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Retraction

Retracted: Multifunctional Therapeutic Approach of Nanomedicines against Inflammation in Cancer and Aging

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This article has been retracted by Hindawi following an investigation undertaken by the publisher [1]. This investigation has uncovered evidence of one or more of the following indicators of systematic manipulation of the publication process:

(1) Discrepancies in scope
(2) Discrepancies in the description of the research reported
(3) Discrepancies between the availability of data and the research described
(4) Inappropriate citations
(5) Incoherent, meaningless and/or irrelevant content included in the article
(6) Peer-review manipulation

The presence of these indicators undermines our confidence in the integrity of the article's content and we cannot, therefore, vouch for its reliability. Please note that this notice is intended solely to alert readers that the content of this article is unreliable. We have not investigated whether authors were aware of or involved in the systematic manipulation of the publication process.

Wiley and Hindawi regrets that the usual quality checks did not identify these issues before publication and have since put additional measures in place to safeguard research integrity.

We wish to credit our own Research Integrity and Research Publishing teams and anonymous and named external researchers and research integrity experts for contributing to this investigation.

The corresponding author, as the representative of all authors, has been given the opportunity to register their agreement or disagreement to this retraction. We have kept a record of any response received.

References

[1] M. M. Rahman, F. Islam, S. Afsana Mim et al., "Multifunctional Therapeutic Approach of Nanomedicines against Inflammation in Cancer and Aging," *Journal of Nanomaterials*, vol. 2022, Article ID 4217529, 19 pages, 2022.

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Review Article

Multifunctional Therapeutic Approach of Nanomedicines against Inflammation in Cancer and Aging

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Cancer is a fatal disorder that affects people across the globe, yet existing therapeutics are ineffective. The development of submicrometer transport for optimizing the biodistribution of systemically provided medications is the focus of nanomedicine. Nanoparticle- (NP-) based treatments may enable the development of novel therapeutic approaches to combat this deadly disorder. In multifunctional, multimodal imaging, and drug delivery carriers, NPs generally play a major role. They have emerged as potential strategies for the invention of innovative therapeutic procedures in the last decade. The exponential growth of nanotechnologies in recent years has increased public awareness of the application of these innovative therapeutic approaches. Many tumor-targeted nanomedicines have been studied in cancer therapy, and there is clear evidence for a significant improvement in the therapeutic index of antineoplastic drugs. Age-related factors such as metabolic and physiological alterations in old age and inadequate animal models are currently understudied in nanomedicine and pharmacology. This review highlighted the most important targeting approaches, as well as public awareness, therapeutic advancements, and future prospects in age-related metabolic variations, and tumor-targeted nanomedicine studies.

1. Introduction

The area of "nanomedicine" is concerned with the development of all nanosized tools for clinical diagnosis, prevention, and treatment [1, 2]. Nanomedicine is described by the European Medicines Agency (EMA) as purposefully designed systems for medical applications, with at least one element at the nanoscale size, with definable particular properties and characteristics linked to the nanotechnology application, along with the expected clinical advantages of nanoengineering, and must meet the criteria of a therapeutic agent as defined by the European legislation [3]. While the Food and Drug Administration (FDA) does not have its own concept, it has adopted the widely used terminology as possessing at least one dimension in the 1–100 nm size range and recommends that assessments should consider any specific characteristics that the application of nanotechnology may confer [4]. Nanoparticles (NPs) have the potential for theranostics because of their large surface-area-to-volume ratio, which allows for high therapeutic and imaging agent loading, surface functionalization with targeting ligands, and compact scale, which allows for extravasation into leaky vessels [5, 6]. They can be programmed to modulate release in response to environmental factors such as pH, temperature, enzymes, and redox potential [6]. Surface functionalization of NPs with a hydrophilic polymer, such as polyethylene

glycol (PEG), can improve blood circulation times [6, 7]. Targeted delivery combined with a high therapeutic and imaging payload can improve therapeutic and imaging effectiveness while lowering off-site toxicity [8].

