DOI: 10.22270/jmpas.VIC2I2.1829 ISSN NO. 2320–7418

International peer reviewed open access journal

Journal of Medical Pharmaceutical and Allied Sciences

Journal homepage: www.jmpas.com CODEN: JMPACO

Research article

Nano diamonds a newer carrier for anti-cancer drug delivery system

Archana Dhyani *[1], Partha Sarthi Bairy[1], Nardev Singh[1], Ashish Dhyani[2]

[1]Graphic Era Hill University, Dehradun, Uttarakhand, India
[2]Graphic Era Deemed to be University, Dehradun, Uttarakhand, India

ABSTRACT

Nano diamonds had recently gained the importance in the field of biotechnology and biomedical science. Nan diamonds are biocompatible and can be complexes with chemotherapeutics. This opens the door of the Nano diamonds in treatment of cancer. The nano diamonds overcomes the problems associated with conventional therapy by providing the localized drug delivery, reduces the frequency of dosing and provide better patient compliance by overcoming the side effect of conventional chemotherapeutic treatment. In this manuscript the authors focused on unique properties of nano diamonds. The different methods like Chemical Vapor Deposition, Detonation synthesis, High-pressure, high-temperature (HPHT) synthesis, Laser synthesis, and Plasma Etching methods were discussed for formulation of Nano diamonds. The manuscript also gives an insight of importance of nano diamonds in ontological studies along with *in-vitro* and *in-vivo* biocompatibility study of nano diamonds.

Keywords: Nano diamonds, Bio-compatibility, Cytotoxicity, Chemotherapeutics, Anticancer, Oncology

Received - 03-09-2021, Accepted- 08/11/2021

Correspondence: Archana Dhyani * ✉ archana.dhyani89@gmail.com

Graphic Era Hill University, Dehradun, Uttarakhand, India

INTRODUCTION

Cancer, the term itself defines its fearsome situations to the affected individuals and environment around the persons and still the leading cause of deaths across the world. The International Agency for Research on Cancer (IARC) estimated a whopping number of 19.3 million new cases including sex, all the age groups and all genotypes (Figure-1) and approx 10 million of reported death worldwide [1]. As the history reveals, the term chemotherapy first coined by Goodman and Gilman after successful application of nitrogen mustard to treat non-Hodgkin's lymphoma in 1942 [2]. Across the timeline chemotherapy plays a significant role in inhibiting multiplication of cancer cells in target specific manner towards signalling molecules, growth factors, apoptosis modulators, cell cycle enzymes etc. Chemotherapy is used as approach to treat cancer cell along with other treatments. But the successful treatment option with the chemotherapy is limited and has certain limitations like effective delivery of drug to effected cells without providing any harm to the normal cells [3] However, the discovery and prominent application of nanotechnology [4,5] opened the doors for effective monogenic treatment strategies. The nano carriers are now being exploited for decades as drug targeting guns to the particular cells or organ. The nanostructure shape of carbon is one of the new doors in the field of nanotechnology for cancer treatment. In this context, the use of nanotubes, nano diamonds, various fullerenes, graphene oxide, and gold nano clusters has been increases in modern science and technology era [6]. In the past few years nano diamnonds (NDs) had gain importance all over the globe because of its low toxicity profile among all other carbon nano materials [7-9]

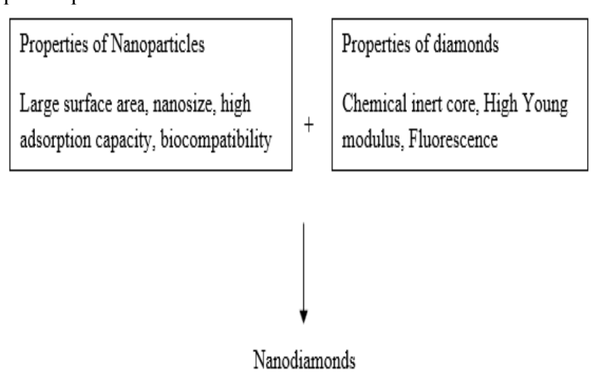
The very usable bulk and surface properties of NDs makes them unique among carbon-based nanoparticles. Being originated from carbon makes them very stable and non-toxic towards biological cells and tiny sizes (<100 nm) helps to use their surface at maximum level so that they can carry other materials on their surface towards smallest pores of biological organs. Exploring these important properties, they are now useful in various fields of sciences [10] but a lot more needs to be done in field of medical sciences. Nano diamonds can be used as carriers because of biocompatibility, scalable method of preparation and ability to bind with number of bioactive molecules and shows better therapeutic efficacy, sustain release, better patient safety and thus increases the patient compliance [11]. The NDs consists of nano crystal in which carbon atoms are bonded as tetrahedral fashion in a 3-dimensional (3D) lattice which gives the property of a diamond. The outer portion consists of a shell

DOI: 10.22270/jmpas.VIC2I2.1829 ISSN NO. 2320–7418

containing a coat of functional groups like hydroxyl (-OH), carbonyl (>C=O), amine (-NH_2), amide (-CO-NH_2) carboxyl (-COOH), sulphuric acid (-SO_3H) and many more (Figure 2) to act as binding domain for other delivering molecules. In complex term, one can say that each particle of NDs has sp^3 bonded carbon atoms which is covered by a layer of sp^2 bonded carbon atoms [12, 13, 14]. These NDs are not naturally abundant carbon materials but can be artificially prepared in large scale by high-temperature–high-pressure procedures (HTHP), chemical vapor deposition (CVD) and detonation method. The different non-toxic readily available polymers which are used to enhance the biocompatibilities of NDs are poly lactic co glycolic acid (PLGA), polylactic acid (PLA), polyvinyl alcohol (PVA), polyethylene glycol (PEG), Poly (ε-caprolactone) and polyvinylidene fluoride (PVDF). All these biopolymers are approved by FDA (Food and Drug Administration) for the preparation of nano diamonds in biomedical field [15].

