

# Nanodiamonds: Advanced carriers for anticancer drug delivery

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**Abstract:** Diamond nanoparticles discovery and extensive applications in modern biosciences. Because of its excellent biocompatibility, it serves as useful platforms that can be implanted within polymer-based microfilm devices. Nanodiamonds complex with a chemotherapeutic show sustained release of the drug for a month, with a significant amount of drug in reserve. It serves the potential for highly localized drug release as a complementary and potent form of treatment with systemic injection towards the reduction of continuous dose, and as such, attenuation of the often-powerful side effects of chemotherapy. Nano-diamonds are very economical, allowing the wide impact of these devices for a range of physiological disorders like supporting as a local chemotherapeutic patch, or as a pericardial device to suppress inflammation after open heart surgery. Nano-diamond patch could be used to treat a localized region where residual cancer cells might remain after a tumour is removed. Nano-diamonds may be used to discover a wide range of therapeutic classes, including small molecules, proteins, therapeutic antibodies, RNAi.

**Keywords:** Nanodiamonds, nanoparticles, tumour, therapeutics, proteins

## 1. Introduction

The improvement of therapeutic delivery agents has become necessary due to the difficulties that the disciplines of biological agents and medical therapies are currently confronting, such as poor pharmacokinetics and chemo resistance. Nanodiamonds (NDs) have become popular carriers among the various platforms under investigation because of their biocompatibility, scalable production procedures, and characteristic surface-mediated binding of a broad range of bioactive chemicals. Furthermore, it has been demonstrated that ND platforms enhance therapeutic efficacy, preserve drug release, and improve therapeutic safety profiles (1). The use of nanodiamonds in biotech and medicine is now advancing steadily. In fact, nanodiamonds are the ideal intracellular carriers of bioactive chemicals due to their biocompatibility, reduced size, and strong surface chemical interaction. Nanodiamonds were found to be able to enter cell cytoplasm using confocal imaging, although they remained stuck in nuclear membranes, only partially penetrating the nucleus (2).

As theranostic agents required for the development of customised medicine, nanoparticles have found utility in the treatment of malignancies, the study of autoimmune illnesses, and cardiovascular disorders. These nanoscale devices should combine imaging, tracking, and monitoring capabilities

with targeted substance delivery to tumours, biological processes, or particular organs (3-7).

Detonation, vapour deposition, or elevated, high-pressure techniques can all be used to synthesise nanodiamonds, which can vary in size between 1 to 100 nm (8). They have a huge surface area, stiff structure, chemical stability, octahedral symmetry, and inexpensive production costs (9,10). Exciting breakthroughs that range from basic to translational have been made as a result of the use of nanomedicine in cellular, preclinical, and clinical research, especially in the field of cancer.

The use of chemicals modified by nanotechnology has been successful in overcoming many of the current obstacles in cancer treatment. These obstacles include, among others, off-target toxicity, low circulation times that result in diminished efficacy, and drug resistance that causes unsatisfactory intra-tumoral retention. The initial clinical achievements in nanomedicine to get over these problems were based on monotherapy, where small-molecule and nucleic acid delivery showed considerable advantages over conventional drug administration. Recent preclinical studies have demonstrated that combination nano therapies, made up of either various classes of nanomaterials or a single nanopatform functionalized with various therapeutic compounds, are more effective at imaging and treating tumours than single-compound delivery. Nanodiamonds, one of the many

potential nanomaterials under development, have drawn more and more attention due to the special chemical and mechanical characteristics of their faceted surfaces. The rational and methodical design of optimal therapeutic combinations employing an implicitly de-risked drug development platform technology, known as phenotypic personalised medicine-drug development, has more recently embraced nanodiamond-based drug delivery (PPM-DD). A significant issue that pervaded all facets of drug research, both nano and non-nano, was successfully resolved by the application of PPM-DD to quickly identify globally optimum drug combinations (11).

## 2. Historical Background

The Union of Soviet Socialist Republics first documented the manufacture of nanoscale diamond particles in the 1960s (12). But they went unnoticed by the rest of the world until the middle of the 1980s, when they started to be used in motor oil additives and wear-resistant coatings. Today, there are many ways to make diamond nanoparticles for industrial use, including grinding down bigger diamond micro particles, laser ablation, and purifying detonation soot. It wasn't until 1988 (13) that ND manufacturing in the United States was first reported; nevertheless, it wasn't until the late 1990s that interest in NDs for use in biomedicine really began to take off. Since then, the area has developed substantially, with NDs being used in numerous applications ranging from cancer therapy to nanoscale magnetic resonance imaging (14,15).

