NANOTECHNOLOGY IN CANCER: A COMPREHENSIVE STUDY

Abstract

Cancer is a global health issue and results from abnormal multiplication of cells in the body leads to different types of cancer, which shows distinct performance and response to various types of treatments. With lifestyle modifications, emerging new diseases and drugs, exposure to potentiallygene-mutating substances increases the risk of cancers. Current cancer epidemiology shows that cancers of the lung, liver, stomach and breast are thedeadly cancers among the world population and account for nearly 44% of deaths globally every year. Treating cancer is a complex area of research, with the advancement in the knowledge of Nanoparticles and CRISPR technology the development of safe and efficient cancer therapies is focused. Nanoparticles like liposomes, carbon nanotubes, and quantum dots are commonly used for nanomedicine in cancer treatments. Nanotechnology is the most focused research area as it promises effective cancer diagnosis and treatments in the near future. This review article is about the present trends of nanoparticles in diagnosing and treating various types of cancer and its symptoms.

Keywords: Cancer; Tumour; Nanotechnology; Nanoparticles; CRISPR.

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I. INTRODUCTION

Cancer is the most leading cause of death worldwide. Usually, the cells have controlled growth but under certain conditions, the cells begin to grow and multiply continuously forming a tumour, or cancerous growth as it is not just a single disease but a group of diseases affecting humans[1]. Our body is made up of cells, every day millions of cells divide and form new cells replacing the old and damaged cells, when this normal process breakdown, abnormal cells start growing and multiplying in an uncontrolled manner resulting in a tumour that can spread to surrounding tissues forming a benign tumour and can also travel to distant places in the body forming new tumour called a malignant tumour and the process is called Metastasis. All tumour cells show six hallmarks of cancer[2].Absence of signalsleading uncontrolled cell division, Continuous cell growth and division even in the presence of anti-growth signals, ignorance of apoptosis, infinite cell divisions, angiogenesis, tissue invasion and metastasis. Each type of cancer shows unique features, but the process of precancerous cells to cancerous cells development is similar. Cancer does not develop all at once, instead it's a long and complex process including series of genetic changes. Each genetic change results precancerous cells to acquiresome traits that together contribute to the malignant growth [3]. Apart from genetic factors there are several demographical and epidemiological factors like tobacco and alcohol consumption, low nutritious diet, exposure to harmful radiations, environmental pollutions, age, area of living etc contribute to cancer. There are more than 200 types of cancersthe most common are breast, prostrate, liver, and lung cancer. In the last decade, nanotechnology has shown tremendous impact in diagnosis and treatment of various cancer. Nanoparticles has eased the process of drug transport within a specific intended time and to the specific target location and acting precisely only on unhealthy cells, causing no harm to healthy cells.

II. CANCER PREVALENCE RATE

1. **Prevalence Rate Worldwide:** It is estimated there were 10 million deaths recorded from cancer and 18.1 million new cases of cancer worldwide in 2020. The cancer cases 4.4 million (44%) in females and 5.5 million (55%) in males, the male: female ratio is of 10:8 and it is also estimated that there will be 28 million new cases of cancer each year by 2040 worldwide. As per the report of GLOBOCAN 2020, The world age-standardised mortality (ASR) rate shows that there are 84.2 cancer deaths for 100,000 females in the world and 120.8 cancer deaths for every 100,000 males. The lung, liver, stomach, and anus cancer are the four most common causes of cancer deaths and account for four deaths in ten that is, 44% of all the recorded deaths [4].

   In 2020, GLOBOCAN reported that all types of cancer incidence and mortality according to world region for both sexes combined is one-half of all cases and 58.3% of cancer deaths are estimated to occur in the world's largest continent, Asia with 59.5% of the world population. Europe, which represents 9.7% of the global population, reported 22.8% of total cancer cases and 19.6% of cancer deaths. America had recorded 20.9% of cancer cases and 14.2% of mortality. As per statistics, the share of cancer incidence in Asia is 49.3% and in Africa is 5.7% the share of cancer deaths in Asia is 58.3% and in Africa is 7.2% which is higher than the cancer incidence rate. The most common 10 types of cancer for both men and women combined account for more than 60% of new cancer cases and more than 70% of cancer deaths. The most commonly diagnosed cancer in

female is breast cancer with 11.7% of total cases, followed by lung cancer with 11.4% of cases, accounting for 18.0% of the total cancer deaths worldwide, colorectal cancer with 10.0% of cases worldwide, prostate cancer with 7.3% and stomach cancer with 5.6% cases worldwide. colorectal canceraccounts for 9.4% of deaths, liver accounts for about 8.3% of cancer deaths, stomach cancer accounts for about 7.7% deaths and female breast cancers are the reason for 6.9% of cancer deaths worldwide. In men lung cancer occurs more frequently and it is the leading cause of death, followed by prostate and colorectal cancer. Breast cancer is the most prevalent cause of death in females, followed by colorectal cancer and lung cancer [5].

