e-ISSN: 2248-9126
Vol 3| Issue 1| 2013| 9-13. Print ISSN: 2248-9118

Indian Journal of Pharmaceutical Science & Research

www.ijpsrjournal.com

A REVIEW ON POTENTIAL APPLICATIONS OF NANOCRYSTAL TECHNOLOGY

Raghvendra* and Amlan Mishra[1]

* Department of Pharmaceutics, Aligarh College of Pharmacy, Aligarh, 202001, Uttar Pradesh, India.
[1]Department of Pharmacology, Smt. Vidyawati College of Pharmacy, Jhansi, 284128, Uttar Pradesh, India.

ABSTRACT

Nanotechnology will affect our lives tremendously over the next decade in very different fields, including medicine and pharmacy. Transfer of materials into the nanodimension changes their physical properties which were used in pharmaceutics to develop a new innovative formulation principle for poorly soluble drugs: the drug nanocrystals. The drug nanocrystals do not belong to the future; the first products are already on the market. Nanocrystals have a wide variety of proven and potential applications. They have been used in the manufacture of filters that refine crude oil into diesel fuel. Nanocrystals can also be layered and applied to flexible substrates to produce solar panels. Researchers at the University of Queensland (Australia) have yielded promising results in this field. Titania nanocrystals can be suspended in liquid form and applied to surfaces, making it possible to literally paint a solar panel onto an exterior wall or roof. Nanocrystals are emerging as key materials due to their novel shape and size-dependent chemical and physical properties that differ drastically from their bulk counterparts. The main challenges in this field remain rationally controlled synthesis and large scale production. This article presents a brief review on potential applications of Nanocrystal technology. An attempt is also made to overview on the brief description of nanocrystals as well as associated technology.

Keywords: Drug nanocrystals, Nanocrystal, Crystalline, Nano-Particle, Nanotechnology.

INTRODUCTION

Nanocrystals

Today nanotechnology is encountered all around our daily lives. Whether it be in the production of computer chips (where the need to fit more integrated circuits per square millimeter is evident to produce chips with more computing power, the increasing field of biotechnology (where new tools to easily interact with proteins in ever smaller sizes are needed [1] or simply cosmetic research and products (where nanonized agents can provide a whole range of benefits. In all these fields the need for ever decreased size is common. The nanonization of products, whether for medical use, the food industry (e.g., nanoencapsulated vitamins for so called functional food or the application of drugs for pharmaceutical use, is an important factor both on the economical, as well as on the medical or pharmaceutical side. From the first write-through paper (where microencapsulated ink was used as a thin layer on the back of the top-sheet and the impact of the typewriter broke the capsules to release the ink to the lower sheet [2], nanotechnology has helped to achieve progress all around us. In drug delivery and clinical applications the technology to nanonize (i.e., to reduce in size to below 1000 nm) is one of the key factors for modern drug therapy, now and in the years to come.

B.D. Fahlman has described a nanocrystal (Fig.1) as any nanomaterial with at least one dimension $\leq$ 100nm and that is single crystalline [3]. More properly, any material with a dimension of less than 1 micrometre, i.e., 1000 nanometers, should be referred to as a nanoparticle, not a nanocrystal. For example, any particle which exhibits regions of crystallinity should be termed nanoparticle or nanocluster based on dimensions. These materials are of

Corresponding Author:- **Raghvendra** Email: raghvendra_mpharm@rediffmail.com

huge technological interest since many of their electrical and thermodynamic properties show strong size dependence and can therefore be controlled through careful manufacturing processes. It is well known that, at the nanoscale, materials exhibit fascinating optical, electronic, and magnetic properties that differ drastically from their bulk counterparts.

A typical example is gold, which in the bulk form is a non-magnetic, yellow noble metal. In contrast, 10 nm Au particles absorb green light and thus appear red, 2 3 nm Au particles exhibit considerable magnetism, and smaller Au particles can even turn into insulators [4]. The novel properties of nanostructured materials enable them to find potential applications in many new and promising fields such as nanofabrication, nanodevices, nanobiology, and nanocatalysis. Crystalline nanoparticles are also of interest because they often provide single-domain crystalline systems that can be studied to provide information that can help explain the behaviour of macroscopic samples of similar materials, without the complicating presence of grain boundaries and other defects. Semiconductor nanocrystals in the sub-10nm size range are often referred to as quantum dots.