## 3. Types of nanodiamonds, their uses, and their mechanisms

Out of all the many types of nanodiamonds, explosions produce the most fascinating ones. Covalent bonds, electrostatic contacts, and/or hydrophobic interactions allow Detonation Nanodiamond (ND) to be easily changed and attached to other molecules and compounds. After their synthesis, these compounds remain stable for several months. Other cutting-edge methods rely on self-assembled nanodiamonds in regulated configurations, are embellished with nanoparticles, or are encapsulated in polymers (16).

Medical and biotechnological applications for nanodiamonds are numerous. Additionally, they can be used to transport medications and biomolecules such as DNA, RNA, and proteins inside

live cells and animals. Because nanodiamond substance and cell physiology and structure have such high compatibility, this event occurs. In fact, it was discovered that among nano-carbons (such as carbon black, fullerenes, and carbon nanotubes), nanodiamonds were the least harmful since they often do not significantly increase oxidative stress or apoptosis when applied to cells (17). The internalisation of nanodiamonds by cells was discovered to be mediated by clathrin. The cytoplasm, as well as the perinuclear region, are all places where cell endocytic vesicles transport and arrange nanodiamonds, but not the nucleus. However, Martn only put up a contentious theory showing that fenton-treated nanodiamonds might penetrate the cell nucleus directly. According to published reports, nanodiamonds can be exocytosed out of cells after being absorbed by them. The size, surface, concentration, and treatment time of the nanodiamonds, as well as the temperature and cell line used, all affect these processes, which are not standard (18,19).

Fluorescent microscopy can also identify nanodiamonds because of the nitrogen-vacancy centres, which are auto-fluorescent structural flaws. Additionally, because of their greater refractive index than cytoplasm, nanodiamonds exhibit significant light scattering signals that enable even optical microscopy with good contrast to easily differentiate them in cell compartments.

## 4. Nanodiamonds: For Cancer Treatment Approaches

Scientists have been investigating the use of nanodiamonds more recently as more is understood about the electromagnetic characteristics of nanodiamonds' facet interfaces when they carry chemicals in natural systems, the ways their inanimate core can be beneficial in certain applications, and as an implies to take full advantage of their tunable surfaces. Detonation nanodiamonds (DNDs) and fluorescent nanodiamonds (FNDs) are the two primary categories of nanodiamonds utilised in medical applications, in order to highlight the main applications of nanodiamonds at the moment.

The researchers point out that imaging both DNDs and FNDs is increasingly being considered as a technique to enhance magnetic resonance imaging, and more recently, FNDs are also being looked as a tool to follow stem cells to learn more about their capacity for regeneration. There is now a lot of research being done on drug delivery to

determine what kinds of medications stick best to nanodiamond facets, especially those utilised in chemotherapy applications.

Similar to this, a great deal of study is being done on bio-distribution and toxicity to determine how nanodiamonds can be ingested, applied topically, orally, or otherwise introduced into a living system.

Another advantage of using nanodiamonds is their low cost of production and use, despite being linked to valuable jewels because mining waste can be used to obtain them (11).

### 5. Detecting Cancer with Nanodiamonds in Early Stages

Recently, scientists created microscopic synthetic diamonds that potentially help the fight against cancer by illuminating cancerous regions in MRI images. The ground-breaking method may be especially useful in identifying tumours like brain and pancreatic tumours, which are difficult to uncover early on. Since brain and pancreatic cancer are two of the most lethal malignancies, improved treatment may be possible. The foundation for this work was earlier investigation into the potential of nanodiamonds as a vehicle for the delivery of anti-cancer drugs. In that study, scientists found that nanodiamonds could penetrate cell barriers without damaging them, making them effective chemotherapy medicine delivery systems. Nano diamonds are particularly important for administering drugs during chemotherapy since they are often non-toxic and non-reactive.