2. **Prevalence Rate In India:** As per the reports of the Global Cancer Observatory (GLOBOCON), India ranked third with the highest incidence of cancer cases after China and the USA holding second and first position respectively. According to the GLOBOCAN prediction cancer cases in India would experience a surge of 57.5% of cancer cases from 2020-2040. The cancer cases in India in the year 2022 were found to be 14,61,427 which means 100 out of 100,000 cases. It is estimated that one in nine Indians are likely to develop cancer in their lifetime. In men, lung cancer and females, breast cancer were the leading cancer types. In childhood cancer (the cancer of 0-14 years old),lymphoid leukaemia was the most common type of cancer accounting for 29.2% of cases in boys and 24.2% of cases in girls. It is estimated that there will be an increase in the incidence of cancer cases by 12.8% in 2025 when compared to 2020[6].

III. CAUSES OF CANCER

Many factors that contribute to cancer including demographical, epidemiological and genetic factors. The external factors include physical carcinogens (ultraviolet light and radiation); chemical carcinogens (tobacco smoke, asbestos, etc.); and biological carcinogens (viruses, bacteria, and parasites)[7].

1. **Demographical And Epidemiological Factors:** As per WHO, nearly 33 percent of cancer deaths are due to tobacco and alcohol consumption, lack of physical activity, low nutritious diet, and unprotected exposure to harmful radiations and UV rays that can mutate normal cells into cancerous cells; According to National Toxicology Programme, certain chemicals in the environment are carcinogenic such as aflatoxins, arsenic, coal-tar, ethylene oxide, formaldehyde, environmental pollution.

   - **Age:** Age is one of the main determinant factors of cancer. Several biological changes linked with the aging process like accumulation of oxidative stress and DNA damage, senescent cells accumulation and immunosenescence can lead to development of cancer. Cancer can develop at any age, but most type of cancer like breast cancer (post-menopausal), oropharyngeal, anal, kidney and stomach cancer etc become more common among the adults aged 50-65 years. Nearly half of all the cancers occur in people over the age of 70 years [8].

   - **Obesity:** Obesity has been associated with several common cancers including colorectal, oesophageal, breast, pancreatic, liver, kidney, uterine and gall blader cancer. Nearly 4-8% of all cancers are attributed to obesity. Overweight results in 17% increased risk of cancer mortality. Obesity accounts for about 4.7% of cancer

cases in men and 9.6% new cases of cancer in women. Biological changes due to obesity including altered fatty acid secretion, metabolism, immune dysregulation, chronic inflammation have been linked to cancer development [9].

- **Environmentaland Occupation:** Environmental pollution has been linked to various cancers. Environmental carcinogens like ultra violet radiations, asbestos, benzene, formaldehyde, radon, nitrates, pesticides, polycyclichydrocarbonsetc are highly prevalent in the environment, food products, and workplace. The National Institute for Occupational Safety and Health has identified more than 130 substances as potential carcinogens including aromatic amines, lead, chromium, mercury, mineral oilscan contribute to carcinogenesis among working adults. Exposure to non-ionizingradiations cause brain cancer; exposure to 1,3-butadiene can cause leukaemia, sarcoma; exposure to air pollution cause lung cancer and exposure to pesticides, mineral oils and solvents can cause breast, prostrate cancer and non-Hodgkin`s lymphoma[10].

- **Diet:** Diet is another risk factor of cancer. In the USA, nearly 30-35% of cancer deaths were linked to diet. Most carcinogens consumed in diet, such as nitrates, nitrosamines, pesticides, and dioxins come fromfood, cooking and food additives. Consumption of red meat has been linked to several cancers, such as gastrointestinal tract, colorectal, prostrate, gastric, pancreatic, oral and breast cancer.Bisphenol from plastic container contaminate food and may increase risk of breast cancer. Food additives such as azo dyes and nitrites has been associated with the risk of carcinogenesis[11].

- **Smoking and Alcohol:** Smoking tobacco increases the risk of developing 14 types of cancer. Tobacco contains about 50 carcinogens including, benzopyrene diol epoxide, has been linked to lung cancer. Tobacco smoking accounts for about 25-30% of all the cancer deaths and 87% of deaths from lung cancer[12].Alcohol consumption is linked to several types of cancer, including cancer of upper aerodigestive tract, liver, colorectum, andbreast cancer. Approximately,4% of cancers globally are due to alcohol consumption [13].

- **Other Conditions:**Type 2 diabetes is highly linked with a risk of developing colon, breast, liver, bladder, rectum and pancreatic cancer. The association between diabetes ands cancer may be due to common risk factors such as, ageing, obesity, and diet. Hyperinsulinemia, hyperglycaemia and inflammation can be possible link between cancer and diet [14].Infectious agents like virus accounts for most infection caused cancerssuch as human papilloma virus (HPV), Epstein Barr virus, herpes virus, HIV, HCV (Hepatitis C virus) are associated with the risk of skin cancer, anogenital cancer, liver cancer, Kaposi`s sarcoma, Hodgkin’slymphoma. It is estimated that nearly 17.8% of the globalcancers burden is associated with infections[15].

2. **Genetic Factor:** Mutation in normal cells convert them to cancerous cells, As the cancer continues to grow, additional changes will occurwithin the same tumour, different cells may have different genetic changesas each person`s cancer has a unique combination of genetic changes. The 3 main genes that are prone to genetic changes resulting incancer are: [16].

