., 2018. Sol-gel Silica Nanoparticles in Medicine: A Natural Choice. Design, Synthesis and Products. Molecules, 23(8), p.2021.
32. Green Nanotechnology in Cadmium Sulphide Nanoparticles and Understanding Its Toxicity and Antimicrobial Properties." Biomedical Research, vol. 30, no. 5, 2019, 10.35841/biomedicalresearch.30-19-324. Accessed 13 Apr. 2020.

33. Guo, P., Hsu, T., Zhao, Y., Martin, C. and Zare, R., 2013. Preparing amorphous hydrophobic drug nanoparticles by nano porous membrane extrusion. Nanomedicine, 8(3), pp.333-341.
34. Hannele Eerikäinen (2005). Preparation of nanoparticles consisting of methacrylic polymers and drugs by an aerosol flow reactor method.40 (2),pp. 111-142.
35. Hashim, A.A. (2012). Smart nanoparticles technology Chinese journal of analytical chemistr8(3), pp.333-341.
36. Hobson, J.J., Al-khouja, A., Curley, P., Meyers, D., Flexner, C., Siccardi, M., Owen, A., Meyers, C.F. and Rannard, S.P. (2019). Semi-solid prodrug nanoparticles for long-acting delivery of water-soluble antiretroviral drugs within combination HIV therapies. Nature Communications, 10(1).
37. Huang, X., Young, N. and Townley, H., 2014. Characterization and Comparison of Mesoporous Silica Particles for Optimized Drug Delivery. Nanomaterials and Nanotechnology, 4, p.2.
38. J, P. (2016). A Review on Nanoparticles in Targeted Drug Delivery System. Research & Reviews: Journal of Material Sciences, 04(04).
39. Jeevanandam, J., Barhoum, A., Chan, Y., Dufresne, A. and Danquah, M., 2018. Review on nanoparticles and nanostructured materials: history, sources, toxicity and regulations. Beilstein Journal of Nanotechnology, 9, pp.1050-1074.
40. Jenita, J.L. (2012). Formulation and evaluation of microparticles containing curcumin for colorectal cancer. Journal of drug delivery and therapeutics, 2(3).
41. Jia, L. (2005). Nanoparticle Formulation Increases Oral Bioavailability of Poorly Soluble Drugs: Approaches, Experimental Evidences and Theory. Current Nanoscience, 1(3), pp.237–243.
42. Jin, S., Hu, Y., Gu, Z., Liu, L. and Wu, H.-C. (2011). Application of Quantum Dots in Biological Imaging. Journal of Nanomaterials, 2011, pp.1–13.
43. Jog R. and Burgess, D., 2017. Pharmaceutical Amorphous Nanoparticles. Journal of Pharmaceutical Sciences, 106(1), pp.39-65.
44. Johnsen, B.B., Kinloch, A.J., Mohammed, R.D., Taylor, A.C. and Sprenger, S. (2007). Toughening mechanisms of nanoparticle-modified epoxy polymers. Polymer, 48(2), pp.530–541.
45. Joshi S.A, R.K... (2012). Solid Lipid Nanoparticle: A Review. IOSR Journal of Pharmacy (iosrphr), 2(6), pp.34–44.

46. Khan, A., Rashid, R., Murtaza, G. and Zahra, A. (2014). Gold Nanoparticles: Synthesis and Applications in Drug Delivery. Trop J Pharm Res Tropical Journal of Pharmaceutical Research, 13(137), pp.1169–1169.
47. Khan, I., Saeed, K. and Khan, I. (2017). Nanoparticles: Properties, applications and toxicities. ArabianJournalofChemistry pg. 1-24
48. Konwar, R. and Ahmed, A.B. (2016). Nanoparticle: an overview of preparation, characterization and application. International Research Journal of Pharmacy, 4(4), pp.47–57.
49. Krishna Sailaja, A. and Swati, P. (2017). Preparation and Characterization of Sulphasalazine Loaded Nanoparticles by Nanoprecipitation and Ionotropic Gelation Techniques Using Various Polymers. Current Nanomedicine, 7(2).
50. Kudr, J., Haddad, Y., Richtera, L., Heger, Z., Cernak, M., Adam, V. and Zitka, O., 2017. Magnetic Nanoparticles: From Design and Synthesis to Real World Applications. Nanomaterials, 7(9), p.243
51. Kumar, K., 2018. Biosynthesis of Silver Ag Nanoparticles using Plant Derivatives of Delonix elata. International Journal of Trend in Scientific Research and Development, Volume-2(Issue-4), pp.83-86.
52. Lateef, A., Ojo, S. and Elegbede, J., 2016. The emerging roles of arthropods and their metabolites in the green synthesis of metallic nanoparticles. Nanotechnology Reviews, 5(6).
53. Lee, D., Ihm, S. and Lee, K., 2005. Mesoporous silica framed by sphere-shaped silica nanoparticles. Microporous and Mesoporous Materials, 83(1-3), pp.262-268.
54. Liu, Z., Zhou, Y., Maszenan, A., Ng, W. and Liu, Y., 2014. Correction to pH-Dependent Transformation of Ag Naoparticles in Anaerobic Processes. Environmental Science & Technology, p.140128165313009.
55. M.b, g. and r. c, k. (2019). Synthesis of different metal nanoparticles from plant extracts. indian research journal of pharmacy and science, 6(2), pp.1861–1866.
56. Mahmood, R., 2017. Hot Melt Extrusion: An Emerging Drug Delivery Technology. Polymer science, 03(04).
57. Malviya T, Joshi S, Dwivedi LM, et al. Synthesis of Aloevera/Acrylonitrile based Nanoparticles for targeted drug delivery of 5-Aminosalicylic acid. Int J Biol Macromol. 2018;106:930–939. doi:10.1016/j.ijbiomac.2017.08.085
58. Mandel, S., 2019. Nanoparticles are a promising solution to thermal energy challenges in electronic devices. Scilight, 2019(40), p.401101.