Since diamonds have magnetic qualities that allow them to function as MRI beacons, they organised the particles inside a diamond to provide it a "signal" that could be recognized by MRIs. The technique allowed for "monitoring of the molecules' travel in the body" when the hyperpolarized diamonds were connected to compounds that were intended to treat cancer. The use of quantum physics in the fight against cancer is indeed highly novel, but scientists are also discovering other distinctive and fascinating approaches to create brand-new cancer medicines. For instance, a personalised cancer treatment considers the molecular make-up of tumour and a patient's genetics to determine the best and most efficient treatments or pharmaceuticals for that patient. Immunotherapy, a field of study that focuses on using the immune system to combat cancer cells, is another area of research that shows significant promise for treating cancers other than melanoma (20).

### 6. Cancer Drug Delivered By Nanodiamonds Kills Chemo resistant Cancer Stem Cells

Chemo-resistance, or the cancer cells' capacity to resist chemotherapy, is the main factor behind cancer treatment failure. Cancer stem cells, a sub-type of cancer cell that starts tumour growth, are frequently discovered to be more resistant to chemotherapy than the majority of the tumour, which might cause cancer to return after chemotherapy treatment. As a result, there is a great deal of interest in creating new medications or therapeutic approaches that circumvent chemo resistance, particularly in cancer stem cells (21).

According to a study, a chemotherapy medication, attached to nanodiamonds successfully kills chemo-resistant cancer stem cells. Research has shown that chemo-resistant cancer stem cells can be successfully treated with conventional chemotherapy medicines when they are repurposed using nanotechnology. This work created a nanodiamond-epirubicin drug delivery complex by coupling the common chemotherapeutic medication epirubicin to carbon nanodiamonds, carbon structures with a diameter of roughly five nanometres (EPND). In xenograft models of liver cancer, the researchers discovered that while conventional epirubicin and EPND were both capable of eliminating normal cancer cells, only EPND was able to eradicate chemo-resistant cancer stem cells and prevent the development of subsequent tumours (21).

Future applications for nanodiamonds are also possible due to the flexibility of the nanodiamond-based drug delivery system. These include the addition of additional drugs with comparable effects as well as active targeting components, such as peptides or antibodies against tumoral cell surface proteins for aimed drug release. A nanodiamond-drug delivery method can be used for more than just liver cancer, too. It provides a potential strategy for treating a variety of challenging malignancies, especially those caused by chemo-resistant cancer stem cells (21).

### 7. Nanodiamond Application in Cancer Treatment

#### *Nanodiamonds for brain tumours*

Researchers have created a novel medication delivery method that uses nanodiamonds, which are extremely small particles, to deliver chemotherapy

treatments directly into brain tumours. It was discovered that the new approach outperformed conventional therapies in terms of cancer-killing effectiveness and adverse side effects. The most prevalent and deadly type of brain tumour is glioblastoma. Despite receiving surgery, radiation therapy, and chemotherapy, individuals with glioblastoma have median survival duration of less than one and a half years. The blood-brain barrier, a system of protecting blood arteries that surrounds the brain, prevents chemotherapy medications from frequently penetrating it, making the tumours notoriously challenging to treat. Additionally, any medications that do pass through the barrier don't stay concentrated in the tumour tissue long enough to be useful (22).

Nanodiamonds are carbon-based particles with a diameter of around 4 to 5 nanometres and the ability to transport a wide variety of medicinal molecules. Additionally, whereas tumour-cell proteins can expel the majority of anticancer medications from the cell before they have a chance to begin working, they are unable to do so with the nanodiamonds. As a result, drug-nanodiamond combinations stay in the cells for a lot longer without having an impact on the tissue around the tumour (23).

The outcomes also showed for the first time that the amount of doxorubicin that was dispersed outside the tumour was constrained by the ND-DOX delivery. This decreased harmful side effects and increased the amount of the medicine in the tumour for a longer period of time, boosting the treatment's ability to destroy the tumour more effectively without damaging nearby tissue. Rats given ND-DOX had significantly longer survival times than those given merely unmodified doxorubicin (24).

Nanodiamonds can bind to doxorubicin very rapidly and powerfully because they have many facets that resemble the surface of a soccer ball. As further research is done, new chemotherapy drugs for brain cancer will be able to be bonded to nanodiamond surfaces, improving treatment and reducing side effects. This study showed that administering ND-DOX convection-enhanced offers a strong therapeutic delivery method against these dangerous and difficult brain tumours (25).