The discovery and development timeline of nano diamonds points us that it was first produced in 1960's in Union of Soviet Socialist Republics. But the actual recognition of ND blooms after 1980 [12] to entire world where everyone was keen to synthesize or tried to maximizes its utilization in various projects. The manufacturing of nano diamonds started in USA in late 1988 and after 1990, the NDs has gained the focus of different researchers and so gained the huge popularity. Final findings in NDs research helps community to purify their surfaces to yield large scale product at reasonable price [16]. It was also established that NDs are less toxic than other carbon nanoparticles and thus finds application in drug delivery, biomedical imaging and other areas of medicine [17]. Since then ,nano diamond is emerging as real diamond as carbon nanoparticles in the areas of biomedical applications like therapeutics and diagnostics, cardiovascular diseases, autoimmune diseases and most importantly in cancer treatment.

Unique Properties and structure of Nano diamonds



The unique property of ND is due to as it has both properties of diamonds and nanoparticles. ND has sp^3 carbon atoms and thus forms the large crystal structure. Since it has core structural design in which the inner core shell has sp^3 bonded atoms while the outer core has sp^2 carbon atoms with functional groups [18]. The surface contains carbonyl, phenols, sulphuric acid. ND also contains carbonic acid groups, anhydride, hydroxyl groups and peroxide groups in smaller amount. Due to presence of carboxylic acid group the suspension of ND is stable in water and thus can form complex with water soluble drugs [19]

Figure 1a: Global cancer cases distribution types including all age groups & sex. Source: GLOBOCAN, 2020

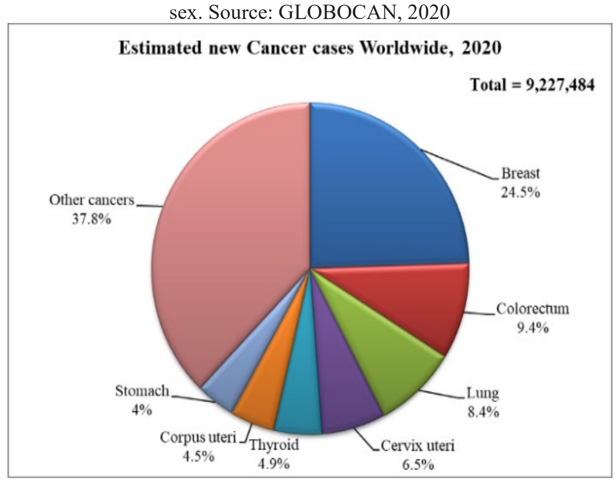
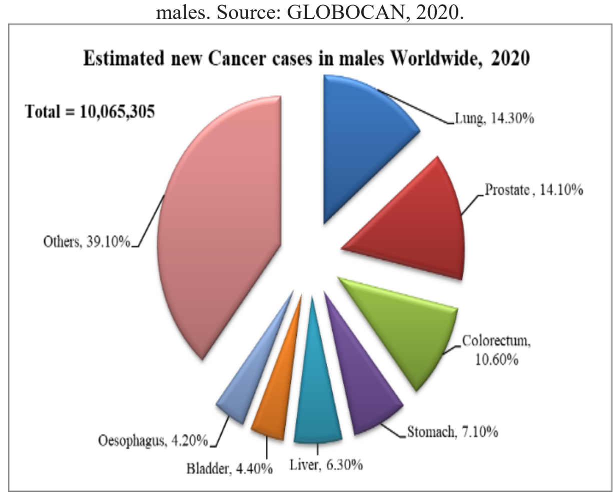
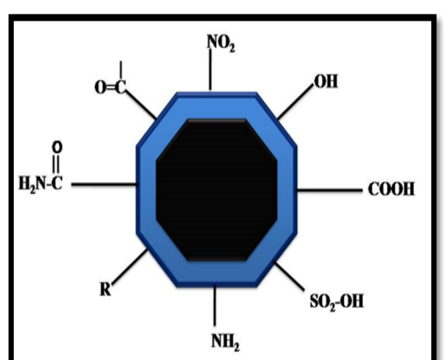


Figure 1b: Global cancer cases distribution types including all age groups of males. Source: GLOBOCAN, 2020.



Synthesis Methods

However, NDs are synthetic carbon particles and can be prepared in laboratory with well-equipped instruments along with proper separation and purification techniques to obtain them in a ready to use form. The popular methods to prepare nano diamonds include:



DOI: 10.22270/jmpas.VIC2I2.1829 ISSN NO. 2320–7418

Chemical Vapour Deposition (CVD):