59. Mathew, M., Krishna Kumar, K., Dinesh Kumar, B. and Nair, S.K. (2017). Antibiotics nanosuspension: a review. Journal of Drug Delivery and Therapeutics, 7(2).
60. Merisko-Liversidge, E.M. and Liversidge, G.G. (2008). Drug Nanoparticles: Formulating Poorly Water-Soluble Compounds. Toxicological Pathology, 36(1), pp.43–48.
61. Mohamed Isa, E., Ahmad, H. and Abdul Rahman, M., 2019. Optimization of Synthesis Parameters of Mesoporous Silica Nanoparticles Based on Ionic Liquid by Experimental Design and Its Application as a Drug Delivery Agent. Journal of Nanomaterials, 2019, pp.1-8.
62. Mohanraj, V.J. and Chen, Y. (2007). Nanoparticles - A review. Tropical Journal of Pharmaceutical Research, 5(1).
63. Naik, B., Gandhi, J., Shah, P., Naik, H. and Sarolia, J., 2017. Asenapine maleate loaded solid lipid nanoparticles for oral delivery. International Research Journal of Pharmacy, 8(11), pp.45-53.
64. Narayan, R., Nayak, U., Raichur, A. and Garg, S., 2018. Mesoporous Silica Nanoparticles: A Comprehensive Review on Synthesis and Recent Advances. Pharmaceutics, 10(3), p.118.
65. Natsuki, J. (2015). A Review of Silver Nanoparticles: Synthesis Methods, Properties and Applications. International Journal of Materials Science and Applications, 4(5), p.325.
66. Ostafin, A. (2019). Nanotechnology: Nanoparticle Characterization and Application in Pharmacology and Toxicology. Journal of Nanomedicine & Nanotechnology, 10(3).
67. Pantidos, N., 2014. Biological Synthesis of Metallic Nanoparticles by Bacteria, Fungi and Plants. Journal of Nanomedicine & Nanotechnology, 05(05).
68. Patel, B., Patel, J. and Chakraborty, S. (2014). Review of Patents and Application of Spray Drying in Pharmaceutical, Food and Flavor Industry. Recent Patents on Drug Delivery & Formulation, 8(1), pp.63–78.
69. Patil, H., Tiwari, R. and Repka, M., 2015. Hot-Melt Extrusion: from Theory to Application in Pharmaceutical Formulation. AAPS Pharm SciTech, 17(1), pp.20-42.
70. Patra, J., Das, G., Fraceto, L., Campos, E., Rodriguez-Torres, M., Acosta-Torres, L., Diaz-Torres, L., Grillo, R., Swamy, M., Sharma, S., Habtemariam, S. and Shin, H.,