#### *Nanodiamonds for breast cancer*

Doxorubicin, an anticancer medication, was bonded to nanodiamonds by researchers. They admin-

istered either this substance or doxorubicin alone to mice with liver tumours, and then evaluated the drug levels in the tumours two days later (26). In comparison to mice given doxorubicin alone, they discovered that mice treated with the nanodiamond compound had doxorubicin levels that were ten times greater and persisted for seven days. Additionally, mice getting nanodiamond-doxorubicin had smaller tumours and lived longer (27,28).

Then, doxorubicin-resistant breast cancer was used as a test subject for the nanodiamonds. There, too, the nanodiamond-doxorubicin mixture performed better. Surprisingly, by releasing the medicine more gradually, the nanodiamonds actually lessened its toxicity. Doses which would have killed mice if administered as free medicine did not even cause them to lose weight when the drug was carried on nanodiamonds (29).

However, the idea of delivering drugs using nanodiamonds is still in its infancy. The idea has to be refined more because synthetic polymers can be tailored in terms of their composition and properties (30,31).

### **8. Nanodiamond-drug delivery under control**

Drug molecules can be conjugated to the surface functional groups of ND, such as hydroxyl and carboxylic groups, because to their hydrophilic characteristics. To successfully deliver chemotherapy agents to the specific loci and release in the physiological circumstances, maximising the efficacy and trying to minimise the side effects resulting from the undesired drug-tissue interactions, effective targeting and controlling of delivery of drugs has been the focus of efforts. In this regard, protein desorption from ND was modelled after the hormone insulin (32).

Physical adsorption in an aqueous solution produced a non-covalent bond between bovine insulin and DND, which showed pH-dependent desorption in sodium hydroxide settings. When the ND-insulin matrix is exposed to an alkaline environment, protein is produced, mediating the interaction between both the ND and insulin. The desorbed insulin retained its functionality, according to MTT and reverse transcription polymerase chain reaction (RT-PCR) analyses, but the adsorbed insulin remained inactive. This shows that ND may be an effective transporter of the necessary proteins by physical adsorption. As a result of the medication's varied acid sensitivity

and the carrier surface's mildly acidic extracellular fluid in a tumour environment or inside the tumour, the active drug can be released from the carrier to the tissue. By adsorption, the anticancer agent cis-dichlorodiammineplatinum (II) (CDDP, cisplatin) has so far been loaded onto ND surface. At pH 6.0, CDDP is released from the composite at a rate that is significantly higher than it is at pH 7.4. Thus, the ND-CDDP complex may release more medicines than it would in normal tissue in an environment with higher acidic extracellular fluid, such as the cytoplasm of cancer cells or the environment surrounding a tumour (31,32)

The preparation of pH-responsive DOX loaded nanodiamond for targeted anticancer therapy has been done using a similar technique. Sodium citrate medium was used to manufacture DOX adsorbed onto PEGylated nanodiamonds in this technique (33).

### 9. More about Nanodiamonds

An allotrope of carbon called nanodiamonds (NDs) has a size range of truncated octahedral shape, and a size of 5 nm. Two are connected. In the crystal structure of NDs, face-centered cubic (FCC) lattices are tightly packed and interpenetrating. Of the two overlapping FCC lattices, one is moved one-quarter of its distance towards the other. Length of the elemental cube space's diagonal. A crystalline diamond can also be said to be present in an ND. Core made out of an ideal lattice. Additionally, this core is encased in an amorphous shell that combines sp<sup>2</sup> (diamond) and sp<sup>3</sup> (graphitic) linkages. NDs display several special qualities include tiny particles and a high specific surface good chemical stability, as well as adsorption capabilities this makes them an appealing possibility for biomedical uses. Additionally, because of their distinct physicochemical fluorescent materials, detonation nanodiamonds (DNDs), and The research community is very interested in nanodiamonds (FNDs) technology applications, which benefit the scientific community. DNDs can be created through the detonation process and are easily functionalized with various biological molecules through hydrophobic and electrostatic contacts, as well as or covalent connections. The usage of DNDs in biotechnology applications, including medication delivery and bio molecule transport Transport inside a living cell or microbe. Additionally, NDs are capable to

by converting incoming radiation into heat, you can potentially due to their use in thermal therapy. NDs recently have being researched for potential uses in treating cancer theranostics, including hyperthermia, photodynamic treatment, drug delivery nanosystems, and cancer imaging nanosystems as well as agents for photo- and thermoacoustics (34).

