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A REVIEW ON NANO CRYSTALS - A NEW DEVELOPMENT BY NANO TECHNOLOGY OF DRUG DELIVERY

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ABSTRACT

Nano technology & Sciences was approaching a goal to outcome of desired product by using nano technology by assembling of atoms together in a controlled & specified designs with nano structures materials regarding this. Now a day's Nano crystals was an important formulation rather mainly used in case of poor water soluble drugs to increase their levels of Bioavailability solubility, dissolutions rate with high stability followed by low toxicity.

As these nano crystals was prepared in form of nano suspension by top down & Bottom up methods. Which are mostly used in industries as these can be manufacture in use of various routes of administration. Their complete biological roll regarding their target to the specific pathogenic sites were discovered with useful ways.

KEYWORDS: Nano crystals, target drugdelivery, bio availability, permeability, target efficiency.

INTRODUCTION

Now a day's novel drug delivery systems have explored all over pharmaceuticals technologies these important & excited challenges through the human subjects for the targeted drug delivery systems.

Nano suspensions werea wonderful techniques which was used for the targeted drug delivery. Some of them was Nano carriers micelles, liposomes etc., and one of them were Nano crystals.

Generally now a days Nano crystals attaining more increase than other novel drug delivery systems because other delivery systems contains many solubilizing agents & binding agents these agents produce an adverse effect which are not used in formation Nano crystals.[1,2,3]

In some preparations they use hydroxylpropyi –B-cyclodextrin & cremopher EL. These are used in commercial drugs the causes hypersensitivity & nephrotoxicity.

These preparation of micelles, liposomes were an scale up difficulties, high manufacturing cost & platform instability, limited drug loading these all difficulties were been improved by using Nano crystals.[3,4]

Nano crystals were been used for delivery of poor water soluble drugs to tissue, organ, cell to attain an effective therapeutic effects.

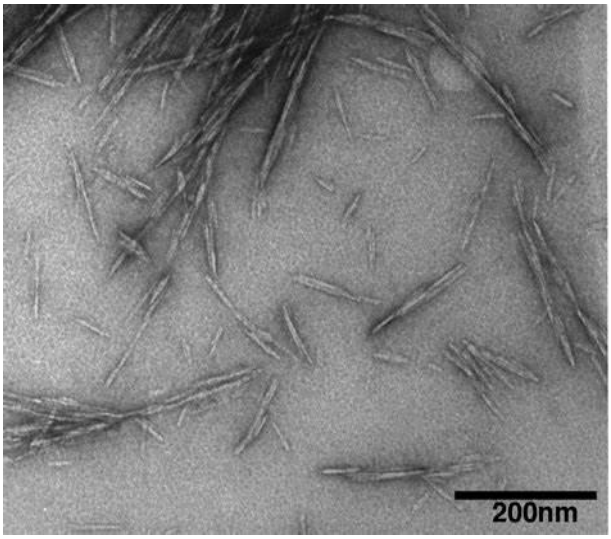
Nano crystals are of ranging from particle size are smaller than the 1 um.[1,3,5]

These Nano crystals offers of drug loading of 50%-90%. so leads to maximum therapeutic concentration at low dose these only needs surfactants & or polymers.

For I improved targeting efficiency these can be injected orally & though IV injection. The Nano crystals injected through IV are not willing to dissolve rapidly distribution. In blood because they have low volume of as these are recognized as exogenous materials & targeted by phagocytic system of cells & 90% were transported to liver & 50% to spleen.

In order to reduce the triggering by phagocytic system were use poloxamer & PEG & thus increase the circulation in blood, thus loading increased permeability & retention effects.