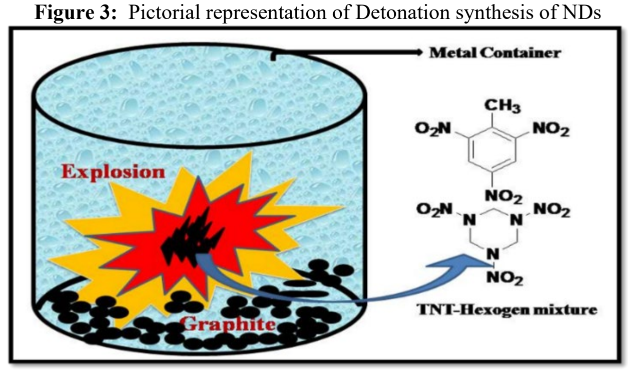
The history of using CVD method for formation of nano crystalline layers has a long history back. For the first time gaseous mixture of Hydrogen-Carbon is used to produce diamonds in the year of 1961. This method is also used now-a-days for the fabrication of nano crystalline structures having size range 10-200nm. In earlier time the nanocrystalline film of size 2-5 nm were prepared by Gruen and his team in Argonne National Laboratory [20]. In this technique, they used hydrogen plasma and inert gases like nitrogen, argon, helium. These inert gases were responsible for acceleration of the nucleation process which ultimately leads to the formation of nano crystalline films of size range 3-5 nm named as ultra-nano crystalline diamond (UNCD) [21]. The structure and morphology of film depends on nature or composition of the gaseous mixture that are used for the fabrication of nano diamonds. The different gases used are hydrogen, carbon-di-oxide, carbon monoxide, and methane [22, 23]. The commonly used gaseous medium is methane/hydrogen mixture and the proportional ratio controls and determines the final size of prepared diamonds in nanoscale range. The vapor phase can initiate by the use of energy source such as flames, plasma and hot filaments to form hydrogen and methyl free radicals. These free radicals help in the continuation of diamond growth over starting phase [24].

Gottlieb et al, 2016 synthesized and reported the NDs and graphene on the samples of copper using hydrogen-methane gas mixture. Raman spectroscopy was employed to determine the quality of graphene and NDs while the optical methods were used for plasma study. They concluded that the CVD method can be used for synthesizing hybrid films of graphene and diamonds. Hurtado et al.,(2020) proposed the method for the formation NDs in aqueous dispersion by CVD method. The NDs were further observed for their size and stability using light scattering method while the surface morphology was analysed by Transmission Electron Microscopy (TEM). The size of NDs was found to be 22 nm and zeta potential was found to be −35 mV. The prepared ND shows cytotoxicity against murine embryonic fibroblast in the concentration range of 0.5–2.2 μg/mL.

Detonation synthesis

This is probably the best and widely used industrial process to synthesized NDs. The detonated nano diamonds were first found in Russia by a team headed by Danilenko in 1963 in Russia [25]. The NDs were formed by the reactions that take places between explosives like RDX and Tri Nitro Toluene (TNT) with carbon materials in a reactor. Most commonly graphite as ND precursor mixed with high quality explosives of TNT-Hexogen mixture (Figure: 3) in varying ratio of 60/40 or 70/30 employed for detonation in oxygen free environment. Inert atmosphere like Argon gas was utilized in drying process but in wet process of detonation synthesis, coolants like ice, nitrogen, and carbon-di-oxide used to achieve rapid cooling of detonated shoot to stabilize the diamond particles. Due to the certain situation in the reactor the carbon species present in the reactor were converted into crystals of diamonds. The explosion increases the temperature and pressure at that point where graphite-diamond conversion is most favourable kinetically but it demands rapid cooling to prevent the sudden reverse transition to graphite [26]. Here wet processes have high advantage and yield in industrial scale over dry process. The obtained crystals of diamonds have a size range between 4-5 nm which should be purified from the non-carbon, non-diamond impurities and from metallic impurities of containers (1-8% w/w) [27]. The prepared powders of detonation nanodiamonds (DNDs) were washed chemically by using a combination of strong acids (HNO_3/ $HClO_4$/H_2SO_4) to obtain C-sp3 inner core (pure diamonds) surrounded by the outer C-sp2 core surface materials [28].

Figure 3: Pictorial representation of Detonation synthesis of NDs



High-pressure, high-temperature (HPHT) synthesis

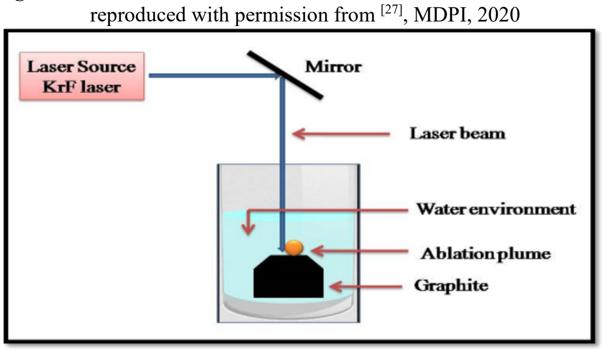
This process of NDs production requires elevated stress conditions like temperature up to 2200^{0}C and pressure up to 7-10GPa [29]. Usually, graphite or carbon aerogel used as diamond precursor and sometimes ruby crystals are used to view the pressure [30]. The technique generally produced diamond particles in micrometre size inside the hydraulic press which needs to be milled in nana diameter. The product is placed to centrifugation and filtration to extract the nano diamonds. The main advantage of this technique includes less nitrogen impurities (up to 200ppm) in final product rather than up to 2000 ppm which is found in DND technique [29]. There are certain limitations in HPHT NDs like we can obtain the smallest size of final materials as 10-20 nm and this process can't produce diamonds in bulk quantities so industrial application is ruled out Ekimov (2019) studied the production of NDs of Adamantane using this HPHT technique. The nano crystals have been synthesized by temperature above 1300–1400°C and a pressure of 8 GPa whereas the huge scale production of ND has been 9.4 GPa in a temperature of 1250–1330°C. The study reveals that diamond microcrystals were formed by graphite re crystallization[31]

Laser Synthesis

For the first time Pulsed Laser Ablation (PLA) method was used for the formation of nanoparticles the year 1987 [32]. The main advantages of PLA method are that it is reproducible; products of high quality are obtained which are free from metallic impurities. But the process is restricted by its highly expensive nature. In this method the krypton fluoride laser (KrF laser) [27] produced laser pulse in a fixed wavelength and for fixed time duration applied on diamond precursor (graphite) in various environments (Figure 4). Water, cyclohexane or nitrogen is used as graphite dipped environments kept in glass or polystyrene chamber [33, 34]. The laser beam causes generation of waves which result in the hydro shock and phase explosion in top layer. The size and surface chemistry of nano diamonds was based on the proper selection of parameter of irradiation and fluid. The liquid environment acts as collector of ablation layer from graphite as suspended nanoparticles. The final task in the method is to collect the particles after cooling. PLA technique is having the fast-cooling rate of 10^{10}-10^{11} K/sec [35] and this rapid cooling favours the NDs deposition in liquid layer.