Cancer is a disease marked by the abnormal division of dysfunctional cells that can infect and spread to other tissues, resulting in metastases. Proliferative signaling, growth suppressor evasion, cell death resistance, replicative immortality, angiogenesis induction, and invasion and metastasis activation are all characteristics of neoplastic disorders [9–11]. Using NPs in anticancer therapies, imaging, diagnosis, and drug delivery has revolutionized the sector. The latest NP-based drug delivery techniques seek to develop conventional drug delivery modalities and improve administrative procedures for multiple cancer therapies. The ability of NPs to administer drugs directly to cancerous cells is their most noteworthy attribute, as opposed to chemotherapeutic drugs [12–14]. This technique confers promising benefits, including better medication efficacy and fewer side effects, protecting therapeutic drugs from the harsh microenvironment (such as elevated acidity in the stomach and high levels of enzymes and proteases in the bloodstream) until they reach targeted tumor cells, regulated drug distribution over a time span with required doses, and low exposure of contaminants [15, 16]. Nanomedicine is the use of nanotechnology in medicine to solve the limitations of traditional pharmaceuticals and improve their medicinal value. In contrast to their traditional medicinal formulations, anticancer drug-loaded NPs have already shown a stronger pharmacokinetic profile (half-life, controlled release) and tumor aggregation. Furthermore, the NP-based method facilitates multidrug coencapsulation and codelivery, which decreases toxicity and drug resistance [17, 18].

Alzheimer's and Parkinson's diseases (AD and PD), stroke, amyotrophic lateral sclerosis (ALS), Hutchinson's disease (HD), and HIV-1-associated dementia (HAD) are some most debilitating diseases of the twenty-first century [19]. This group of diseases has little to do with host biology and more to do with advancing age, environmental cues, and/or a disordered immune system [20–24]. Theranostical nanomedicine has emerged as a major and promising disease prevention approach because of its ability to combine diagnosis and therapy [25, 26]. NPs migrate through the BBB (blood-brain barrier) owing to a pathway called receptor-mediated endocytosis. Multiple NPs can quickly cross the BBB by interacting with proteins and protein-related receptors, owing to functionalization and alteration. NPs engineered with surfactants like polysorbate 80 also assist drug passage through BBB, as altered NPs have been shown to absorb particular plasma proteins [27]. In the presence of electromagnetic fields, gold nanoparticles (AuNPs) have been shown to stimulate the generation of induced dopamine neurons for PD care [28]. Functionalized single-walled carbon nanotubes (SWNTs) have been shown to restore natural autophagy defects in lysosomal proteolysis, thus promoting the removal of autophagic substrates, implying that SWNTs could become novel neuroprotective nanomedicine for AD therapy [29–32].

Thus, the present review is focused on the recent advancements based on NPs for cancer and aging therapeutics. Some potential future opportunities, clinical studies, and patents in the field of cancer and aging disorders nanomedicine are also reviewed.

2. Sources and Modulators of Inflammation in Tumor and Aging

Maturing and aggravation work at different degrees of intricacy influencing numerous tissues and organs just as the insusceptible framework and our connected biological systems (gut microbiota). Both of these variables are thought to prompt the fundamental incendiary condition, through the unevenness of favorable to provocative as well as mitigating go-betweens [33–36].

2.1. Immunosenescence. Many progressions in inborn and procured insusceptibility have been distinguished and considered unsafe in the older, subsequently the term immunosenescence. Maybe then, a basic unidirectional decrease in safe capacity, immune senescence, is an intricate cycle including various reorganizational and normatively controlled changes. Then again, in the older, certain immunological boundaries are regularly fundamentally diminished and great capacity is contrarily connected to the wellbeing status. Albeit intrinsic resistance is moderately very much saved in the older, and gained insusceptibility is more helpless because of both the utilitarian decrease related with age and the antigen weight to which an individual has been uncovered during their lives. This constant antigenic pressure, which influences the resistant framework during life and prompts a reformist actuation of macrophages and related cells, assists with evaluating the fiery status. This outcome is an increment in incendiary middle-person movement, which is connected to the presence of persistent diseases [34, 35, 37].