Fig.1. Images for Nanocrystals

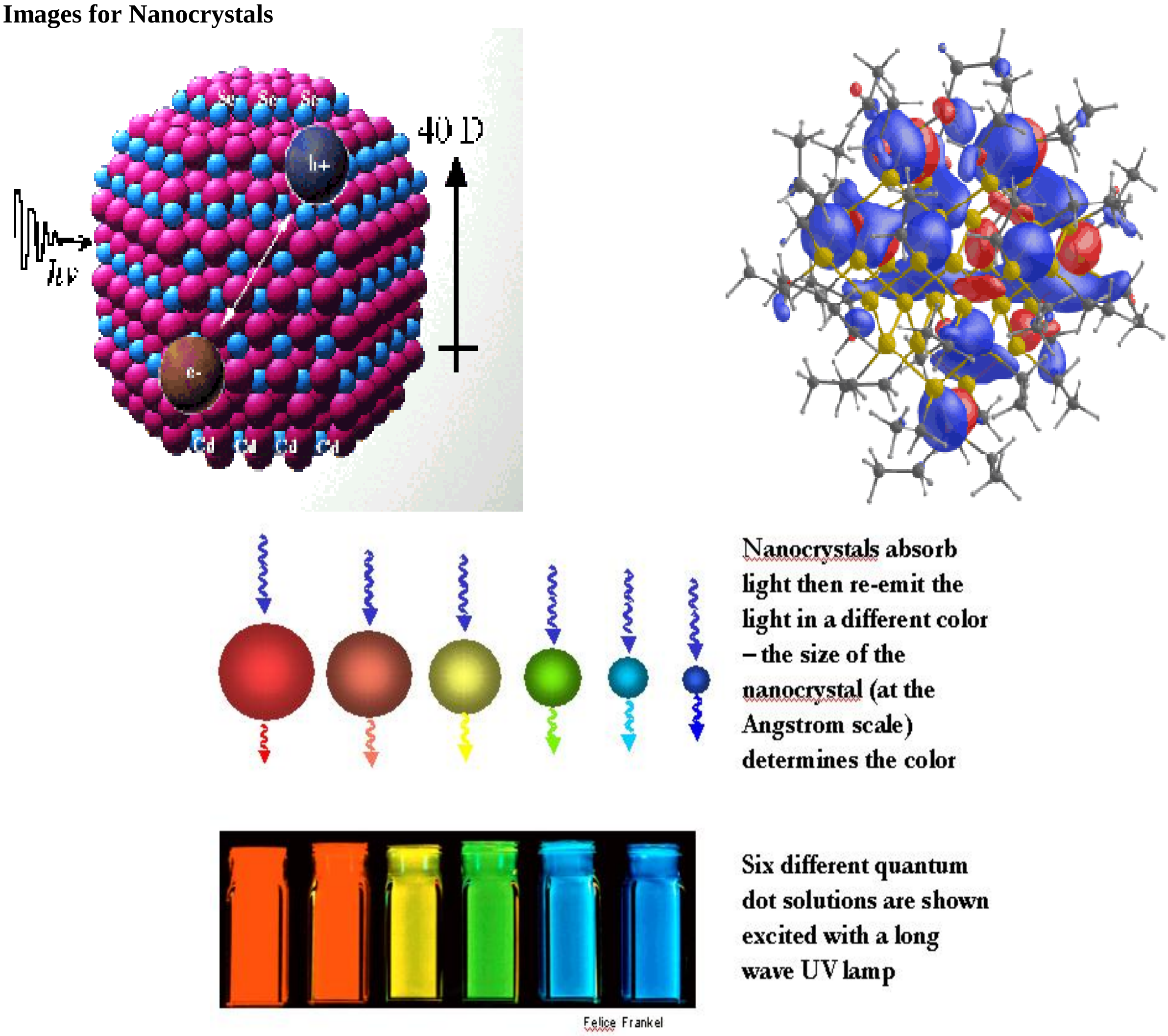

Table 1. List of Some Drugs Developed With Nanocrystal Technology

Product	Drug	Technology by/licensed to
Rapamune	Sirolimus	Elan/Wyeth
Emend	Aprepitant	Elan/Merck
Tricor	Fenofibrate	Elan/Abbot
Triglide	Fenofibrate	SkyePharma/First Horizon Pharmaceuticals