Lin (2020) [33] synthesized and characterized NV canters enriched NDs in nitrogen environment using PLA techniques. Thomas A et al. in 2021 [40] fabricated the NDs from the dispersion of graphene. The size of ND was found to be less than 50 nm. The NDs also found to have characteristics of absorption at 226 nm.

Figure 4: Pictorial scheme of PLA in water environment. Modified and reproduced with permission from [27], MDPI, 2020



Plasma Etching

Plasma is a new and innovative state of matter developing success among research community and replacing conventional wet lab synthesis through its rapid selectivity and specificity on the reactive starting materials [37]. Targeting the chemical bonds in molecular level followed by etching it can create nano materials also. The diamond samples of various origin and shapes are subjected to plasma treatment which yields nano crystalline structure of diamonds. The options of obtaining plasma etching include radio frequency (RF), direct current (DC), electron cyclotron resonance (ECR), microwave (MW), inductively coupled plasma (ICP), neutral loop discharge (NLD) [38]. It is another top-down process like HPHT NDs synthesis where we can fabricate diamonds of various sizes and shapes via coupling of plasma along with some gases. The gases used are in combination of H_2/O_2, CH_4/O_2, H_2/Ar CF_4/O_2 or as a single administered agent [39]

Biocompatibility of nano diamonds

The bioactivity and bioavailability of NDs it is utmost important to profile their selective cytotoxicity's to mark them safe to use in future sense. However, scientifically it is done by experimenting, collecting and reporting *in-vitro* and *in-vivo* data.

In-vitro cytotoxicity

The *in-vitro* cytotoxicity determination of carbon nanomaterial is very important in determining the safety profile to screen out unwanted possibilities that may hamper the in-vivo studies. Strand, 2007 [40] was the first person who reported the cytotoxicity of NDs. The study he had done reveals that the NDs show less generation of reactive oxygen species when the NDs were incubated with mitochondrial cell line. Progressing their previous work, they have compared biocompatibility of carbon nano materials such as detonated nano diamonds, single and multi-walled carbon nanotubes and carbon black in lung cancer and neuronal cell lines for period of 24 h in a concentration ranging from 25 to 100 µg/mL. The biocompatibility was evaluated for morphological and sub cellular effects of nanomaterial on membrane permeability of mitochondria and generation of reactive oxygen species. The bioavailability order shows NDs as safe than other in order of nano diamonds> carbon black > multi walled carbon nanotube > single walled carbon nanotube [41]

The cytotoxicity was also measured and reported by Liu et. al., (2007) [42] on human lung epithelial cancer cells A549 and normal fibroblasts HFL-1 cell lines. The results indicate that up to concentration 0.1-100 µg/ml, do not reduce the viability of cells or change the expression of protein profile. Vaijayanthimala et al., (2009) [48] studied the mechanism of uptake of NDs by Hela cancer cells and pre-adipocytes (3T3-L1) in detail. The study concluded that the uptake of ND was energy dependent clathrin-mediated endocytosis. It was found that surface charge on ND was also responsible for cellular uptake. Similarly, lots of *in-vitro* cytotoxic assessment [44-46] had been done to prove the safe biocompatibility profile and good to go for *in-vivo* studies.

***In-vivo* biocompatibility**

In-vivo studies are done in experimental animals to validate helpful data outcomes to access the biocompatibility in true physiological environments. Conceptualizing the same Wang and his co-workers [47] for the first time studied the pulmonary toxicity of NDs through intrathecal administration in experimental mice. The study parameters were supported by transmission electron microscopic images and found to have wide distribution of NDs in entire lungs including alveoli and bronchia. But the histopathological studies revealed the beneficial effect of NDs without any toxicity on lungs.

Zhang and his co-workers [48] studied the two morphological parameters after intrathecal instillation of NDs and reports shows toxicity to lungs, liver and kidney in dose dependent manner. NDs at 0.8, 4 and 20 mg/kg dose level shows proper bio-distribution pattern in organ level of Kun Ming mice. However, the reported toxicity caused by ND was not as much of carbon nanotubes.

Another study was conducted by Schrand et. al.,(2009) revealed that the oral administration of NDs used to study the effect of ND hydrosol on mice. The NDs given to the mice was found to be between 16 mg to 450 mg in hydrosol. In mice diet the water is replaced by 0.002 to 0.05 wt% ND in hydrosols. The result reveals that ND hydrosol does not cause death or any organ failure or organ damage. The ND hydrosol did not affect the reproductive organ of the mice [49].

NDs IN ONCOLOGY

Because of unique characteristics as carbon based nonmaterial and high efficiencies NDs are widely useful in field of petroleum industry as lubricant for engine oils, electronics and signal processing using their quantum properties, nano composites, catalysis and so on but the vast application has been explored and tested in the field of biomedical areas [12, 50]. NDs have the properties both of nanoparticles and diamond which is being used in different biomedical fields like targeted drug delivery, genomics, proteomics, immunomodulatory, biomedical and imaging procedures. ND is used as safer choice to incorporate medication and in targeted drug delivery because of its high efficacy and small toxicity profiles. NDs itself possess some cytotoxic properties against some viable microorganisms [51, 52] and with other chemicals it causes threat for harmful pathogens.