The use of polymer encapsulation of Nano crystals process & use of immobilized ligands the surface of Nano crystals. The possibility of targeting efficiency was increased & stabilized.[1]



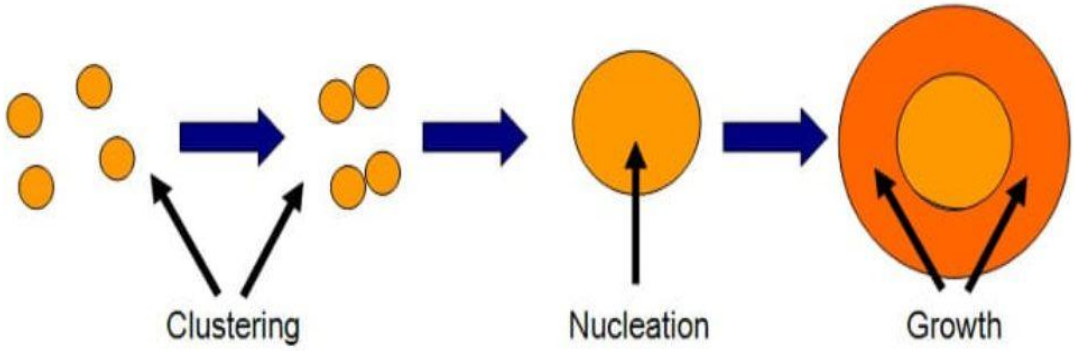
Fig; 1; microscopic structure of nano crystals.

Advantages

- Formulation of Nano crystals does not require more scale up to process
- These Nano crystals have more therapeutic index because they high drug loading efficiency.[7,8,11]
- They have high surface area upon increased drug bio availability & high dissolution rate
- Low usage of polymers & other solubilizing agents thus leading to adverse effects
- These have more aqueous solubility of API.[7,9,10]

Disadvantages

Poor rapid solubility due to low volume of distribution In production crystallization leads to nucleation & crystals growth leads inappropriateaggregation of rystals.[12,13]



These Nano crystals have low stability issues when compared to amorphous molecules.

Method of preparation

Several method of preparation have been implemented for nano crystallization techniques to reduce the particle size, those been classified as bottom up & top down & both top down & bottom up method & spray drying methods all these methods were attained to alter size & shape of nano crystals to an a required property Top down method was mostly used because of their advantageous than the bottom up method & it was called as Nano sizing.[2,3,14]

In all above of these spray drying method of preparation is more practical & rapid product formation were seen

1) Bottom up method
   Precipitation
2) Top down method
   Milling
   High pressure homogenization
3) Top down & bottom up method
4) Spray drying
5) Other techniques

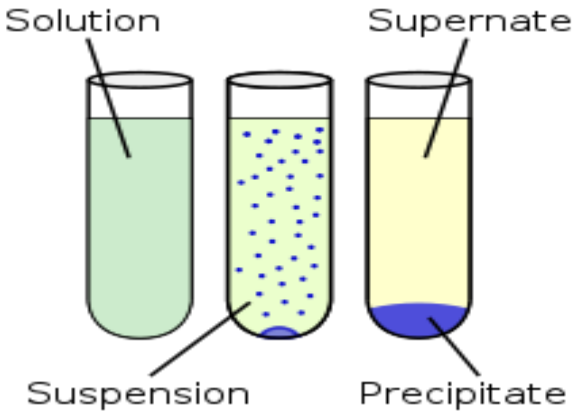
Bottom up technology

In this bottom up technology precipitation method was done were our Nano crystals formed was inform of precipitation these are then filtered & then analyzed.

a) Precipitation method

In the precipitation firstly we have to take drug & it should be dissolved in a solvent & it was added to non-solvent leads to formation of precipitation these were collected as Nano crystals.[14,15]

Specifications: the drug should be dissolved in at least 1 solvent or else it causes stabilization problems.[15,16]