2.2. Cellular Senescence. Cell senescence is described by a condition of perpetual cell-cycle capture because of openness to distressing boosts like telomere disintegration, oncogene initiation, reactive oxygen species (ROS), synthetics, and ionizing radiation [38]. As a result, cell senescence is widely regarded as a cancer component; however, evidence linking this interaction to hyperplastic and progressive disorders through continuous exacerbation is still being developed [37, 38]. In spite of their development capture, senescent cells are metabolically and transcriptionally dynamic and they set up a complex crosstalk with their microenvironment through the combination of an assortment of secretory proteins [39, 40]. A senescence-associated secretory phenotype (SASP) is a vital component in our present comprehension of the connection between cell senescence, aggravation, and malignancy improvement [41].

2.3. Self-Debris Triggers of Inflammaging. Attributable to expanded turn of events and additionally lacking expulsion, maturing is related to a continuous amassing of harmed macromolecules and cells (self-flotsam and jetsam). These

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byproducts are delivered because of cell/organelle injury and are gotten from cell and metabolic cycles. Self-garbage, as endogenous threat-related sub-atomic examples, can emulate bacterial items and damage-associated molecular patterns (DAMPs). Therefore, intrinsic invulnerability receptors perceive weakened cell and organelle components, ROS, and metabolites (for example, ATP, unsaturated fats, urate gems, ceramides, cardiolipin, amyloid, succinate, peroxidized lipids, progressed glycation finished results, modified N-glycans, and HMGB1) [40, 42]. The upregulation of irritation-related pathways and middle people are set off by the Toll-like receptor family (TLR), intracellular NOD-like receptors (NLRs), and cytosolic DNA sensors. TLRs, specifically, cause irritation by initiating NF-κB and activator protein 1 (AP-1) by means of Myd88. The initiation of NLRs (especially Nlrp3) by DAMPs brings about the development of an inflammasome and the resulting emission of a few proinflammatory arbiters. The natural invulnerable reaction to DAMPs gets tenacious and maladaptive as self-trash gathers, prompting inflammation [43].

2.4. Gut Microbiota. The gut microbiota bacterial populace contains the greater number and convergence of organisms in the human body, and it has appeared to assume a part in an assortment of physiological and neurotic cycles. The advantageous capacity of this environment comprised of microbiota, gut-associated lymphoid tissue (GALT), and intestinal mucosa is dependent on a physiological poor-quality irritation to look after homeostasis. The microbial organization of the gut microbiota fluctuates with age, with pervasiveness of Bacteroides in the older contrasted with a higher presence of Firmicutes in more youthful grown-ups. A few investigations have likewise discovered an association between microbial variety, feebleness evaluations, and natural elements in old individuals, like dietary examples. In this sense, changes in gut microbiota arrangement have all the earmarks of being inseparably connected to the maturing-related, long-haul changes in the gastrointestinal parcel (for example, decrease of intestinal motility, helpless dentition, and adjustment of salivary qualities). Critically, changes to the gut microbiota in the older will rush the beginning of dysbiosis and increment the commonness of pathogenic species in the intestinal microbial synthesis, which has been connected to raised degrees of the foundational support of provocative markers (IL-6, IL-8, TNF-α, and CRP). The connection between gut dysbiosis and malignant growth is in this way not restricted to a direct pathogenic pretended by explicit microorganisms on the intestinal epithelium, yet additionally to general environment insanity that has foundational outcomes through provocative pathways [44–51].

2.5. Obesity, Nutrition, and Metaflammation. Numerous individuals, particularly in Western nations, partner maturing with an increment in instinctive fat, which adds to weight and insulin opposition [52]. Moreover, epidemiological proof proposes an association between a high body mass index (BMI) and an assortment of malignancies, including pancreatic disease, prostate disease, colon malignant growth, postmenopausal bosom malignancy, and numerous others [53, 54]. Notwithstanding the way that the subatomic associations among stoutness and malignant growth are as yet being investigated, it is presently commonly concurred that corpulence causes a constant incendiary state [55]. Metainflammation is a second-rate, constant fiery condition coordinated by metabolic cells in light of an overabundance of supplements and energy in weight-actuated aggravation [56]. Hefty irritation is described by the way that it is set off by metabolic signals and happens inside metabolic cells, for example, the adipocyte. Extreme supplement admission, particularly glucose and free unsaturated fats, causes pressure, which actuates provocative intracellular flagging pathways. C-jun N-terminal kinase (JNK), IκB kinase (IKK), and protein kinase R (PKR) are the primary intracellular supporters of the initiation of aggravation in metabolic tissues [57].