Nano diamonds for the management of breast cancer

The unique architecture of NDs with potential binding groups at surface helps them to carry medicines and high penetrability and low toxicity makes them effective cancer guns. Several anti-cancerous medicines were tested utilizing several in-vitro and in-vivo studies making them as ND-supraparticles[53] Doxorubicin loaded nano diamond (ND-DOX) is a revolutionary discovery in management of breast cancer a decade back and still lots of progressing. ND-DOX used in management of breast cancer (4T1) and lung cancer models (LT2-M) with prime advantages like the complex prevent the doxorubicin to expel out from its core while the half-life of ND-DOX complex were increased ten times of doxorubicin alone. The other benefits of using this complex are the reduction of mortality when high dose of DOX were delivered, causes size reduction of tumours and also causes absence of myelo suppression [54]. Locharoenrat, 2019 [55] studied the efficacy of the same complex on human breast adenocarcinoma MCF-7 cell lines. They found that the ND-DOX complex permeates through the cells and shows increased cytotoxicity towards targeted cells. The ND-DOX complex has high cytotoxicity because of ability of doxorubicin with ND to permeate the cells with the passive diffusion mechanism. The results also reveal that the complex causes reduction in IC50 values also precise to be 0.40 mg/ml to establish its anti-proliferative property.

Not only limited to Doxorubicin, the NDs are also tested as complex with Mitoxantrone (MTX). A published work in 2014 [56] reported a study of ND-MTX Complexes in MDA-MB-231-luc-D3H2LN (MDA-MB-231) triple negative breast cancer cell line. The study suggested that the ND effectively binds with MTX with high loading efficiency. ND-MTX shows the greater extend of drug release in acidic media via endocytosis process by the cell. The in-vitro studies suggest that the complex enhanced the efficacy of ND-MTX in MDA-MB-231 cell.

Landeros-Martínez et. al., (2016) [62] constructed a complex of Nano diamond-tamoxifen as a drug delivery carrier to Breast cancer. Yuan and his co-workers in 2019 [58] formulated doxorubicin–polyglycerol nano diamond conjugate that reverses the caner induced immunosuppression against triple negative breast cancer. Garg and his teammates [59] utilizes other anticancer drugs like Unci acid, 5-Flurouracil and Curcumin in increasing concentration in ND complexes and reported their in-silico and in-vitro effects on MCF-7 cell lines.

ND in liver cancer

The drug efflux capabilities of nano diamonds complex also tested for curing hepatic cancers. NDs is used not only to target medicaments in liver cancers but also used to improve imaging for detection purpose [60]. Improved the solubility of the UNCo646 molecule as G9a inhibitor for hepatocellular carcinoma drug delivery in mice model [61]. ND-DOX complex also been tested for liver cancer in mouse where the complex is capable of inhibition of tumor growth and causes apoptosis in liver tumor models. Along with improved efficacy the complex helped to reduce DOX toxicity in a significant manner [54]. DOX delivery in human liver cancer cell (HepG2) reported to improve using polyethylene glycol in ND complex via clathrin dependent endocytosis. Epirubicin-adsorbed NDs also marked as efficient complex overcoming the chemo resistance in cancer cells. The complex enhances the tumor retention by enhancing the endocytic uptake and thus it can potentially harm the cancer and non-cancer stem cells [62].

ND in Colorectal cancer

Doxorubicin hydrochloride (DOX-HCl) forms the complex with NDs having 2-8 nm and targeted on HT-29 colon cancer cell line and found to have innate activity and efficacious results of DOX-HCl in all the tested bioassay parameters [63]. The microtubule inhibitor anticancer agent Paclitaxel (PTX) along with Cetuximab

(Cet) also introduced in colorectal cancer using NDs as ferrying agents in targeted tissues. The promising results indicates marked reduction of tumor size in nude mice and the complex also enhances the mitotic catastrophe and induction of apoptosis in-vivo as well as in-vitro parameters [64].

ND in prostate cancer

The various ND-drug complexes have been explored for their prostate cancer efficiency by scientist Salaam and his teammates through one decade. He utilized already established tetra-peptide Asp–Gly–Glu–Ala (DGEA) as binding protein along with ND-DOX cytotoxic bullets. This newer complex binds to integrins in metastatic phase of prostate cancer which allows more accumulation of DOX in target cells followed by desired apoptosis [65]. They studied that ND-DOX complex on hormone-refractory prostate cancer (HRPC) cell line PC3 through in vitro assay. The study result shows a significant pH dependant efficacy of the complex over DOX alone [66]. Another potential agent Docetaxel is also combined with NDs applying on in vitro assay and it was found to be effective against the PC3 cell viability with effective drug release [67]

ND in pancreatic carcinoma

Pancreatic tumours in starting phase or in metastatic phase are devastating for patients and NDs helped the therapeutic community to achieve some great results via effective delivery system. The PEG coated ND-DOX molecules act as magic bullets in both the in-vivo and in-vitro models of pancreatic ductal adenocarcinoma (PDAC). The superior results of complex over DOX alone were demonstrated via 3D models [68]. On continuation of the promising results of the work, the authors introduced multiple drugs irinotecan and curcumin for the PDAC, human pancreatic carcinoma AsPC-1 cells and reported the efficacious results. NDs alone or in combination with drug-polymer complexes are beneficial for down regulating interleukins expression also [69]. Lu M et. al., studied the Gemcitabine (GEM) loaded amine functionalized NDs in double polymer grafted delivery system to observe their drug release and cytotoxicity over human AsPC-1 cells [70]. Furthermore, the GEM is combined with peptide gly-phe-leu-glyto make it responsible for controlled release. This peptide-Gemcitabine then combined with NDs having particle size of 90 nm to target the pancreatic carcinoma. The cytotoxic studies were characterized on BxPC-3 pancreatic carcinoma cells via MTT assay. It was found that the ND-complex of GEM shows superior activity over GEM alone [71].