#### *Nanosystems for cancer imaging based on nanodiamonds*

Nanodiamonds have a variety of distinctive qualities, including biocompatibility, chemical and photo physical stability, and fluorescence emission from their NV centres. The use of (NDs) as a contrast agent for cancer is well suited. On account of the NV sites incorporated into the diamond matrix, NDs are known to generate strong red photoluminescence. Auto-fluorescence (from cells and tissue) and other background noise sources have been found to frequently impair fluorescence-based imaging systems, especially in vivo. The wide-field time-gated fluorescence imaging approach can get over this issue. Because NDs have far longer fluorescence lifetimes than auto-fluorescence (up to 20 ns), it is conceivable to use temporal gating to provide background-free detection in vivo. The blood arteries in mouse ears were also successfully imaged in vivo by these authors for lung cancer cells. For the in vivo imaging of blood-circulating tumour cells, this method may be helpful. It was discovered that background-free imaging might be altered by an external device both in vivo and in vitro applied during imaging through an oscillating magnetic field using a fluorescence microscope. When compared to traditional fluorescent imaging techniques, this combined approach significantly increased the signal-to-noise ratio, as demonstrated by the usage of solely FNDs (size 100 nm in vivo using a mouse model). A brand-new fluorescent ND platform with FND labelling, fluorescence detection, and imaging was demonstrated by Wu et al. Monitoring of transplanted stem cells in living creatures using FLIM and FACS technologies for long-term monitoring and analysis. For the first time, these combined approaches were employed to analyse the in vivo function of FND-labelled LSCs following transplantation and to assess the engraftment potential after around a week. Has extensive application to other stem cells as well (35).

### **10. The creation of multi-drug PEGylated nanodiamonds to stop the growth of tumours and disease in a genetically modified mouse pancreatic cancer model**

#### *Creation of PEGylated NDs*

We coupled the carboxylated NDs with poly (ethylene glycol) (PEG) moieties to increase their stability and dispersibility. The EDC and sulfo-NHS acid-amine coupling reaction technique was used to create PEGylated NDs by forming an amide link between ND-COOH and mPEG-amine. PEGylation was confirmed by FTIR measurement following purification, and high-resolution TEM (HR-TEM) was employed to confirm the NDs' atomic structure (36). The nanodiamonds' crystalline structure was confirmed by HR-TEM images of the NDs. The lattice spacing between diamond faces clearly reveals the diamond structure, as seen by the arrows. To sum up, in the current work, we have shown in animal models of PDAC, PEGylated NDs enhanced simultaneous medication delivery and therapeutic improvement. These outcomes shown for the first time that the anti-inflammatory/anti-cancer compound curcumin and the chemotherapy medication irinotecan bind to NDs (37). This study also covers, for the first time, the application of computerized all-atom model of NDs for structural design execution as a method to develop effective nano-carriers for drug delivery. Following a full description and evaluation of the drug loaded NDs in vitro and in vivo, two genetically altered, spontaneous PDAC mice were used. It's interesting to note that we found NDs suppressed IL-9 and IL-10 to have immunomodulatory effects in vivo. The findings discussed here will give the development direction when taken as a whole (38).

### **11. Drug-Resistant Breast and Liver Tumour Treatment Using Nanodiamond Particles as Systemic Chemotherapeutic Delivery Agents**

The vast majority of tumour treatments in situations of metastatic cancer fail as a result of drug resistance, which is a prevalent issue in cancer therapy. ND-anthracycline agents are among the ND-drug agents that have been synthesised; they are highly scalable and potently bind the drug molecules, leading to noticeably improved efficacy and safety. A very promising approach to combating drug resistance based on nanomedicine would be

the quick synthesis of drugs that are too large to be effluxed from a tumour mass and that are nanoparticle-tagged, along with the ability to prevent early systemic release, systemic toxicity, and off-target effects. Due to the remarkable scalability of its synthesis methodology, NDX is among the most promising platforms for this indication, according to a recent study. Injecting NDX particles into a mouse's tail vein allowed for systemic administration. Even at high ND dosages, subsequent toxicity assessments of serum IL-6 and serum ALT showed no apparent toxicity, proving that the NDs were well tolerated. It was assessed how NDX injections affected myelosuppression. Treatment of Dox alone caused significant drops in white blood cell counts below threshold levels, whereas administration of NDX had no apparent myelosuppression. Chemotherapy's dose-limiting adverse effect, myelosuppression, can have serious consequences such as superinfections and patient mortality (39).