Fig. 2. Nanocrystal Technology

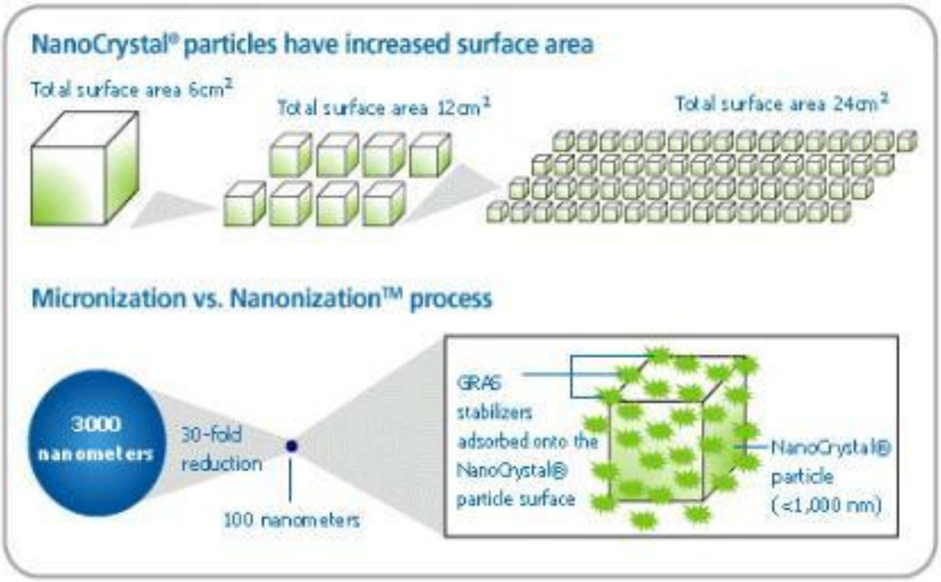

Table 2. Advantages and Disadvantages of Different Methods for the Production of Nanocrystals

Technology	Advantages	Disadvantages
Precipitation	▪ finely dispersed drug ▪ good control of desired size	▪ needs to be stabilized ▪ organic solvent residue ▪ not universally applicable, only drugs with certain properties are possible (e.g., soluble in at least one solvent)
Milling	▪ low energy technique ▪ proven by 4 FDA approved drugs	▪ residue from milling media ▪ can be a slow process (several days) ▪ needs to be stabilized ▪ large batches difficult to produce due to size of milling chamber
Homogenization	▪ universally applicable ▪ no problem with large batches ▪ fast method (several minutes possibly) ▪water free production possible (several minutes possibly)	▪ high energy technique ▪ great experience needed

Crystalline nanoparticles made with zeolite are used as a filter to turn crude oil onto diesel fuel at an ExxonMobil oil refinery in Louisiana, a method cheaper than the conventional way. A layer of crystalline nanoparticles is used in a new type of solar panel named SolarPly made by Nanosolar. It is cheaper than other solar panels, more flexible, and claims 12% efficiency. (Conventionally inexpensive organic solar panels convert 9% of the sun's energy into electricity.) Crystal tetrapods 40 nanometers wide convert photons into electricity, but only have 3% efficiency. The term NanoCrystal is a registered trademark of Elan Pharma International Limited (Ireland) used in relation to Elan's proprietary milling process and nanoparticulate drug formulations. A nanocrystal is a crystalline particle with at least one dimension measuring less than 1000 nanometers (nm), where 1 nm is defined as 1 thousand-millionth of a meter (10^{-9} m).Nanocrystals have a wide variety of proven and potential applications. They have been used in the manufacture of filters that refine crude oil into diesel fuel. Nanocrystals can also be layered and applied to flexible substrates to produce solar panels. Researches at the University of Queensland (Australia) have yielded promising results in this field. Titania nanocrystals can be suspended in liquid form and applied to surfaces, making it possible to literally paint a solar panel onto an exterior wall or roof. Possible future uses of nanocrystals include [5]-:

- Production of hydrogen
- Removal of pollutants and toxins
- Medical imaging
- Bio-tags for gene identification
- Drug manufacture

- Protein analysis
- Flat-panel displays
- Illumination
- Optical and infrared lasers
- Opt isolators
- Magneto-optical memory chips
- Self-organized smart materials.