ND for brain cancers

Brain is very sophisticated human organ and very difficult to deliver the drugs limited by the presence of blood brain barrier. Recently researchers focused on ND to target the drug directly in brain tumours. The spectroscopic ability of NDs also helps for imaging of brain tumours via supplying luminescence materials utilizing NV centres of NDs [72, 73]. Slegerova J et. al., designed fluorescent NDs coated with biocompatible polymers to target glioma cells for effective cancer imaging with selective specificity [73]. This newer method has greater cancer killing ability with fewer side effects than the already existing drug delivery treatment strategies [74]. Among the different type of brain tumours Glioblastoma is the most common type and despite of many treatment approaches like surgery, radiation, chemotherapy the survival time for the patient is less than one and a half year. The hypothesis was framed that ND modified drug can be given by direct injection method called convection enhanced delivery (CED). This method was used to inject ND-Dox directly in brain tumours in rodent models. Result of the study revealed the proper distribution pattern of the ND-DOX complex in target tumour cells and surroundings in brain without any adverse effects.

CONCLUSION

Nano diamonds are the biocompatible carriers which can be utilized for various biological applications like drug delivery, bio-sensing and bio-imaging. There are the different methods used for fabrication of nano diamonds as discussed in the manuscript. ND also found compatible both in-vitro and in-vivo. Nan diamonds have the capability to penetrate cell wall and acts as a carrier for chemotherapy. They are cost effective and can be produced in large quantities. Thus, the nano diamonds have future application in various diagnostic and therapeutic fields.

ACKNOWLEDGEMENT

The authors are thankful to Graphic Era Hill University and Graphic Era Deemed to be University, Dehradun for providing all the facilities and support for the study.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest among them.

REFERENCE

1. Sung H, Farley J, Siegel RL, et al, 2021. Global cancer statistics 2020 globocan estimates of incidence and mortality worldwide for 36 cancers in 185 countries, CA a cancer journal for clinicians, 71 209-49.
2. Chabner BA, Roberts TG, 2005. Chemotherapy and the war on cancer, Nature Reviews Cancer, 5, 65-72.
3. R Mahjub, Jatana S, Lee SE, et al, 2018. Recent advances in applying nanotechnologies for cancer immunotherapy, J Controlled release, 28, 239-63.
4. Sun T, Zhang YS, Pang B, 2014. Engineered nanoparticles for drug delivery in cancer therapy, Angew Chem Int Ed, 53, 12320–12364.
5. Merkel TJ, De Simone JM, 2011. Dodging drug-resistant cancer with diamonds, Sci trans med, 9), 73ps8.
6. Qin SR, Zhao Q, Cheng ZG, et al, 2019. Rare earth-functionalized nano diamonds for dual-modal imaging and drug delivery, Diamond and Related Materials, 1,173-82.
7. Zhang K, Zhao Q, Qin S, et al, 2019. Nano diamonds conjugated up conversion nanoparticles for bio-imaging and drug delivery,