- **Oncogenes**: Proto-oncogenes regulate the normal growth of cells and their division and it is present in our normal cell, but when these genes are altered, they may become cancer-causing genes(oncogenes) and unable to control the growth of the cells and allowing abnormal cancer cells to grow and survive. The mutated proto-oncogene is referred to as cellular oncogenes or c-onc

- **Tumour Suppressor Genes:** Studies found that normal cells have a gene with tumour suppressor activity, these genes can recognize abnormal growth and reproduction of cancer cells and can suppress their division or growth. If the tumour suppressor genes are mutated or become inactive, can lead to malignancy. For example, TP53(tumour suppressor gene) codes for the protein p53 and controls cell division. Changes in the TP53 gene can lead to Li-Fraumeni syndrome, (inherited or family cancer syndromes) and bring the risk of several types of cancer.

- **DNA Repair Gene:** This gene recognizes errors in replication and helps in fixing damaged DNA. Mutations in these genes tend to develop additional changes in other genes and the errors in DNA can be transmitted to new cells to become cancerous. As with other types of genetic mutations, the changes in DNA repair genes can be either acquired during one's life or inherited from parents. For example, the BRCA1 and BRCA2 genes when undergoing mutation possess a high risk of breast and ovarian cancer.

IV. TYPES OF CANCER

There are more than 200 types of cancers and the most common cancers are breast cancer, lung, liver and prostate cancers, they are classified based on the body organ and tissue they start[17].

1. **Bladder cancer:** The uncontrollable growth of cells in the bladder causes bladder cancer. Back pain, painful urination, polyuria, and haematuria are the most common symptoms. Water contaminated with arsenic, smoking, urinary tract infections, and mutations are the main cause of bladder cancer. Bladder cancer can be non-muscle invasive bladder cancer (cancer that has not invaded muscle wall of the bladder) and Muscle-invasive bladder cancer (cancer that invades the muscle wall of the bladder through the lining of the bladder). Childhood bladder cancer is a very rare type of cancer.

2. **Breast cancer:** Breast cancer starts in lobules and ducts. There are different kind of breast cancer depending upon which cells in breast turn into cancer, the most common types of breast cancer are Invasive ductal carcinoma (cancer of the duct that and can grow outside the ducts into other parts of the breast and then to another part of body) and Invasive lobular carcinoma (cancer in lobules of breast which spreads to other part of breast and body). Breast cancer causes pain in the breast, irritation of breast skin, lumps in the breast, nipple discharge, change in size and shape of the breast etc. The mutation to genes, like BRAC1 and BRAC2(tumour suppresser genes) can lead to breast cancer, A female who suffered breast cancer is at higher risk developing breast cancersecond time, and non-cancerous breast diseases like lobular carcinoma and atypical ductal hyperplasia can sometime become a risk factor for breast cancer and some other risk factors for breast

cancer are radiation therapy, use of drug diethylstilbesterol and inheritance etc. Mammograms are x-ray images of breasts used to detect early signs of breast cancer [18].

3. **Colorectal cancer:** The cancer of the colon or rectum is called colorectal cancer; According to CDS (Centre for Disease Control and Prevention) it is a leading cause of cancer death in the USA. Colorectal cancer can be screened for characteristic precancerous polyps (abnormal growth in the colon and rectum) which can turn into cancer [19].The risk of colon cancer increases with age, Crohn's disease or ulcerative colitis (inflammatory bowel disease), genetic syndrome like familial adenomatous polyposis or hereditary polyposis colorectal cancer (lynch syndrome) other than these lifestyle factors like lack of physical activity, obesity, alcohol and tobacco consumption etc. syndromes of colorectal cancer include blood in stool, diarrhoea, constipation, abdominal pain, aches, or cramps, unexplained weight loss etc.

4. **Kidney cancer:** Kidney cancer can occur both in adults and children. Kidney cancer is of different kind such as renal cell cancer, transitional cancer, and Wilms tumour. This is also called renal pelvis cancer, and the person with such cancer mightshow some of the symptomslike haematuria, lump in kidney area, lower back pain, often feeling tired etc. The risk factors includehigh blood pressure, overweight, smoking, person suffering from hepatitis C infection andgenetic inheritance etc [20].

5. **Liver cancer:** When cancer cells form in the tissues of liver causes cancer. There are different types of liver cancer among which Hepatocellular carcinoma and cholangiocarcinoma (bile duct cancer) arethe main type of adult liver cancer. It is the leading cause of cancer-related deaths worldwide. A hard lump, jaundice, tiredness, pale or chalky stool, dark urine etc. are the symptoms of liver cancer.