Effectiveness was almost non-existent with unaltered Dox administration at 100 g equivalent. A significant reduction in tumour size was achieved after NDX delivery at the same dosage equivalent. Unchanged Dox administration led to accelerated animal mortality when the drug dosage equivalent was doubled. All of the animals survived when the lethal dosage was administered by ND, and the tumour treatment efficacy was substantially improved, resulting in the study's smallest tumours. This showed how the ND platform could mediate significant enhancements to chemotherapeutic tolerance.

This early example of preclinical NDX administration showed that even when a treatment is bound via physisorption, there is no premature drug elution. This was supported by the fact that premature drug release would have produced no therapeutic benefit because the Dox would have been effluxed and separated from the ND as well as apparent myelosuppression due to the circulation of free drug. The lack of myelosuppression and large increases in efficacy supported the idea that the powerful interaction between NDs and Dox acted as a key mediator of greatly improved safety, even in a passively targeted system (39).

### **12. Nanodiamonds Encapsulated in Liposome's for the Treatment of Triple-Negative Breast Cancer**

An effective passively targeted technique was initially established by the systemic delivery of NDX for the treatment of drug-resistant liver and breast

tumours. The continuous development of NDX toward clinical usage was supported by the improved drug tolerance and therapeutic efficacy seen even with the deadly Dox dosage. In a recent investigation, an alternate NDX complex was created in which Epi was used in place of the Dox molecule (40). The MDA-MB-231 triple-negative breast cancer (TNBC), which has been demonstrated to overexpress the epidermal growth factor receptor EGFR, served as the disease model in this investigation. Therefore, the ND-Epi complexes were encapsulated in liposomes that had the EGFR antibody surface functionalized. This architecture was used to maximise drug loading on the ND surface because the ND-anthracycline interaction was able to confirm that it could improve intratumoral drug preservation to prevent diffusion and improve efficacy, vascular system half-life by a factor of 10, and completely remove myelosuppression, among other benefits. Thus, these ND-Lipid hybrid particles (NDLPs) aggressively targeted the previously scalably generated ND-anthracycline complexes. The procedure of rehydrating lipid thin films made of cholesterol, biotinylated lipids, and ND solution was used to create NDLPs. The anti-EGFR antibodies were attached to the liposome surface using biotin-streptavidin chemistry. A variety of techniques were used to characterise NDLP synthesis, including zeta potential analysis, dynamic light scattering (DLS), Fourier transform infrared spectroscopy (FTIR), flow cytometry, cryogenic transmission electron microscopy (cryo-TEM), and cryo-TEM to visualise NDLP formation. These techniques were used to measure the success of NDLP synthesis and to distinguish the NDLPs from free NDs and lipids. The presence of lipids was determined using inductively coupled plasma atomic emission spectroscopy (ICP-AES) and the conjugation of the anti-EGFR antibody was verified using an enzyme-linked immunosorbent test (ELISA). The effectiveness of anti-EGFR functionalized NDLP targeting was thoroughly evaluated *in vitro*. Epidermal Growth Factor (EGF) flooding tests showed that anti-EGFR antibody conjugation and targeting abilities were successful because the targeting efficacy gradually decreased as the EGF concentration increased. Targeted and untargeted NDLP complexes, as well as phosphate buffered saline (PBS) and unmodified Epi, were used as test conditions in order to determine preclinical efficacy. Similar to unmodified Dox treatment, unmodified Epi administration led to accelerated animal mor-

tality. Drug tolerance was promptly improved by untargeted NDLP treatment because early mortality was no longer seen. Furthermore, there was a definite delay in tumour growth. It is intriguing to note that the delivery of the anti-EGFR functionalized NDLPs caused tumours to regress until they were no longer discernible, which is a promising result for actively targeted ND-chemotherapeutic substances. This study offered one of the most thorough analyses of ND serum and urine toxicity in terms of ND biocompatibility. No apparent toxicity was observed following the injection of ND and NDLP in any of the patients, further demonstrating the promise of the ND platform for drug delivery (40).

### 13. The Promising Prospects of Nanodiamonds for Biomedical Use

The three main applications of ND in biomedicine that are envisaged are imaging, analytical diagnostics, and cancer therapies (i.e., drug delivery). The field of nanomedicine will also likely be impacted by other clinical applications of NDs for platforms for nerve stimulation, prosthetic devices for retinal implants, and instruments in cell surgery.