Top down technology

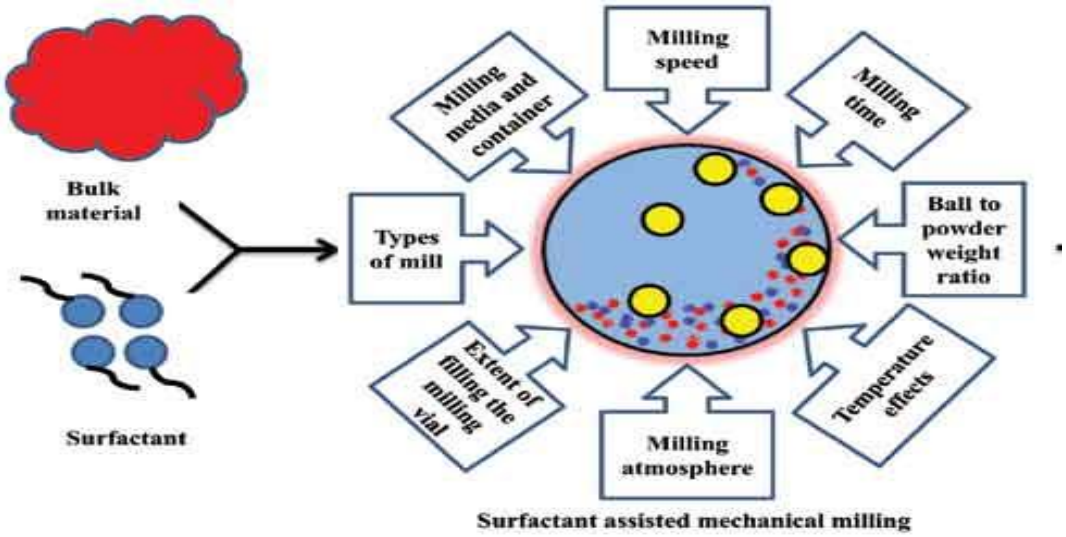
Top down techniques was most commonly used & have beneficence than the bottom up method. This method this was also called as Nano sizing. This technique bears the large particles in to small sized particles.[2,14]

a) Milling method

In a milling technology bead or ball or a pearl milling was achieved to achieve minimization of particle size in a milling chamber milling media, dispersion medium, stabilizer& drug was added. Shear forces were acquired with in the milling media & then size reduction of crystals takes placed.[14,17]

The beads may cause erosion & contamination to prevent this type of problems the beads or pearls were coated with ceramics or titanium or polystyrene resins.

In this milling process wastage of products were seen because complex chamber internally causes adherence of product to the walls of chamber this can be presented by using agitations Milling time depends on temperature, viscosity, surface contact etc. of the drug.[14,18]



Surfactant assisted mechanical milling

b) High pressure homogenous method

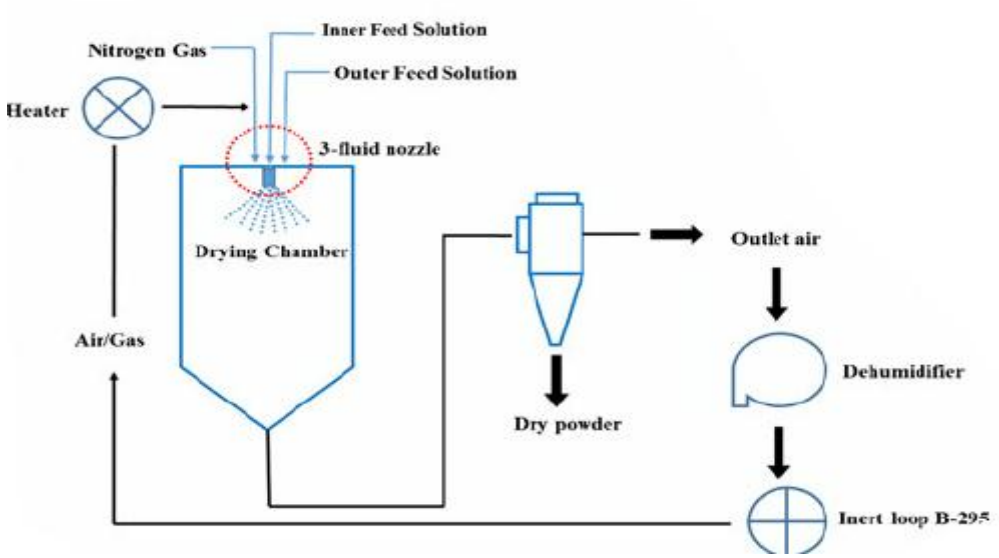
In this method two fluids stream (turbulent flow) were colloid with each other at right angles thus upon causes reduction of particle size.[1,19,20]

3) Top down & bottom up technology

In this method both the top down & bottom up methods were been used. It was useful technology for a drug with a high melting points & more partition coefficients.[21,22]