3. Immunity and Inflammatory Mechanisms in Aging

Maturing is connected to insusceptible framework changes that increment powerlessness to irresistible illnesses, malignancy, and immune system sicknesses, just as the inability to help wound recuperating and immunization reaction. Maturing influences both versatile and inborn invulnerable capacities and is brought about by a blend of changes in safe framework cells, lymphoid organs, and circling solvent factors that impact insusceptible cells and their microenvironment. The bit-by-bit-expanded weakness to incendiary illnesses seen with maturing is because of a gentle enactment of aggravation, which is a sign of maturing. The combined impacts of typical maturing lead to the marvel known as "immunosenescence," which alludes to the reformist debilitating of the safe framework [58].

Despite the fact that our comprehension of old-enough-related changes in the versatile safe reaction is genuinely best in class [59], our comprehension of maturing measures including the intrinsic resistant framework actually requires further examination. We are principally inspired by the dysfunctions of the inborn safe reaction as they add to maturing measures. Monocytes, macrophages, neutrophils, dendritic cells (DC), and natural killer (NK) cells are intrinsic invulnerable framework cells that experience huge phenotypic and practical changes as they develop. It is accounted for by changes in the complete number of circling inborn-resistant cells or the overall level of various subpopulations. Old-style (CD14++/CD16), nontraditional (CD14+/CD16++), and moderate (CD14++/CD16+) monocyte subsets can be recognized as dependent on the general articulation of CD14 and CD16 [60, 61].

4. Pathways Linking Innate Immunity, Inflammation, and Cancer

Aggravation and malignancy are two cycles that are connected. The possibility that irritation and disease are connected traces all the way back to Virchow in the nineteenth century. The connection between irritation and malignant growth can be considered as far as two pathways.

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Irritation and malignancy are two cycles that are connected. The possibility that irritation and malignancy are connected traces all the way back to Virchow in the nineteenth century [61]. The connection between irritation and disease can be considered as far as two pathways. Predominant and latent qualities drive neoplastic cell change, which causes irritation in tumors that aren't related to an excess of aggravation (for example, bosom carcinoma and gliomas). The development of an incendiary microenvironment is organized by malignant growth causing hereditary occasions [62]. In created danger, the incendiary parts fluctuate significantly among tumors and seething, nonsettling irritation drives harmful movement [63]. The tumor microenvironment (TME) is presently perceived as a significant factor in the advancement of neoplasia. We pulled back from a pervasive malignancy cell-driven perspective on the idea of disease [62, 64, 65] regarding general malignant growth standards. Provocative cells, especially macrophages, add to the advancement of an immunosuppressive microenvironment as well as cooperating with tumor cells and stroma. Immunosuppressive particles like cytokines (IL-10 and TGF) and designated spot barricade triggers like PDL1 are accessible to mononuclear phagocytes [66].

5. Tools of Nanotechnology

The equipment, programming, and supplies used to gauge and control structures on the nanoscale are known as nanotechnology apparatuses and instruments. Magnifying lens, tests, lithography situation, control and creation frameworks, programming, and different extras are among the things accessible. These instruments are seldom selective to nanotechnologies. Most of them came from different ventures, particularly semiconductors and chipmaking, where submicron producing standards fueled the correspondences blast. Science, physical science, and materials science have all had an impact, and nanotechnology is exceptional in its interdisciplinarity. This BCC report centers around nanotechnology devices and instrumentation, or the advances, items, and applications that permit researchers and laypeople to accomplish nanotechnology work. The capacity of instruments and apparatuses to quantify, sense, create, and control matter at the nanoscale is basic to each part of essential nanoscale science just as business nanotechnology advancement [67].