2018. Nano based drug delivery systems: recent developments and future prospects. Journal of Nanobiotechnology, 16(1).

71. Piras, C., Fernández-Prieto, S. and De Borggraeve, W., 2019. Ball milling: a green technology for the preparation and functionalisation of nanocellulose derivatives. Nanoscale Advances, 1(3), pp.937-947.
72. Poopak F,Ali Akbar,, Saeed M. G.Jalaledin Modified .Rifampin Nanoparticles: Increased Solubility with Slow Release Rate 2017 The International Journal of Mycobacteriology | Ppgno.1-6
73. Rashid, M.U., Bhuiyan, M.K.H. and Quayum, M.E. (2013). Synthesis of Silver Nano Particles (Ag-NPs) and their uses for Quantitative Analysis of Vitamin C Tablets. Dhaka University Journal of Pharmaceutical Sciences, 12(1), pp.29–33.
74. Rizvi, S.A.A. and Saleh, A.M. (2018). Applications of nanoparticle systems in drug delivery technology. Saudi Pharmaceutical Journal, 26(1), pp.64–70.
75. Sadeghi, S. (2012). Hybrid Nanoparticle Systems: New Materials for Sensing and Functional Bio-Applications. Journal of Nanomedicine & Nanotechnology, 03(03).
76. Savjani, K., Gajjar, A. and Savjani, J., 2012. Drug Solubility: Importance and Enhancement Techniques. ISRN Pharmaceutics, 2012, pp.1-10.
77. Sekar, Padmini V, et al. “Green Nanotechnology in Cadmium Sulphide Nanoparticles and Understanding Its Toxicity and Antimicrobial Properties.” Biomedical Research, vol. 30, no. 5, 2019, 10.35841
78. Shah, D.P., Patel, B. and Shah, C. (2015). Nanosuspension technology: a innovative slant for drug delivery system and permeability enhancer for poorly water soluble drugs. Journal of Drug Delivery and Therapeutics, 5(1).
79. Shah, M., Fawcett, D., Sharma, S., Tripathy, S. and Poinern, G. (2015). Green Synthesis of Metallic Nanoparticles via Biological Entities. Materials, 8(11), pp.7278–7308.
80. Shelake, S., Patil, S. and Patil, S., 2018. Formulation and Evaluation of Fenofibrate-loaded Nanoparticles by Precipitation Method. Indian Journal of Pharmaceutical Sciences, 80(3).
81. Singh, Priyanka, et al. “Biological Synthesis of Nanoparticles from Plants and Microorganisms.” Trends in Biotechnology, vol. 34, no. 7, July 2016, pp. 588–599.s

82. Singh, S., Dobhal, A.K., Jain, A., Pandit, J.K. and Chakraborty, S. (2010). Formulation and Evaluation of Solid Lipid Nanoparticles of Water Soluble Drug: Zidovudine. Chemical and Pharmaceutical Bulletin, 58(5), pp.650–655.
83. Soma, D., Attari, Z., Reddy, M., Damodaram, A. and Koteshwara, K., 2017. Solid lipid nanoparticles of irbesartan: preparation, characterization, optimization and pharmacokinetic studies. Brazilian Journal of Pharmaceutical Sciences, 53(1).
84. Sreelakshmi, C., Datta, K., Yadav, J. and Reddy, B., 2011. Honey Derivatized Au and Ag Nanoparticles and Evaluation of Its Antimicrobial Activity. Journal of Nanoscience and Nanotechnology, 11(8), pp.6995-7000.
85. Stine, K.E. (2015). Principles of toxicology. Boca Raton: Crc Press.7-17
86. Suhailah, S.A.-J. and Soheir, N.A.E.-R. (2017). Effect of quercetin nanoparticles on the kidney of the streptozotocin-induced diabetes in male rats: A histological study and serum biochemical alterations. African Journal of Biotechnology, 16(39), pp.1944–1952.
87. Suriati, G., Mariatti, M. and Azizan, A. (2014). Synthesis of silver nanoparticles by chemical reduction method: effect of reducing agent and surfactant concentration. International Journal of Automotive and Mechanical Engineering, 10, pp.1920–1927.
88. Tippayawat, P., Phromviyo, N., Boueroy, P. and Chompoosor, A., 2020. Green Synthesis Of Silver Nanoparticles In Aloe Vera Plant Extract Prepared By A Hydrothermal Method And Their Synergistic Antibacterial Activity.
89. Vijay Kumar, N. (2016). Nanoparticles for Improved Delivery of Poorly Soluble Drugs. Journal of Drug, 1(1), pp.18–27.
90. Yanes, R. and Tamanoi, F., 2012. Development of mesoporous silica nanomaterials as a vehicle for anticancer drug delivery. Therapeutic Delivery, 3(3), pp.389-404.
91. Zhang, H., Wu, S., Tao, Y., Zang, L. and Su, Z., 2010. Preparation and Characterization of Water-Soluble Chitosan Nanoparticles as Protein Delivery System. Journal of Nanomaterials, 2010, pp.1-5.
92. Zhang, X., Liu, Z., Shen, W. and Gurunathan, S., 2016. Silver Nanoparticles: Synthesis, Characterization, Properties, Applications, and eutic Approaches. International Journal of Molecular Sciences, 17(9), p.1534.
93. Zhao J, Pan X, Sun X, Pan W, Yu G, Wang J. Detection of metronidazole in honey and metronidazole tablets using carbon dots-based sensor via the inner filter effect. Luminescence. 2018;33(4):704–712. doi:10.1002/bio.3467

94. Zheng, Y., Zheng, Y. and Ning, R. (2003). Effects of nanoparticles SiO2 on the performance of nanocomposites. Materials Letters, 57(19), pp.2940–2944.