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Review Article

Dentistry Section

The Baffling Human Body and the Boundless Nanomaterial Boon- A Trap for Cancer Crab

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ABSTRACT

Life is a balance of infinite physiochemical balanced harmonies and the basic unit cell is responsible in maintaining it. Cardiovascular diseases and Cancer are the prime causes of death worldwide. Cancerous cells break the harmonious balance and result in uncontrolled growth and spread. Emerging among the existing modalities for management of cancer, as a ray of hope is Nanotechnology based treatment. Dendrimers, Quantum dots and nanobubbles contribute significantly as part of nano based diagnosis and treatment in the management of cancer. Dendrimers are nanoparticles which employ the principle of Trojan horse strategy in that encapsulation and conjugation of anti cancer agents helps in targeting the cancerous cells specifically without affecting the adjacent healthy cells. Quantum dots are cadmium based nanoparticles which when exposed to UV light glow and help in destroying the cancerous cells in the incipient stage. Nanobubbles are generated with short pulses of laser, which helps in identifying the individual cancerous cells and explodes them. Apart from them other technologies such as liposomes, fullerenes, carbon nanotubes, nanoshells, paramagnetic nanoparticles, nanoburrs, respirocytes, microbiovores, nanopores, smart coating and nano bandaid contribute a great lot as boundless nanomaterial boon for the management of cancer, cardiovascular problems and overall systemic health.

Keywords: Cancer, Dendrimers, Nanobubbles, Quantum dots

INTRODUCTION

Human existence is a mystery of infinite physiochemical balanced harmonies and the basic unit cell maintains it all at different stages of life. However, the destiny of life in the form of death is a miserable end point and no doubt baffling pathologies play a key role in this regard with cardiovascular disease and cancer being the prime reasons worldwide for this pathetic breaking point.

Focusing on the key culprit, Cancer - The beginning of Cancer happens when a cell takes the liberty to violate the normal check points on uncontrolled growth and spread. Healthy cells have a harmonious balance of molecular checks that dictate when the cell must remain silent and when it should undergo division. Disruption of this delicate and sensible check point mechanism occurs due to various endogenous and exogenous factors acting on the cell disturbing the balance and leading the cell to undergo uncontrolled proliferation (cancer).

Hippocrates introduced the word carcinoma from the Greek word Karkinos which means crab since he correlated the persistence and spread of cancer simulating a crab [1]. This crab like growth has been tackled since ages with advances in science. Despite advances in science, man is always at risk from the effects of science at different levels. Medical management of pathological conditions with drug faces a twin challenge of safety and efficacy. The modern science has showered its merciful face solving these twin problems in the form of nano technology.

HISTORY OF NANOTECHNOLOGY

Nanotechnology introduced in 1959 by late Nobel Physicist Richard P Faynman and highlighted by K Eric Drexler in the mid 1980's emerging from the greek word nano which means dwarf can be defined as the science and engineering involved in the design, synthesis, characterisation, and application of materials and devices whose smallest functional organization, in at least one dimension, is on the nanometer scale or one billionth of a meter [2].

Definition

Nanotechnology has currently been defined in three dimensions wherein the first dimension relates it to the development of a technology and associated research at three levels namely atomic, molecular and macromolecular within the measurement of nanosize scale which ranges approximately 1-100 nanometers. In the second dimension it deals with systems and devices which have properties and functions based on nanobiomaterials due to their small and or intermediate dimension. In the third dimension it is concerned with the ability to regulate or manipulate at the level of an atom. These three dimensions connote nanotechnology as per the National nanotechnology initiative [3].

No doubt, tackling human pathologies is an art and astonishingly tiny particles as part of nanotechnology serve as a unique platform with bundles of boundless nanomaterials. The following are a few of them playing the role of a tricky trap for the cancer crab as well for the welfare of human body as a whole.

NANOTECHNOLOGY AND CANCER

Dendrimers

They are a unique form of Nanotechnology which arises as a hope from the myriad of new treatments, for cancer [4]. It employs the cunning trick of Trojan horse strategy wherein the dendrimers serve as smugglers in carrying the anticancer agent to the cancerous cells specifically; thereby sparing the adjacent normal cells [5,6].