6. Nanotechnology in Cancer

Nanotechnology has the greatest advantage on cancer diagnosis and therapy over other function. There are several numbers of ongoing researches including the designing of nanodevices against cancer which have the ability to detecting tumor at the early stage of cancer and also the location within the body that will further be helpful for delivering chemotherapy or drug on the record location where malignant cells are being developed. Recent research shows that nanotechnology is being developed for detecting tumor and as well as developing nanodevices that will lead to cancer treatment. The best cure for cancer can be possible by diagnosing tumor and taking required steps for prevention. Nanodevices such as nanowires have special features like specificity and selectivity through which it can easily detect molecules of malignant cells, and protein produced by cancer cells resulting in diagnosis of tumor can be achieved. Having detected the tumor, it can be destructed by nano-shell-assisted photo-thermal therapy that can absorb light of the near-infrared region (NIR) and penetrate tissues. It works by producing heat that aids to destruct tumor. The greatest advantages of thermal therapy are destroying tumor cells that cannot be destroyed by surgery [68].

6.1. Aptamer Nanomedicines for Cancer Therapy. Aptamer can be a special tertiary structure that can detect small molecules like protein as well as cells [69–71], although it has similarity to antibody [72] and because of this its high molecular weight hampered to penetrate into solid tumor but it is significant in cancer therapeutics. There has some strong evidence that aptamer nanomedicines have promising effects on gene therapy, drug therapy, and tumor imaging. Typically, aptamer nanomedicines work by inhibiting the growth of tumor cells. However, there have been some barriers on the designing and application of aptamer at the desired target. In that case, SELEX is the significant aspect to produce aptamer for required target cells [73, 74]. Aptamer is screened from a library that is composed of different molecules. By some intermediary process, the target-specific candidate can be elucidated which will further be enhanced by PCR (DNA) or RT-PCR (RNA). The exaggerated candidate can be activated by isolation or transcription for the selection process. These processes should be continued until the best performing aptamer can be achieved by the SELEX process which will make capable the aptamer for target recognition. But in some cases, these aptamers are unable to stimulate or inhibit the target. So in that case, the researcher should obtain a specialized process to generate aptamer or conjugate aptamer which can produce desired therapeutic outcomes [75]. Aptamers are significantly potential because they are designed as safe, well-controlled, and robust delivery systems [76].

6.2. Lipid-Based Nanostructure for Cancer. Lipid-based nanomedicines have promise to exert potential effects on the special drug delivery system of cancer treatment [77]. They contain therapeutic agents inside. Lipid nanoparticles like liposome have cationic groups on the head that binds to an ionic nucleic acid and hydrophobic drug containing the liquid membrane and inside contains hydrophilic drugs [78] resulting in unfortunate virus. To improve liposome-mediated gene transduction, it requires combining potent promoters such as multilamellar vesicle (MLV) liposomes with a transcriptional activator like HMG-1, 2 protein that can increase the response of cationic liposomal genes. Liposome-mediated gene expression can be strong by the combination of the Egr-1 promoter and radioisotope [79]. Lipid-based magnetic nanomedicines have promising effects on both drug delivery and early detection of the disease condition and also treatment and diagnosis [80].

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6.3. Approach of Nanomedicine in Gut Cancer Axes. Nanotechnology as well as nanomedicine greatly is impacted by gut bacteria. Gut bacteria can enhance carcinogenesis by toxic metabolites [81] or by attachment of bacteria to the tumor microenvironment [82]. These carcinogenic bacteria can be induced from undigested food or toxins like colibactin, lipopolysaccharides, and hepatic bile metabolites. Various types of dietary habits can produce carcinogenic or class in a protective metabolism that can stimulate and prevent intestinal carcinogenesis (Figure 1(a)) [83]. Gut microbiota such as *Fusobacterium nucleatum* can interfere on the chemotherapy of cancer [84]. Especially induce chemoresistance instead of apoptosis on colorectal carcinoma [85] by activating autophagy. Another research suggests that gut bacteria like *E. coli* have the tendency to direct mutation on human intestinal colorectal carcinoma [86, 87]. The gut liver axes facilitate the movement of toxic metabolites from the gut to the extraintestinal part resulting in hepatocellular carcinoma [88, 89]. Bile acids are transformed into toxic intermediates that can attack the cell wall of bacteria though it will be further converted to secondary bile acids that can ultimately induce carcinogenesis [90].