Nanocrystal Technology and products based on this technology

NanoCrystal Technology is one of the earliest scalable technologies for nanosizing the drugs (Table 1, Fig. 2). Rapamune was the first product based on this technology approved in USA. Rapamune was previously available only as an oral solution in bottles or sachets. The oral solution requires refrigeration storage, and must be mixed with water or orange juice prior to administration. The new tablet developed with NanoCrystal technology provides patients with more convenient administration and storage than Rapamune oral solution. In 2000, Elan Pharmaceuticals received FDA approval for its NanoCrystal technology, by reformulating Rapamune®, a Wyeth drug (sirolimus). The new formulation overcame the drug's relative insolubility by reducing the particle size to less than 200nm, and subsequently coating the active compound with GRAS (Generally Regarded as Safe) surface stabilizers. Many nanotechnologies are developed and are under investigation for their application. As this area of research is in its early stage of growth one can hope for many more surprises and new applications [6].

Nanocrystals are the important components for next generation nanoscale devices [7] and the successful operation of these devices will be easily accomplished by using nanocrystals with distinct sizes and shapes. By assembling and patterning nanocrystals in a manner similar to assembling "Lego" blocks, the fabrication of next generation devices that are extremely fast, efficient, and small can be possible [8].

It has been found that size and shape of nanocrystals are key factors for the determination of their unique chemical and physical properties. Bulk materials have their own characteristics and innate properties such as colour, phase transition temperature, and band-gap energy. However, nanocrystalline materials no longer retain such bulk properties and exhibit unprecedented novel phenomena associated with nanoscale dimension [9]. There are various possibilities to produce nanocrystals in the desired shape and size. Basically three principles can be used: milling, precipitation methods and homogenization methods, as well as a combination thereof. The properties of nanocrystals may be listed as follows-:

- Size below 1µm
- 100% drug, no carrier
- Generally needed to be stabilized
- Crystalline or amorphous structure
- Increase of dissolution velocity
- Increase in saturation solubility
- Amorphous particle state offers advantages

The advantages and disadvantages of different methods for the production of Nanocrystals may be summarized in Table 2.

CONCLUSION

When the size of the material is reduced to less than 100 nanometers, the realm of quantum physics takes over and materials begin to demonstrate entirely new properties. Hence nano-design of drugs by various techniques like milling, high pressure homogenization, controlled precipitation etc., are explored to produce, drug nanocrystals, nanoparticles, nanoprecipitates, nanosuspensions (which for ease of understanding commonly mentioned as nanocrystals). As decreased size will increase the solubility of drugs hence, this technology is explored to increase oral bioavailability of sparingly water soluble drugs. On the other hand engineering of nanocrystals will avoid the use of toxic solvents and surfactants to develop injectable solutions of sparingly water soluble drugs. It is also possible to develop formulations for various routes of administration where size is the critical factor (injectables, ophthalmics and topical preparation). A nanocrystal is a nanoparticle with a crystalline structure. Usually, nanocrystals are used in a "cluster" formation. Semiconductor nanocrystals that are less than 10 nanometers in diameter are called quantum dots. Due to the ability of such nanocrystals to change the wavelength of light, research and development currently is focusing on optical electronic applications.

REFERENCES

1. Merkle RC. Biotechnology as a route to nanotechnology. *Trends Biotechnol*, 17, 1999, 271–74.
2. Cinzia De Vita VC. Nanostructured hybrid materials from aqueous polymer dispersions. *Adv Colloid Interface Sci*, 108, 2004, 167–85.
3. Fahlman BD. Materials Chemistry, Springer: Mount Pleasant, Michigan, 2007, 1, 282-283.
4. Dingsheng Wang, Ting Xie, Yadong Li. Nanocrystals: Solution-Based Synthesis and Applications as Nanocatalysts. *Nano Res*, 2, 2009, 30-46.
5. Anonymous 1. http://whatis.techtarget.com/definition/nanocrystal
6. Anonymous 2. http://www.nanopharmaceuticals.org/NanoCrystals.html

7. Markovich GC, Collier P, Henrichs SE, Remacle F, Levine RD, Heath JR. Nanocrystals and their properties. *Acc. Chem. Res*. 32, 1996, 415.
8. Muller RH, Jacobs C, Kayser O. Nanosuspensions as particulate drug formulations in therapy: Rationale for development and what we can expect for the future. *Adv Drug Deliv Rev*, 471, 2001, 3–19.