6. **Lung cancer:** According to Centres for Disease Control and Prevention (CDC), lung cancer is the most common cancer in the US and has a higher mortality rate than other cancers. Cancer starts in the lungs and can spread to lymph nodes and other organs. Lung cancer has two types **small cell** and **non-small cell.** Non-small cell lung cancer is more common than small cell lung cancer, and it includes adenocarcinoma and squamous cellcarcinoma. Cigarette smoke is the main cause of lung cancer resulting in 80% to90% of lung cancer deaths, tobacco smoke consists of a mixture of several toxic chemicals out of which 70 are known to cause cancer; second-hand smoke is also a risk factor for lung cancer, Radon gas in nature is the second most leading cause of lung cancer as per the report of U.S. Environmental Protection Agency, it causes 21,000 lung cancer deaths each year. Asbestos, arsenic, silica and chromium are linked to cause lung cancer on prolonged exposure. Chest pain, shortness of breath, haemoptysis, wheezing, feeling of tiredness, lymph node enlargement etc. are the symptoms of lung cancer [21].

7. **Prostate cancer:** Men across the world are at risk of prostate cancer but African-American men are more likely to get prostate cancer than other men due to their genotype. According to a study, 13 men out of 100 American men are prone to cancer, resulting in death of 2-3. Increase age and genetic inheritance are the most promising risk factors fordeveloping prostate cancer. Interrupted flow of urine, frequent urination, blood in urine or semen, painful ejaculation etc. are few symptoms. Prostate-specific antigen

tests and Digital rectal examination are tests commonly used for screening prostate gland cancer.

8. **Thyroid cancer:** When cells in the thyroid gland divide uncontrollably causes thyroid cancer. Every year 12,000 men and 33,000 women develop thyroid cancer resulting in the death of nearly 950 men and 1,100 women. The types of thyroid cancers are papillary, follicular, medullary and anaplastic and out of these four, papillary is the most common type. A swelling on the side of the neck includingdysphagia, dyspnoea etc. Exposure to radiation near the neck region can stimulate the cell to divide out of control and leads to cancerous growth. Thyroid cancer can be treated successfully if detected early [22]. Types of cancer based on cells or tissue they start.

9. **Carcinoma:** Carcinomas are the cancer of epithelial cells or tissues that line the skin and internal organs accounting for 85% of all cancers. Different types of cells can develop different kinds of carcinoma, they are squamous cell carcinoma (carcinoma of squamous cell, cell lining the skin, throat and food pipe);[23]. Adenocarcinoma (startsin glandular cells; Transitional cell carcinoma (cancer that begins in transitional cells or tissues, these cells are present in the lining of thebladder); Basal cell carcinoma (basal cells are found in the deepest layer of the skin and the cancer that starts in these cells are basal cell carcinomas).

10. **Sarcomas:** Sarcomas start in connective tissue; they account for less than 1 % of total cancer. There are two types of sarcomas; Bone sarcoma (sarcoma that starts in bone cells) andsoft tissue sarcomas (they are rare sarcomasthat start in cartilage and muscle; cancer in cartilage is called chondrosarcoma and the cancer of the muscle cells is called rhabdomyosarcoma or leiomyosarcoma) [24].

11. **Leukaemia**: Leukaemia is the cancer of white blood cells. They are not as common as carcinomas and account for only 3% of all cancer cases, they are most common in children younger than 15 and adults older than 55. Different types of blood cancer show different symptoms such, as fatigue, fever and chills, pain in bones and joints, stomach problems, cardiovascular problems, vomiting, and night sweats.[25]. Smoke, exposure to radiation and certain carcinogenic chemicals, family history, genetic disorders like Down syndrome etc. can triggernormal WBC cells to become cancerous.

12. **Lymphomas and Myelomas**: Lymphoma is acancer of the lymphatic system or lymphatic tissues, when lymphocytes start to divide abnormally, the abnormal lymphocytes accumulate in the lymph nodes, bone marrow or spleen which can later grow into tumours and account for nearly 5% of all cancers. Painless lymphadenopathy in Hodgkin lymphoma; abdominal pain in non-Hodgkin; lump in the neck; tiredness; pain in the leftside of the shoulder and chest, weight loss are a few symptoms of lymphoma.Myelomas is the cancer of plasma cells. Plasma cells are produced by bone marrow. When the plasma cells divide abnormally causes myeloma. It nearly accounts for 1% of all cancer cases. Aches in bones, joints and muscles, back pain, and tiredness are common symptoms of myelomas[26].

V. GENERAL SYMPTOMS

Different types of cancer show different symptoms. Each type of cancer causesmany symptoms, and these symptoms may also appear under other conditions like injury, infection and other problems that are non-cancerous. Note, that cancer does not cause pain in all individuals [27].

Common symptoms include changes in appetite, indigestion, dysphagia, Nausea, vomiting and heartburn, stomach ache, painful ulcers are the symptoms of gastrointestinal track. Haematuria, haematochezia, trouble in urinating, painful urination, difficult bowel movement are the symptoms of kidney. Changes in the organs or site of cancer growth; lumps in the breast, lumps in under arm, nipple discharge, itchy, red, scaly breast skin are the symptoms of breast cancer, oral changes-white or red patches on the tongue, bleeding, pain or numbness in the lips or mouth are the symptoms of mouth cancer.