4) Spray drying

Nano crystals were prepared by one of the method of spray drying.[22,23] In this method either prepared slurry, paste, emulsion, suspension were passed through atomizer then these are formed into small droplets & then settled as dried powder, by the adjusting the concentration, viscosity, temperature, spray rate the particle size & drying speed can be optimized.[21,24,25]

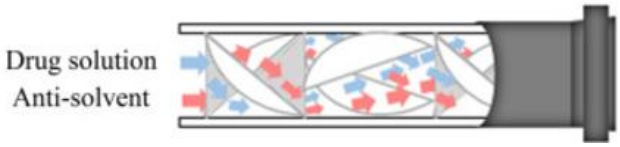


5) Super critical fluid method

In this super critical fluid method first a solvent was added in the Super critical anti solvent was added the solute molecules.[21,26] Then it attains super saturation that creates the precipitation of Nano crystals & then these are filtered & then used for after process.[27,28]

6) Impinging jet crystallization

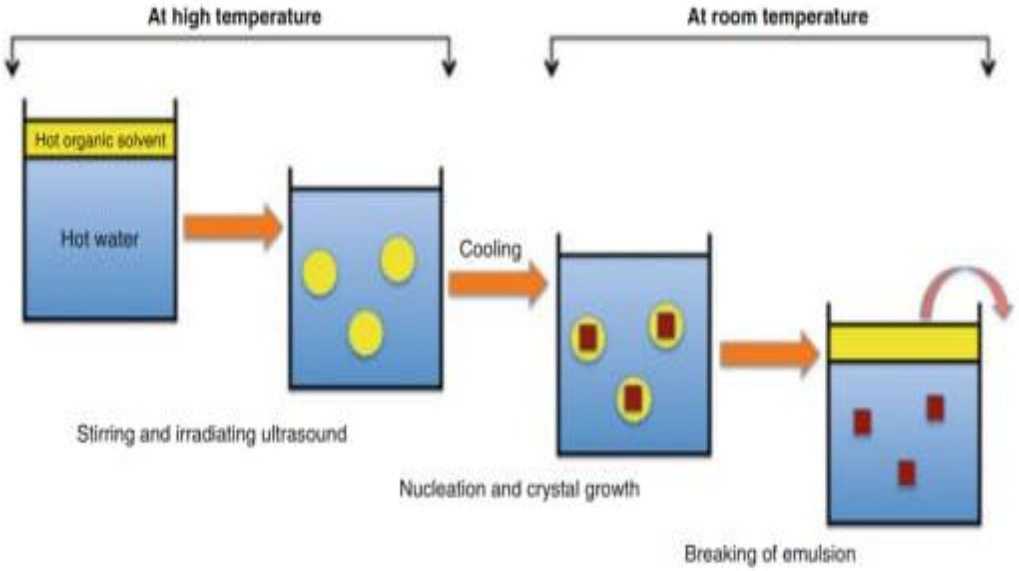
In this method a jet are used to create an impingement & achieves high intensity mixing of fluids of solvent, anti-solvent & ensure were intended to be mixed at high intensity this combined micro mixing leads to produce controlled crystal growth with an required crystal size.[21,29,30]



7) Emulsion method

In this emulsion method mixing of organic solvent with the aqueous phase occurred at high temperature & mixing attains emulsion.[31] Then the mixture was subjected to cooling upon cooling the solute molecules gradually forms as crystals.[32,33]

Then to this solution on anti-solvent was added for breaking of emulsion was seen were organic solvent was separated & solute were dispersed in aqueous medium those were collected & dried.[22,34]



Characterization of Nano crystals

1) Particle size analysis

The particle size analysis of Nano crystals (powder form) were determined by placing on weight amount water in a beaker containing 0.1% PVA by using dynamic light scattering size was analyzed & diameter was determined by using mean particle size distribution.

2) Scanning electron microscopy

The surface morphology was determined by the scanning electron microscopy in this the sample were mounted on top of the sticky carbon tube which are holder on metal disc which was coated with gold & palladium in blazers.