#### *Delivery of Medicine and Cancer Treatment*

Its capacity to successfully counteract the mutagenic effects of cancer medications alone or in combination with chemotherapy and radiotherapy, as well as reduce the incidence of new tumours, makes ND, an insoluble solid powder, unique. The most favourable ND type (e.g., detonation, HPHT, natural, etc.), dose, surface functionalization, and treatment period can all be chosen in order to optimise the therapeutic efficiency of NDs for a particular drug or delivery application. For instance, directed/sustained medication delivery systems could make use of the time-release and shielding capabilities of ND agglomerates.

#### *Bioanalytical/Diagnostic*

In the near future, it is anticipated that ND films and particles will be used for analyte adsorption, purification, and collection in bioanalytical applications. As shown in Figure, recent studies have shown that ND-probe bioconjugates can be successfully used in diagnostic applications that collect and target proteins, small molecules, and nu-

cleic acids. This work will be extended to additional bio- and organic compounds to determine the breadth of applications because NDs are biocompatible and could be employed as an inert solid support that doesn't affect the chemical or biological function of bound molecules. Due to the chemical and physical characteristics of nanodiamond, Nanodiamond-based biosensors perform better than conventional silicon like and gold-based microelectronic materials by combining very fast detection with high selectivity and sensitivity, especially for high throughput clinical systems. The differences in the type of Nanodiamond particle or film like mono-, poly-crystalline may also make novel devices expansive and allow them to outperform existing performance standards at a lower cost. The packing distance of ordered assemblies of ND particles that we refer to as "ND Rainbows" depends on the particle spacing. Furthermore, the size selection of ND particles has led to the creation of organised photonic crystals that we refer to as "ND Christmas Lights." As a result, these ordered ND particle assemblies may be used in biodiagnostics, such as a substrate for colorimetric indicators.

#### *Imaging*

Fluorophore tagging, optical scattering, Raman mapping, and other imaging modalities of ND enable dynamic monitoring of its interaction with living systems. In the future, NDs might be employed for biomedical imaging that is directed at the human body or inside individual cells.

Of course, in order to improve the signal output owing to endogenous fluorescence of biological tissues, optimization may be necessary as a method of viewing. This can be done by further functionalizing the surface or developing more advanced non-destructive imaging techniques. However, recent *in vivo* and *in vitro* research demonstrates that ND imaging is simple and does not necessitate such considerations. In the future, different types of near-infrared (NIR) fluorescence, tomography (magnetomotive optical coherence, photoacoustic, positron emission, computed scan), ultrasound, or magnetic resonance imaging could be integrated for detection with nanohybrid fluorescent-magnetic-radioactive nanoparticles (MRI).

As a result, nanodiamonds present a promising path for more advanced and perhaps brand-new imaging modalities in biomedicine (41-45).

#### **14. Nanodiamond Application In Medicine**

##### *Nanodiamonds' anti-tumour properties in cell culture*

Exciting findings have been obtained from research into the anti-cancer capabilities of diamond in both its natural and functionalized forms. Diamond powders showed a reduced stress response as shown by human gene expression in human promyeloblastic leukaemia (HL60) cells exposed to dual radiofrequency/microwave plasma activated chemical vapour deposition (RF/MW PCVD). Nanodiamonds or ND composite films, in contrast, have been utilised to successfully deliver anti-cancer pharmaceuticals such dexamethasone (Dex) and doxyrubin hydrochloride (DOX). The cellular response of RAW 264.7 murine macrophages and HT-29 human colorectal cancer cells was observed when the apoptosis-inducing medication DOX was electrostatically loaded onto the surface of 2 to 8 nm NDs or into 50 nm ND aggregates. After that the cells were treated with 25 g/mL unconjugated Nanodiamond, 2.5 g/mL DOX, or the composite ND-DOX of an equivalent concentration, the cell viability was assessed using the MTT assay and DNA fragmentation was investigated using electrophoresis. The findings revealed that ND is naturally biocompatible, DOX is hazardous, and ND-DOX composites exhibit an intermediate, attenuated reaction. The authors made the speculative claim that the shielding properties of ND aggregates could be used to delay DOX desorption in sustained drug release applications while minimising adverse drug side effects on the healthy tissues and cells immediately surrounding the drug delivery system. Examining the mechanisms involved in the production of apoptosis by NDDOX composites revealed that prolonged incubation of cells resulted in gradual apoptotic cell death, which suggested that DOX was slowly eluting from the ND surface and aggregate interior. After pre-treatment with lipopolysaccharide (LPS), a recognised inhibitor of DOX-mediated apoptosis, which greatly reduced cell death, more evidence for DOX-mediated apoptosis following addition of ND-DOX composites was demonstrated.