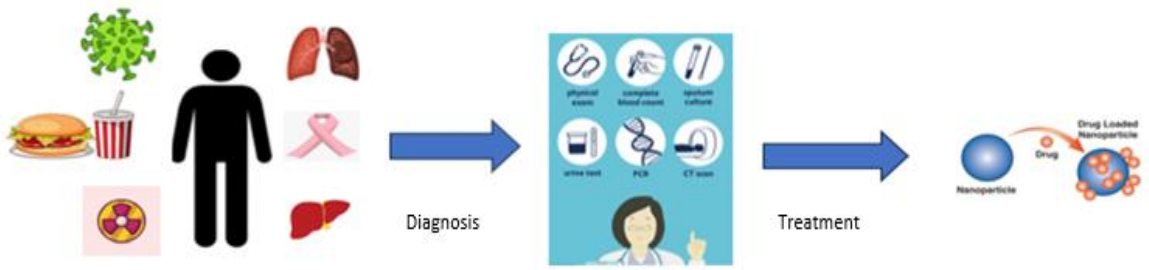

Figure 1: Shows risk factors of cancer and applications of nanoparticles in diagnosing and treating various kinds of cancer.

VI. NANOPARTICLES AND CANCER

1. **Definition:** Nanotechnology has contributed to cancer diagnosis and treatment over the years with specificities by the use of nanomaterials or nanoparticles. Nanoparticles (NPs) are defined as particles with at leastone of its dimensions in the nanoscale (i.e, 1-100nm). The composition of NPs is complex, comprising the surface layer, the shell layer and the core, which is the central portion of NP[28].Nanoparticlesowes unique propertieslike high surface: volume ratio, submicron size, and enhanced drug delivery system, usually not found in bulk samples of the same material, thus can be used as an efficient tool for drug delivery. Nanoparticlescarryinganti-cancer drugs can be administered by oral or parental routes.Each of these nanoparticles can transport different anti-cancer drugs at a time (called the synergetic anti-cancer effect), this helps to avoid the development of resistance by tumours and also reduces drug toxicity [29].

2. **Types of Nanoparticles:** Depending on the overall shape of the nanoparticles, it can be classified as 0D (zero dimensional nanomaterials have all dimensions measured within the nanoscale; example incudes, nanoparticles and quantum dots), 1D (one dimensional nanomaterials have two dimensions at the nanoscale and one dimension at the macroscale, forming needle like shaped nanomaterials like nanorods and nanofibers),**2D** (two dimension nanomaterials have one dimension at nanoscale and two dimension at the

macroscale, exhibiting plate or sheet like shape example includes, nanoplates and nanosheets), 3D (three dimension nanomaterials have no dimension at nanoscale, forming a bulk nanomaterials example includes nanocomposites and nanomaterials)[30].

Nanoparticles like liposomes, micelles, dendritic macromolecules, quantum dots, and carbon nanotubes have been used for cancer treatment and diagnosis. Liposomes are the most widely used nanoparticle for drug delivery. They are nanospheres composed of a phospholipid bilayer membrane (synthetic or natural) and aqua-phase nuclei. Its amphiphilic property allows hydrophilic drugs to stay in monolayer liposomes and hydrophobic drugs in multilayer liposomes and a few drugs can beincorporated into the liposomes by changing the buffer (from acidic buffer to neutral buffer). A combination of saturated drugs with organic solvents forms liposomes of size 500 nm, that can enter the tumour and can fuse with tumour cells by the process of endocytosis and release drug in intercellular space. The liposome of size 100 nm has a longer half-life can penetrate the tumour easily and can stay there for along time. Whereas, the liposome of larger size has ashort half-life as it can be easily marked and destroyed by mononuclear cells of our immune system. The tumour specific-antigen can be easily targeted by specificliposome-bound antibodies and can release anti-cancer drugs in the tumour. Many liposomal drugs have been approved by the FDA. Adriamycin is a liposomal drug used in the treatment of ovarian cancer[31].

- **Carbon nanotubes** are another type of nanoparticle used in the delivery of anti-cancer drugs.The physical and chemical properties of carbon nanotubes such as surface area, mechanical strength electrical and thermal properties makecarbon nanotubes a suitable candidate for wide-scale biomedical use, including drug delivery. Based on size and structure carbon nanotubes can be, single-walled carbon nanotubes (made up of monolithic cylindrical graphene) and multi-walled carbon nanotubes (made up of concentric graphene). carbon nanotubes can absorblight from near-infrared regions that cause nanotubes to get heated up and can easily penetrate tumour cells[32]. Due to its non-invasivepenetration property, it is regarded as the most competent carrier for deliveringdrugs into living cells. Carbon nanotubes incorporated with drugs such as paclitaxel (hydrophobic anticancer drug)can be used in the treatment of breast, ovarian and other cancers[33].

- **Polymeric micelles**: Polymeric micelles are nanoparticles; they are the first polymers used for drug delivery systems. They are used as drug carriers for hydrophobic drugs as they can hold the drug via a covalent bond or hydrophobic core interaction, polymeric micelles are thermodynamically highly stable, it has endothelial cell permeability and is required in a small amount making them suitable drug carrier for cancer therapy. They can be administrated either orally or through parental routes. The major drawback of polymeric micelles is theymay cause some side effects like cytotoxicity [34].