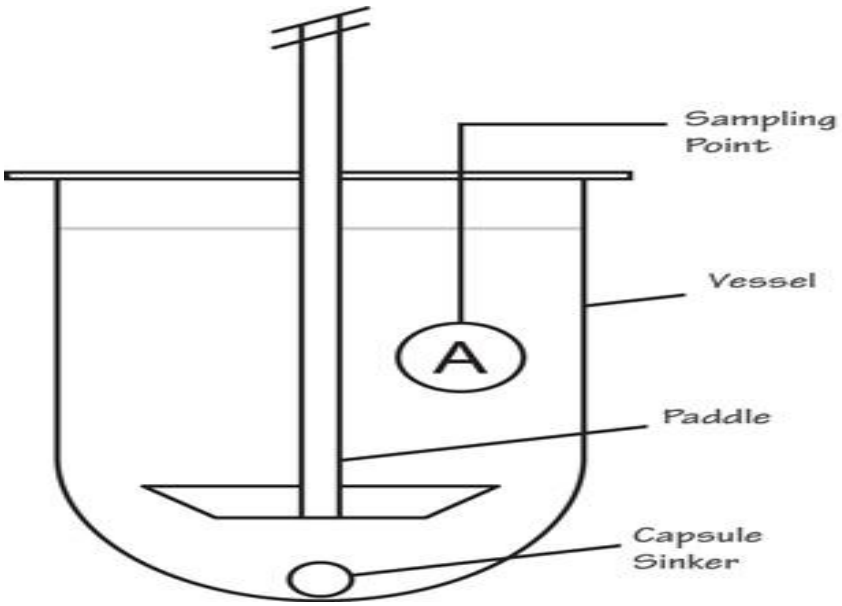
3) Drug content

The drug content was been analyzed by using UV spectrophotometer in order to confirm the purring of the samples.

The drug dosage form was dispersed in the aqueous media & then this aqueous media was centrifuged then the upper saturation fluids was collected & identified at UV 291 nm or else drug in aqueous media was filtered by using filtered paper of diameter 0.8 m & the filtrate coming out the filter paper it was dissolved in 4% SLS solution & the concentration of drug was determined.[35]

4) Dissolution studies

The drug which was designed in a suitable dosage form was dispersed in a dissolution medium of 900ml of USP apparatus of paddles which maintains at 37 ± 2^{o}c temperature at every 10-15 minutes of interval the sample was collected & the absorbance was analyzed at UV 291 nm.[36]



5) Stability studies

The formation prepared was stored at different temperature $4^0c\pm2^0c$ temperature & 35^0crespectively after certain time at interval samples were taken & absorbance & drug contents were taken & absorbance & drug contents were analyzed.[37,38]

X-Ray diffraction

The formed nanocrystals were investigated for their crystaline properties with the comparisions of a atorvastatin calcium powder over range of 2θ from 5° to 50° with filtered Cu-Ka radiation.

F T-IR: F T-IR is a common which was employed in investigation of nanocrystals as they detects the presence of IR active functional groups in bond with either organic or inorganic crystalline samples. It reveals the characteristics Interactions spectral bands of surfactants / proteins/ polymers in bond with nano material (on surface)[35]

Applications

Nano crystals are prominent used for cancer treatment rather than the drug carriers Drug loading was up to 100% Prevents the drug from the enzymatic degradation Much less toxic was gained by preventing solubilizing agents & does not use solvents By binding or encapsulating with ligands or poloxamer the pharmacokinetics properties were improved.

Used as hybrid Nano crystals in this were the water soluble dye with radiolabelled was dissolved in solvents & these get embedded in the crystals lattice & upon reaching to the target site or tumor site they acts as bio imaging.

CONCLUSION

Nano technology has suppressed various limited advantages or dis satisfied factors of conventional system by improving the solubility parameters of two soluble drugs by ensuring with high permeability followed by dissolution, stability & bioavailabilityrates as these preferable can be given through any routes by absence of in convince these are passively delivered to MPS cells & MPS rich organs. The parameters of Nano crystals will greatly influence the in vivo distribution. The used stabilizers or cross linkers will enhance with stability and enhanced retention chances to the targets.

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