After being seeded with RAW264.7 murine macrophages, the biocompatibility of the single or multilayered ND-PLL films was evaluated. Similar to free-floating NDs, the ND-PLL films did not alter the macrophages' release of pro-inflammatory

ry cytokines (TNF, IL-6, and iNOS), which is important for many different cancer signalling pathways. Dexamethasone (Dex), a powerful synthetic glucocorticoid steroid hormone that has anti-inflammatory and immunosuppressive properties, has also been found to lessen LPS-induced cytokine production when added to the ND-PLL thin films. The amounts of fluorescently tagged Dex in water were evaluated with UV-Vis spectroscopy to validate the desorption and elution of Dex from the PLL-ND composite substrates. A sustained release throughout 24 hours, which corresponds to the time period of the cell tests, was suggested to be the driving force behind the Dex release mechanism (46-49)

*Nanodiamonds' anti-cancer properties  
in both humans and animals*

The success of in vitro drug delivery and cell targeting using NDs has increased interest in researching the therapeutic effects of NDs in cancer-prone mice, canines, and people. The impact of DND on lifespan was examined in the Af line of mice with ascites Erlich cancer. These mice were chosen as the study subjects because they are frequently used as laboratory animals for radiation research and because the findings may be generalised to people. Six 106 ascite Erlich cancer cells were injected into each mouse, after which the effect of DND on the mice's level of spontaneous mutation was calculated. When compared to the control group, the experimental mice treated with ND suspensions lived around 38% longer. The UNCD-treated mice continued to be active right up to their deaths. Furthermore, administration of DND made by the "Diamond Centre" at high concentrations (2.5% to 3% aqueous suspensions) had no deleterious effects on the mouse sex cells.

Other studies in dogs with terminal cancer demonstrated that oral suspension of NDs might stop the dogs' growling and whining from discomfort while also restoring intestinal function and boosting their immune systems.

Following chemotherapy and radiotherapy, Dolmatov and colleagues' studies on human patients with stage IV cancer showed that aqueous and oil suspensions of DND can improve health regardless of the initial tumour location (breast, intestinal, or stomach). Orally administered DND had a pronounced favourable impact in every case, extending life expectancy, boosting the will

to live, lowering pain thresholds, restoring intestinal function, enabling mobility, and raising blood indices. Additionally, as toxins were actively eliminated, polyps on the bladder's interior walls decreased, and immune system function was improved. These changes also affected the colour and smell of the urine.

Additionally, after rinsing with it, paradontosis and other purulent processes in the mouth and throat, such as wounds and cuts, quickly healed (46-49).

## 15. Conclusions

The last few years have seen incredibly strong research into the chemistry and biology of nanodiamonds, which has resulted in a new type of nanodiamond that is potentially nearly unidentifiable and significantly superior than its predecessors. In terms of purity, size selectivity, inhibition of aggregation, colloidal stability, surface functionality, and photoluminescence, the ND products produced as a result of this concentrated study are comparable to other nanoparticles. As a result, the authors of this the near uses as future well as due to their potential distinctive new surface scientific fields paper predict that NDs will gain more attention in and of diamond study and core qualities, applications. We think will establishing tight working ties with researchers outside the nanodiamond community is essential for the productive development of nanodiamond products as well as for promoting and utilising their potential in biotechnology and medicine.

The conclusion drawn from the aforementioned paragraphs is that the use of nanodiamonds in the treatment of cancer appears promising and a potential strategy due to their multiple advantages, including the absence of side effects, target action, nontoxic nature, and inability to create inflammation. Nanodiamonds have the ability to pass through cell walls without harming them, making them potential drug delivery vehicles for chemotherapy. In addition, they can be functionalized with almost any type of therapeutic and are easily suspended in water, both of which are crucial for biomedical application.

They can also be made in huge quantities at a low cost. Nanoparticles are used in the treatment of cancer as well as the investigation of autoimmune disorders and cardiovascular conditions. As therapeutic agents required for the development of customised therapy, they are now of interest.

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