- **Dendrimers:** Dendrimers are spherical polymer cores with branches. They can be synthesised by using various molecules such as polyacrylamide, polyglycerol-succinic acid, polyglycerin, propionic acid, melamine, etc. These dendrimers exhibit various chemical structures and physical properties like alkalinity, charge and hydrogen bond capacity which can be regulated by changing the groups on the surface of dendrimers.

Several molecules or anti-cancer drugs can attach to each dendritic molecule, due to the covalent binding of drugs to each dendritic peripheral group forming dendritic drug conjugates. Dendrimers various physiochemical and biological properties like size, charge, lipid bilayer interactions, cytotoxicity, multi-ligand groups, biological distribution, etc. make them suitable nanoparticles for drug delivery. It is found that cancer cell with folate receptor on their surface binds with dendritic molecule and the ability of dendrimers to bind to DNA forming DNA-polyamidoamines that enhances the killing of cancer cells [35].

- **Quantum Dots**: Quantum dots are nanocrystals made up of semiconductor material of size range between 2 to 10 nm. It possesses electron property which is intermediatory of as emiconductor and an atom. Quantum dots can accumulate in a specific part of the body and deliver the drug in that area, this ability of quantum dots to concentrate in specific internal organsmakes them abetter option against untargeted drug delivery and may cause no side effects [36].Quantum dots when combined withbiomolecules like peptides and antibodies can target the tumour easily. Researchershavefound that quantum-dot-based probes can detect breast cancer and quantum-dot immunohistochemistry is highly efficient than immunohistochemistry. quantum dot immunostaining is the most efficient method for thedetection of various tumour biomarkers. Quantum dots are the most efficient nanocrystals in cancer screening and treatment.

Other than these nanoparticles some inorganic and organic nanoscale molecules are used as nanocarriers for drug transport. Nanoparticles of some metals like gold and silver are used as nanocarriers, Silver (Ag) nanoparticles have wide biomedical applications due to their high surface/volume ratio, making it easy to synthesise, having surface properties with good penetration power giving intrinsic anticancer effect[37].

3. Applications of Nanoparticles

- **Personalized nanomedicine:** Disease development depends generallyon genetics and pathophysiological causes. Though every human has a very similar genetic makeup, yet everyone remains unique. Therefore, the use of approaches that emphasizes the uniqueness of a person, diseases and drug with reduced side effects are important. Administering medicine to an individual based on his or her sex, nutrition, uniqueness and with less side effects are called personalised medicine.Personal medicines used against cancer and other diseases has shown positive results. Personalized nanomedicine mainly focuses on genetics and epigenetic abnormalities. As they are nanosized medicines it is easier to deliver with high specificity, such nano based personalized medicine can be used against cancer and other diseases due to its specificity, reduced toxicity and maximum efficiency in disease treatment[38].

- **In proteomics:** Nanoparticles when subjected to the biological system, they come in contact with cellular and serum proteins surrounding it and forms a structure known as protein corona. The protein corona affects the interaction of nanoparticles with biological system hencegoverns the application in medical field. The number of proteins in cancer cells and serum can be studied under cancer proteomics, that

supports identifying proteins and biomarkers that aids in diagnosis and treatment. Cancer proteomics using nanoparticles helps in understanding cancer pathogenesis, and drug resistance mechanism[39].

- **Tumour microRNA delivery and profiling:** MicroRNA (miRNA)are emerging biomarkers that are a significant target for cancer therapy and diagnosis. Thenanoparticles-based miRNA techniques use base primingnature of nucleic acid for profiling. Nanoparticles are used for the delivery of miRNAs, microRNA loaded with polycation hyaluronic acid nanoparticles have shownpositive results on lung cancer. Nano based delivery and profiling of miRNA has significant applications in cancer diagnosis and treatment efficiently with reduced side effect[40].

- **In cryosurgery:** Cryosurgery is an advance approach of freeze destroying cancer tissue. The thermal conductivity property of nanoparticlesis being used to freeze the cancer tissue and cause damage to cancer cell. Using nano basedapproach, it is feasible to regulate the direction of ice ball and its growth. The nanoparticles made up of phase change materials are used to protect the adjacent healthy tissues or organs during cryosurgery [41].

- **Drug resistance:** Drug resistance is one of the chief problems in treatment of various diseases including cancer. Thus, to overcome the phenomenon of drug resistance nanoparticles are used, nanoparticlesdue to their ability to carry multiple therapeutic agents, can be used to overcome cancer related drug resistance. Nano based therapeutic drugtarget hypoxia and apoptotic pathway that can over come the drug resistance of tumour[42].

- **In cancer therapy:** Traditional cancer therapies include chemotherapy, radiation therapy, and targeted therapy has limitations such as lack of specificity, cytotoxicity and multi drug resistance posing challenge for cancer treatment. Nanoparticles can overcome the challenges of conventional cancer therapies. Nanoparticles can be used to treat cancerdue to their specificity, biocompatibility, reduced toxicity,precise targetingand can overcome multidrug resistance. Several nanoparticles like liposomes, carbon nanotubes, quantum dots etc are used in cancer diagnosis and treatment[43].