Journal of colloid and interface science, 1, 316-24.
8. Vaijayanthimala V, Cheng PY, Yeh SH, et al, 2012. The long-term stability and biocompatibility of fluorescent nano diamond as an in vivo contrast agent, Biomaterials, 33, 7794-802.
9. Turcheniuk K, Mochalin VN, 2017. Biomedical applications of nano diamond, Nano technology, 28,252001.
10. Moore LK, Gatica M, Chow EK, 2012. Diamond-based nanomedicine, Enhanced drug delivery and imaging, Disruptive Science and Technology, 1, 54-61.
11. Mochalin VN, Shenderova O, Ho D, et al, 2012. The properties and applications of nano diamonds, Nature nanotech, 7, 11-23.
12. Iakoubovskii K, Baidakova MV, Wouters BH, et al, 2000. Structure and defects of detonation synthesis nanodiamond. Diamond and Related Materials, 9, 861-5.
13. Iakoubovskii K, Mitsuishi K, Furuya K, 2008. High-resolution electron microscopy of detonation nanodiamond, Nanotechnology 19,155705.
14. Rehman A, Houshyar S, Wang X, 2020. Nanodiamond in composite, Bio medical application, Journal of Biomedical Materials Research Part A, 108,906-22.
15. Shenderova O, Koscheev A, Zaripov N, et al, 2011. Surface chemistry and properties of ozone-purified detonation nanodiamonds, The J. of Physical Chemistry C, 26, 9827-37.
16. Schrand AM, Johnson J, Dai L, et al, 2009. Safety of Nanoparticles, From Manufacturing to Medical Applications, Nanostructure Science and Technology, 159-87.
17. Slocombe D, Porch A, Bustarret E, et al, 2013. Microwave properties of nanodiamond particles, Applied Physics Letters, 17,244102.
18. Kaur R, Badea I, 2013. Nanodiamonds as novel nanomaterials for biomedical applications, drug delivery and imaging systems, International journal of nanomedicine, 8, 203.
19. Gruen DM, 1999. Nanocrystalline diamond films, Annual Review of Materials Science, 29,211-59.
20. Gruen DM, 2001. Ultra nano crystalline diamond in the laboratory and the cosmos, MRS bulletin, 26,771-6.
21. Spitsyn BV, Bouilov LL, Derjaguin BV, 1981. Vapor growth of diamond on diamond and other surfaces, Journal of Crystal Growth, 52, 219-26.
22. Butler JE, Sumant AV, 2008. The CVD of nanodiamond materials, Chemical Vapor Deposition, 14, 145-60.
23. Park JW, Kim KS, Hwang NM, 2016. Gas phase generation of diamond nanoparticles in the hot filament chemical vapor deposition reactor, Carbon, 106, 289-94.
24. Greiner NR, Phillips DS, Johnson JD, et al, 1988. Diamonds in detonation soot, Nature, 333,440-2.
25. Baidakova M, 2007. New prospects and frontiers of nano diamond clusters, Journal of Physics D, Appl. Physics, 5, 40, 63.
26. Basso L, Cazzanelli M, Orlandi M, et al, 2020. Nanodiamonds, Synthesis and application in sensing, catalysis, and the possible connection with some processes occurring in space, Applied Sciences, 10, 4094.
27. Chang LY, Ōsawa E, Barnard AS, 2011. Confirmation of the electrostatic self-assembly of nano diamonds, Nanoscale, 3, 958-62.
28. Shenderova OA, McGuire GE, 2015. Science and engineering of nanodiamond particle surfaces for biological applications, Bio interphases, 10, 030802.
29. Crane MJ, Petrone A, Beck RA, et al, 2019. High-pressure, high-temperature molecular doping of nano diamond. Sci adv 5, eaau6073.
30. Ekimov EA, Kondrina KM, Mordvinova NE, et al, 2019. High-pressure, high-temperature synthesis of nano diamond from Adamantane, Inorg Mat, 55, 437-42.
31. Yang GW, Wang JB, Liu QX, 1988. Preparation of nano-crystalline diamonds using pulsed laser induced reactive quenching. Journal of Physics, Condensed Matter. 10, 7923.
32. Basso L, Sacco M, Bazzanella N, et al, 2020. Laser-Synthesis of NV-Centers-Enriched Nano diamonds: Effect of Different Nitrogen Sources, Micromach, 11, 579.
33. Amans D, Chenus AC, Ledoux G, et al, 2009. Nanodiamond synthesis by pulsed laser ablation in liquids, Diam Related Mater, 18, 177-80.
34. Yan Z, Chrisey DB, 2012. Pulsed laser ablation in liquid for micro-/nanostructure generation, Journal of Photochemistry and Photobiology C, Photochem Rev, 13, 204-23.
35. Thomas A, Parvathy MS, Jinesh KB, 2021. Synthesis of nanodiamonds using liquid-phase laser ablation of graphene and its application in resistive random-access memory, Carbon Trends, 3,100023.
36. Puliyalil H, Cvelbar U, 2016. Selective plasma etching of polymeric substrates for advanced applications, Nanomatter, 6, 108.
37. Tamburri E, Orlanducci S, Reina G, et al, 2015. Nanodiamonds, the ways forward, InAIP conference proceedings, 23, AIP Publishing LLC.
38. Terranova ML, Orlanducci S, et al, 2015. Nanodiamonds for field emission, state of the art Nanoscale, 7, 5094-114.
39. Schrand AM, Huang H, Carlson C, et al, 2007. Are diamond nanoparticles cytotoxic? The j. of physical chemistry B, 11, 2-7.
40. Schrand AM, Dai L, Schlager JJ, et al, 2007. Differential biocompatibility of carbon nanotubes and nanodiamonds. Diamond and Related Materials.16, 2118-23.
41. Liu KK, Cheng CL, Chang CC, et al, 2007. Biocompatible and detectable carboxylated nano diamond on human cell, Nano techno, 18, 325102.
42. Vaijayanthimala V, Tzeng YK, Chang HC, et al, 2009. The biocompatibility of fluorescent nano diamonds and their mechanism of cellular uptake, Nanotechn, 25, 425103.
43. Li J, Zhu Y, Li W, et al, 2010. Nanodiamonds as intracellular transporters of chemotherapeutic drug, Biomaterials, 31, 8410-8.
44. Zamani M, Aghajanzadeh M, Molavi H, et al, 2019. Thermally oxidized nanodiamond, an effective sorbent for separation of methotrexate from aqueous media, synthesis, and characterization, in vivo and in vitro biocompatibility study, J. Inorganic Organometallic Polymers Materials, 29,701-9.
45. Bondon N, Raehm L, Charnay C, et aL, 2020. Nanodiamonds for bioapplications, recent developments, J Mater Chem B, 8, 10878-96.
46. Yuan Y, Wang X, Jia G, et al, 2010. Pulmonary toxicity and translocation of nano diamonds in mice, Diamond and Related Materials, 19, 291-9.
47. Zhang X, Yin J, Kang C, Li J, et al, 2010. Biodistribution and toxicity of nanodiamonds in mice after intratracheal instillation, Toxico lett, 198, 237-43.
48. Schrand AM, Hens SA, Shenderova OA, 2009. Nanodiamond particles properties and perspectives for bio applications, Critical reviews in solid state and materials sciences,34, 18-74.
49. Torres Sangiao E, Holban AM, Gestal MC, 2019. Applications of nanodiamonds in the detection and therapy of infectious