Clinical Implications

Encapsulation and Conjugation are the binary benefits of the dendrimers. The design of hyper branching proceeding from the centre towards the periphery in dendrimer results in an amazing umbrella that can provide a tailored sanctuary containing voids which provide a refuge from the outside environment where in anti cancer drug molecules can be physically encapsulated [7]. Apart from encapsulation, the concept of conjugation has been made possible by the inclusion of ligands which are intended to bind specifically

to cancer cells. Folate is considered as a Tumour targeting ligand, because the membrane bound folate receptor is over expressed on a wide range of human cancer [8-12]. Also paving a platform for the pandemic HIV are the dendrimers solving the complexities of HIV infection cycle as part of targeted drug delivery system [13].

Quantum Dots

Quantum dots are tunable fluorescent nano particles made of cadmium selenide which glow when exposed to u-v light and are useful in the detection of cancer in very incipient stages and preferentially killing them [14].

Clinical Implications

Early detection of cancer in incipient stage is essential and desirable since usually they are detected only on reaching a certain size when they contain millions of cells that would have metastasized. The Quantum dot technology is easy, economical, and enables quick point-of-care screening of cancer markers. Thus crowning the cancer management by Sentinel lymph node (SLN) imaging in cancer patients for tumour staging and planning of treatment are the Quantum dots which along with near infra red fluorescence system serve as trimodal imaging probe using optical, MR and PET imaging [15,16].

Nano-Bubbles

Advances in cancer research targets to achieve a theranostic approach which is the intersection of diagnosis, therapy and therapy guidance. Achieving the above objective is the tunable theranostic probe in the form of plasmonic (gold) nano particles serving as nano bubbles which help in singling out individual diseased cells and destroy them with tiny explosions [17]. The plasmonic nano bubble is a transient event rather than a particle. The generation of them takes place by the optical excitation of plasmonic nano particles with short pulses of laser. This results in nano particle heating and subsequent evaporation of environment around the nano particle surface.

Clinical Implications

They are useful in early detection and management of residual cancer cells on a thin surface, detection and ablation of metastasis in deep tissues. Other applications include gene therapy, cell level treatments and microsurgery [18], imaging, targeted drug delivery, sonothrombolysis, vascular diseases [19-22].

Liposomes

Developments in nanotechnology is a dynamic travel and drug delivery using nanotechnology is a desperate effort serving humans solving the twin problem and dating back to 1960, spherical nanoscaled drug delivery vehicles referred to as liposomes.

Clinical Implications

They are useful in the incorporation of not only anti cancer agents but also genetic materials, vaccines, anti microbial agents, proteins, enzymes, peptide hormones and chelating agents [23]. The structure of Liposomes with lipid membrane and aqueous core have been a breakthrough especially in targeted delivery of anti-cancer agents thus overcoming the setbacks of conventional chemotherapy. The anti cancer agent can be encapsulated in the lipid membrane or aqueous layer based on the lipophilic or hydrophilic nature of the drug.

Liposomes with antibody directed towards tumour antigen (immunoliposome), and also with an enzyme to activate a prodrug (enzyme linked immunoliposome) contribute significantly as part of targeted drug delivery in cancer management [24].

With respect to oral and maxillofacial region, liposomes play an important role in the management of hemangioma along with urea in inhibiting vascular endothelial cell proliferation. Liposomes play a key role in targeted and dose controlled management of hemangioma [25].

Limitations

The drawback of liposome associated with swift destruction and removal by liver macrophages. However, it is overcome by polyoxyethylene coating and addition of polyvinylpyrollidone polyacrylamide lipids, distearoyl phosphotidylcholine and cholesterol which help the stealth liposomes for prolonged existence and effective action [26].

Amidst the sparkling advantages there exist a few setbacks with respect to liposomes such as decreased blood circulation time due to non-specific binding or immunogenicity, reduced tumour penetration, and high susceptibility to lysosomal degradation after internalization [27].

Fullerenes

Fostering a tiny technology to the fullest extend are the Fullerenes which are carbon based allotropes molecules composed of 60 carbon atoms arranged in a soccer ball-shaped structure and also referred to as bucky balls discovered by Kroto et al., [28].

Clinical Implications

Most significantly they contribute in the management of malignancies wherein they serve as photosensitizers in photodynamic therapy. This is achieved by generation of reactive oxygen species which when stimulated by light destroys the target cell. This property serves the anti microbial effect of fullerenes especially on gram positive bacteria and mycobacterium [29].

By virtue of the specialised molecular structure and anti oxidant activity the fullerenes serve as anti viral drug transport nano structures especially contributing crucially in HIV and Hepatitis infections [30]. Also contribute as new biomarker homing and diagnostic contrast agents for MRI.

Limitations

However the use of fullerenes is contemplated upon due to the inconclusive evidence of its toxicity related to the carbon 60 per se or any other associated factors, experimental artifacts [31].