4. **Nanoparticles Role in Cancer:** Nanoparticles have made significant impact in cancer diagnosis and treatment. The uniqueness of nanoparticles such as size, shape, high permeability, selective binding, surface modification and retention effects etc. makes NPs a suitable candidate for diagnosis and treatment of cancer. Use of NPs along with conventional cancer therapies such as immunotherapy, gene therapy has significant impact. The high specificity of nanoparticles in identifying biomarkers in cancer diagnosis and site-specific nano drug delivery with reduced toxicity has placed NPs in good position in cancer therapy.

    - **Identification of Biomarkers:** Expression of cancer biomarkers indicates the presence of tumour. Biomarkers proteins and its fragments and DNA. Such biomarkers are used to monitor changes in cancer cells and understand nature of tumours. Biomarkers from blood, urine or saliva samples of patient are used to screen for cancer risk. Use of nanoparticles in identifying diagnostics and prognostic

markers, may include the use of quantum dots, nano composting, etc. certain nanosized devices such as biosensors and nanochips are installed in the body to improve prognosis and diagnosis. Nanoparticles such as perfluorocarbon nanoparticles can detect extremely smaller tumour [44].

- **Drug Delivery:** Conventional chemotherapy provided to tumour cells is lethal for the healthy cells, leading to neural toxicity, cardiomyopathy, etc. such adverse effects of chemotherapy could be effectively decreased by using nanoparticles that specifically target the tumour site. Nanoparticles are capable of delivering the insoluble drugs to local and distant tumour sites with reduced side effects. The nanodrugs are biocompatible, non-immunogenic, non-toxic and biodegradable which reduces the adverse effects of cancer therapy. Targeted drug delivery could be achieved by NPs due to the selective binding of nano ligands to the receptors on the surface of tumour cells [45].

- **Gene Therapy:** Genetic and epigenetic factors contribute to carcinogenesis. There are several genes that are actively involved in various cellular processes in tumour cells. Regulations of genes that are involved in cancer cell growth could be inhibited by NP based gene therapy and strategically kill tumour cells. Genes like BCL2L1, ANG, AKT1, CDC34, NFKB2, etc could be efficiently regulated or inhibited by Fe3O4 nano powders and can induce an anti-cancer effect on cancer specific molecular markers.Use of nano particles to deliver viral vectors such as retroviruses and nucleic acids has emerged new approaches such as magnetofection and theranostics. Magnetofection is a viral and non-viral approach that uses supermagnetic nanoparticle under magnetic field for gene delivery. Theranostics monitors the response to treatment and increase the efficiency, it combines therapeutics with diagnostics to develop efficient targeted therapies. The successful gene transfer therapy depends on two important aspects.1. efficient and safe delivery of genes to the target cells and 2. Effective monitoring of gene expression of modified cells and gene delivery by non-invasive imaging techniques can be efficiently achieved by nanoparticles[46].

- **Immune therapy:** The immune system of our body has an important part in the establishment and development of cancer cells. There are several NP based immunotherapy that aims at activating immune system against cancer cellssuch as nano vaccines, artificial antigen presenting cells (aAPCs), and immunosuppressed tumour microenvironment targeting (TME). Liposomes, and gold NPs based nano vaccines specialize in delivering tumour associated antigens and adjuvants to APC that enhances antigen presentation and promote dendritic cells maturation that stimulates the cytotoxic Tells that has anti-tumour function. The artificial APCs interact with MHC-antigen complex that binds to T-cells and co-stimulatory receptors leading to T-cell activation. Targeting the immunosuppressed tumour micro environment (TME) using nanoparticles is done by targeting essential cell types in TME such as regulatory T-cells, tumour associated macrophages, etc. Three factors important for effective cancer therapy includes cancer antigens must be effectively transferred to immune cell, adjuvant and cancer antigens must induce an anticancer immune response when delivered, the immunosuppressive TME must be modified to respond to the anti-cancer immunotherapeutic. Nanoparticles can be used for all the three aspects with reduced side effects [47].

- **Site specific cytotoxicity:** Site specific drug delivery and action are the basis behind the use of nanoparticles in cancer therapy. Intercellular delivery of DNA, mRNA, and protein by nanoparticles, offers site specific cytotoxicity. The binding efficiency of the target ligands on the nanoparticle surface, increase the deposition of drug in cancer cells.As nanoparticles have high drug loading capacity and cytotoxicity, zinc oxide (ZnO) NPs was found to show cytotoxic effect towards cancer cells by inducing apoptosis. Conjugation of ZnO NPs with Fe3O4 NPs increases the cytotoxic potential of the drug. Thus, the use of nanoparticles for the site-specific cytotoxicity has positive results in efficient cancer therapy with reduced side effects, causing no harm to surrounding healthy cells [48].

5. **Current Challenges:** Clinical researchof nanotechnology has been bloomed, and the knowledge has been steeply raised. Most of the clinical research are in vivo and vitro stages, only few of them make it up to clinical trials. There are several challenges in the use of nanoparticles in cancer therapy. Each nano formulation posse particular challenges, the most pressing problem is potential toxicity of nano particles. The potential toxicity of NPs cannot be ignored, a few studies showed that NPs may attach to the surface of biological membranes via electrostatic interactions can cause damage to cells by producing reactive oxygen species, protein denaturation, DNA damage result in cell death [49].NPs and carbon nanotubes (CNTs) can damage the respiratory, nervous and cardiovascular systems. CNTs can induce cell apoptosis, disrupt cell cycle, damage lung tissue and are inflammatory. Quantum dot salso showstoxic effects as they contain heavy metals. There are very few NPs that has been approved as antitumour agents to enter market, rest are still halt at in vivo and vitro stages [50].