diseases, Mater, 12, 1639.
50. Wehling J, Dringen R, Zare RN, 2014. Bactericidal activity of partially oxidized nano diamonds, ACS nano, 24, 8, 6475-83.
51. Jira J, Rezek B, Kriha V, et al, 2018. Inhibition of E, coli growth by nano diamond and graphene oxide enhanced by Luria-Bertani medium, Nano mat 8, 140.
52. Yu Y, Yang X, Liu M, et al, 2019. Amphipathic nano diamond supraparticles for anticancer drug loading and delivery, ACS applied materials & interfaces, 15, 18978-87.
53. Chow EK, Zhang XQ, Chen M, et al, 2011. Nano diamond therapeutic delivery agents mediate enhanced chemo resistant tumor treatment, Science translational medicine, 9,73ra21.
54. Locharoenrat K, 2019. Efficacy of nano diamond–doxorubicin complexes on human breast adenocarcinoma cell lines, Artificial cells, nanomedicine, and biotechnology, 4, 4053-8.
55. Toh TB, Lee DK, Hou W, et al, 2014. Nano diamond–Mitoxantrone complexes enhance drug retention in chemo resistant breast cancer cells, Mol. pharmaceutics, 11, 2683-91.
56. Landeros Martínez LL, Chavez-Flores D, Orrantia-Borunda E, et al,2016. Construction of a nano diamond–tamoxifen complex as a breast cancer drug delivery vehicle, J Nano mater, 27, 2016.
57. Yuan SJ, Xu YH, Wang C, et al, 2019. Doxorubicin-polyglycerol nano diamond conjugate is a cytostatic agent that evades chemo resistance, reverses cancer-induced immuno suppression in triple-negative breast cancer, J nano bio techn, 17, 1-25.
58. Garg S, Garg A, Sahu NK, Yadav AK, 2019. Synthesis and characterization of nano diamond-anticancer drug conjugates for tumor targeting, Dia Relat Mat, 1, 94,172-85.
59. Hou W, Toh TB, Abdullah LN, et al, 2017. Nano diamond–Manganese dual mode MRI contrast agents for enhanced liver tumor detection, Nanomedicine, Nanotechnology, Biology and Medicine, 13, 783-93.
60. Gu M, Toh TB, Hooi L, et al, 2019. Nano diamond mediated delivery of a G9a inhibitor for hepatocellular carcinoma therapy, ACS applied materials & interfaces, 11, 45427-41.
61. Wang X, Low XC, Hou W, et al, 2014. Epirubicin-adsorbed nano diamonds kill chemo resistant hepatic cancer stem cells, ACS nano, 8, 12151-66.
62. Huang H, Pierstorff E, 2007. Active nano diamond hydrogels for chemo therapeutic delivery, Nano letters, 14, 3305-14.
63. Lin YW, Raj EN, Liao WS, et al, 2017. Co-delivery of paclitaxel and cetuximab by nano diamond enhances mitotic catastrophe and tumor inhibition, Sci rep, 7, 1-1.
64. Salaam AD, Hwang P, McIntosh R, et al, 2014. Nano diamond DGEA peptide conjugates for enhanced delivery of doxorubicin to prostate cancer, Beilstein J nanotechn, 5, 937-45.
65. Salaam AD, Hwang PT, Poonawalla A, et al, 2014. Nano diamonds enhance therapeutic efficacy of doxorubicin in treating metastatic hormone-refractory prostate cancer, Nanotech, 25, 425103.
66. Ortiz JD, Joshi S, Singh SR, et al, 2018. Impact of Docetaxel Conjugated Nano diamonds on Gene Expression of Prostate Cancer (PC3) Cells. Biotech, Biomaterials and Biomedical, Tech Connect Briefs 2018, 65-68.
67. Madamsetty VS, Sharma A, Toma M, et al, 2019. Tumor selective uptake of drug-nano diamond complexes improves therapeutic outcome in pancreatic cancer, Nano med, Nano techn, Bio and Med,18, 112-21.
68. Madamsetty VS, Pal K, Keshavan S, et al, 2019. Development of multi-drug loaded PEGylated nano diamonds to inhibit tumor growth and metastasis in genetically engineered mouse models of pancreatic cancer, Nanoscale,11, 22006-18.
69. Lu M, Wang YK, Zhao J, et al, 2016. PEG Grafted-Nano diamonds for the Delivery of Gemcitabine, Macromolecular rapid communications, 37, 2023-9.
70. Ye W, Han H, Li H, et al, 2020. Polymer coated nano diamonds as gemcitabine prodrug with enzymatic sensitivity for pancreatic cancer treatment, Progress in Natural Science, Mat Inter, 30, 711-7.
71. Zhang XQ, Lam R, Xu X, et al, 2011. Multimodal nano diamond drug delivery carriers for selective targeting, imaging, and enhanced chemotherapeutic efficacy, Adv mate, 23, 4770-5.
72. Slegerova J, Hajek M, Rehor I, et al, 2015. Designing the nano bio interface of fluorescent nano diamonds: highly selective targeting of glioma cancer cells, Nanoscale, 7, 415-20.
73. Gupta C, Prakash D, 2017, Gupta S, Cancer treatment with nano-diamonds. Front, Biosci 9, 62-70.
74. Xi G, Robinson E, Mania-Farnell B, et al, 2014. Convection-enhanced delivery of nano diamond drug delivery platforms for intracranial tumor treatment. Nano med, Nano techno, Bio Med, 1, 10, 381-91.

How to cite this article

Archana Dhyani, Partha Sarthi Bairy, Nardev Singh, Ashish Dhyani, 2022. Nano diamonds a newer carrier for anticancer drug delivery system. Jour. of Med. P'ceutical& Allied. Sci., VIC 2 – I 2, Pages – 211 - 218. doi: 10.22270/jmpas.VIC2I2.1829