Carbon Nanotubes

Concurrent with the family of fullerenes are the Carbon nanotubes (CNT) discovered by Iijima in 1991, which are the third allotropic form of carbon along with graphite and diamond constructed by thin sheets of benzene ring carbons rolled up into the shape of a seamless tubular structure.

Clinical Implications

The carbon nanotubes contribute multifariously in cancer diagnosis and as part of targeted drug delivery in cancer management, antifungal therapy, gene therapy, lymphatic targeting, photodynamic therapy, thermal therapy, vaccine delivery for cancer immunotherapy and immunotherapy for immunological diseases [32-36].

Limitations

Carbon nanotubes though have a setback of insolubility yet proper functionalisation of carbon nanotubes makes it hold a special place in cancer as they bypass the bystander effect of conventional chemotherapy wherein neighbouring cells are affected [37].

Nanoshells

Clinical Implications

A new approach of targeted treatment comprising of a silica core and thin metallic shell coating are the Nanoshells developed by West and Halas. When they are exposed to near infra red region of electromagnetic spectrum, they get heated up and result in tissue destruction. They are targeted to tissue of application

by immunological methods. They are useful in cancer therapy, micro metastasis of tumours, whole blood immune assays and management of diabetes mellitus [38].

Paramagnetic Nanoparticles

Clinical Implications

Hyperthermia properties of magnetite nanoparticles have been explored in tackling tumoural tissues more effectively by means of magnetically induced heat. At a temperature above 42–45°C, the magnetic energy absorption of properly coated iron oxide based nanoparticles containing tissues induces a localised heating that permits a targeted cell death. This temperature increase can be used to selectively kill cancer cells and thus play a mighty role in cancer management [39,40].

NANOTECHNOLOGY AND SYSTEMIC HEALTH

Nano Burrs

Clinical Implications

Attaining an admirable place in handling the prime cause of the death in the form of cardiovascular problem are the nanoburrs which are coated with tiny protein fragments that facilitate them to cling to diseased and damaged arterial walls [41].

Thus, Nanoburrs contribute in coronary artery disease management, modulating lipid disorders and preventing plaque thrombosis by reducing angiogenesis within atherosclerotic plaques [42]. Apart from coronary artery disease the nanoburrs also solve vascular permeability and damage related problems in inflammatory diseases and cancer [43].

Respirocyte and Microbiovore

Clinical Implications

As an application of advanced medical system, accounting for vital part of life wherein oxygenation plays a very crucial role and can be supported and provided by Respirocytes which are an artificial nano-medical erythrocyte serving the important functions of the red blood cell in oxygen and carbon dioxide transport. Thus, respirocytes are useful in the perfusion of tissues in conditions such as anaemia, heart attack, asphyxia, lung diseases, choking. Also, respirocytes have potential applications in treatment of various anaerobic and aerobic infections such as chronic refractory osteomyelitis, and necrotizing soft tissue infections and can also help in recovery of burns by decreasing fluid requirements, improving microcirculation, and overcoming the need for grafting [44].

Similar to the respirocytes which serves the function of the red blood cell, the microbiovores serve the function of white blood cells by identifying and digesting pathogens like bacteria, viruses and fungi in the blood stream [45].

Nanopores

Clinical Implications

Paving a promising platform for personalised medicine are the porous Nano pores as part of nano technology designed by Desai and Ferrari which consist of wafers having high density of pores approximately 20nm in diameter which allow entry of oxygen, glucose and insulin and thereby serve as a newer treatment strategy for Insulin dependent Diabetes mellitus through microsphere and nanopump [46,47].

Smart Coating and Nano Bandaid

Clinical Implications

As part of tissue engineering and regenerative medicine, the nano technology has developed a “smart coating” that helps surgical implants bond more closely with bone and ward off infection [48,49].

Serving the area of sterilization are the world’s thinnest band-aid named as “Nano Bansoko” a nanometers-thick adhesive bandage sheet designed for surgical use which amicably aids wound healing process, vascular tissue engineering [50,51].

CONCLUSION

The human body is a scientific mystery of molecules, hence the availability of a technology at molecular level and more interestingly at nano level will pave a challenging platform to solve medical problems and contribute to improvement in human health at the nano scale. Cancer is a not a new challenge and facing this pathetic deadly disaster is the nanomedicine as a part of diagnosis and therapy. The future of medicine in the form of nanotechnology has potential benefits which by far go beyond the imaginations of scientific crowd.

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