   A few studies showed that silver nanoparticles can be toxic and cause damage to various cells and organs of our body and revealed that silver nanoparticles can change the expression of several genes linked with motor neuron disorder and immune function leading to neurotoxicity and immunotoxicity. Though there are many applications of nanotechnology in biomedicine like efficient drug transport much research has shown possible toxic effects of nanocarriers used in cancer treatment. It is found that Adriamycin conjugated nanomaterial that is used to treat several different cancers is associated witha possible risk of cardiotoxicity[51].

6. **Future Perspective:** Nanotechnologypromises efficient cancer treatment by delivering small molecules for cancer detection and therapy. Application of NPs for combination therapy, helps in overcoming multi drug resistance. However, there are several limitations such as immunotoxicity, neurotoxicity and the long-term toxicity. Therefore, the long-term toxicity of NPs to living systems needs to be studied intensively [52].For nanomaterial design, more efforts must be made in understanding toxicity, cellular and physiological factors that regulate NP-based drug delivery. It is also necessary to research the mechanisms of injury in cells due to NPs. From studying nanomaterials to clinical transcription, will require multidisciplinary approachvia clinical, ethical, economical and social perception. Compared to the enormous number of investigations, only a few NP-based drugs are in use, a few are in clinical trials, and most are in the exploratory stage. As both development of NMs and tumour therapies are multidisciplinary field, much research must be focused on tumour biology, molecular biology, and Nanomaterials.

VII. CRISPR – THE GENE EDITING TOOL AND CANCER

CRISPR-associated Cas protein is an adaptive immune system of some ancient bacteria, that has gained much attention from scientists in the last three decades in developing CRISPR-based technologies in programmable gene editing in almost all types of cells. CRISPR-cas in simple terms is a DNA endonuclease that cleaves DNA at a specific target sequence, this mechanism can be used in cancer treatment [28].As we know the major cause for 90% of cancer is genetic changes or alteration. With the improved knowledge of precision medicine, it is easy to detect the mutation or change in a gene that results in normal cell stransferring into cancer cell or tumour and can be removed by various methods, CRISPR has complemented and enhanced this process by simple gene manipulation or editing, allowing fast and precise genetic knockout or separation of the cancer causing mutated gene, alternation of endogenous gene expression, and engineering of cancer-associated genomic mutations or changes. To treat any disease, it is important to know about that disease and this even holds for cancer, understandinggene functions in tumour formation, the contribution of genes in each stage of the cancer and finding effective treatment is very important in creating cancer models. CRISPR enables us to create complex organoid cancer cultures and animal models (for example, KO mice) and in produce combinations of various genetic alternations in the same mice, in one step can be achieved by zygote targeting viaCRISPR-EZ(electroporation of zygote).CRISPR also has its role in screening the cancer, the CRISPR KO efficiently screen gene function in cancer cell and find the genetic changes in it. Chow et al. used CRISPR-Cas9 to screen asubset of cancer drivers in glioblastomas. As many researchisgoing on to understand the use of the CRISPR system in treating cancer both in vivo and ex vivo. Much research has shown that ex-vivo CRISPR-based targeting of T-cells can enhance its antitumour activity following its adoptive transfer. Preclinical in vivo trials have shown the potential of CRISPR in cancer therapies selective activation ofnuclear factor-kB in cancer cells to drive transcription of CRISPR Cas13a,which induces cancer cell-restricted oncogene silencing [29].Despite, of broad application of CRISPR there are limitations to using CRISPR technology in treating cancer such as direct targeting of tumours with CRISPR is a difficult task, and manipulation of patient-derived cells for transplant is again a challenging process. CRISPR can also cause deletions and large-scale chromosomal aberrations, impair normal function of cells, gene disruption etc. Scientists all over the world are working on the applications and drawbacks of CRISPR technologies in use for cancer diagnosis and treatment.

VIII. CONCLUSION

Cancer has remained one of the significant health problems for ages, there is no acute origin of cancer and remains undiagnosed and uncured for long.Cancer has the ability to develop in any of the body’s tissues or organs and each type of cancer shows unique characteristics and features. The current epidemiologicalstatistics suggest the incremental trend of cancer prevalence and the burden of these malignant diseases that disrupt social life and erodes economic resources. Cancer research has mademany remarkable progressthough treating cancer is a complex process. Conventional treatment methods are slowly being replaced by advanced methods like nanomedicine that promise a safe and efficient method of treatment. Current research in oncology focuses on the development of a new advanced approach tocancer treatment and diagnosis. Several new technologies like CRISPR technology are currently under clinical trials and some of them like nanomedicine havebeen

approved.Nanotechnology has contributed to biocompatible nanomedicine that is used for both cancer diagnosis and treatment and bioengineering by CRISPR has creatednew areas of research and opened doors for new cancer treatments in future

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