Undoubtedly, gut microbiota can aid in pathogenesis and progression of bacteria while cyclophosphamide altered the microbial cell as well as biotransformation (Figure 1(b)) [91] on the small intestine that will restrict the tumor and induce anticancer effects. NPs decompose the gut microbiota in molecular and cellular levels that can inhibit hepatocellular carcinoma and colorectal cancer (Figure 1(c)) [92].

7. Novel Prospects in Nanomedicine for Enhanced Tumor Treatment

Through passive targeting NPs works on tumor over several NPs occur on healthy organ. So, the active targeting process facilities the way of functioning of nanoparticles on active areas along with binding to specific receptors on tumor or other endothelium and accumulation on tumor [94]. Folate has the high affinity to the folic acid receptor that can be overexpressed at 100–300-fold in specific tumor [95]. The folate-functionalized PEGylated dendrimers have shown the higher accumulation rate to tumor that is resulting in the reduction on tumor growth. Active-targeted topotecan, a topoisomerase-I inhibitor, showed twofold higher anticancer efficacy against breast cancer with anti-HER2 scFv F5 antibody in comparison with passive-targeted liposomes [96]. The current research works for controlled release from nanoparticles that will functionalize better against tumor cells compared with others in which circumstance ultrasound and increased temperature aid to induce the drug release in tumor [97].

7.1. Tumor-Specific Profiling of the Accumulation of Nanomedicines. For the diagnostic approach, nanoparticles first select the tumor and magnetic nanoparticles (MNPs) can be imaged that will classify tumors in a specific corresponding group according to MNP accumulation and further associated to therapeutic nanoparticles (TNPs). The buildup of high level of MNP in tumor tends to accumulation of high-level of TNP which slows tumor growth. There is a significant difference in cellular level distribution between TNPs and MNPs. MNPs do not have the same cellular level distribution as TNPs that depends on enhanced permeability and retention (EPR) of tumor. MNPs have comparatively strong affinity to tumors than TNPs (Figure 2) [98, 99].

7.2. Impact of Nanoparticle Properties in Tumors. For solid tumor treatment, nanomedicines are administered through systemically and they accumulated to the tumor according to the EPR level [94, 95, 100, 101]. Multiple biological steps lie on the systemic delivery of nanoparticles which will be also affected by the EPR levels like NP-protein binding, blood circulation, extravasation tumor tissue penetration, and tumor cell internalization. Several properties of nanoparticles such as size, stiffness, geometry, surface charge, porosity, elasticity, surface hydrophobicity, and roughness can influence their biological systems which estimate EPR effects and therapeutic results. Having entered to the biological steps like in blood and intestinal fluid, immediately, it forms corona by covering with several biomolecules (Figure 3) [102–105]. So, the NP-protein interaction basically is depending on the physical chemical properties of NPs.

8. Nanomedicine Strategies for the Treatment of Rheumatoid Arthritis

Rheumatoid arthritis (RA) is a chronic autoimmune disease in which the joint tissues develop severe inflammatory microenvironments. Congenital and high infiltrations are found in inflammatory joints. Self-antigen-specific adaptive immune cells induce hyperplasia and increased inflammatory cytokine levels lead to cartilage and bone breakdown, be it irreversible [107].

With the formation of nanoparticles, the development of nanomedicines in RA has increased rapidly. It efficiently accumulates in the inflammatory microenvironment of arthritic joints. It features neovascularization and an abnormal peripheral lymphatic system. Synthetic and biological DMARD delay the development of RA by interfering with the inflammatory cascade in various immune cells. The known mechanism of action is to downregulate production of inflammatory cytokines and inhibit leukocyte migration [108]. Long-term treatment of this disease with antirheumatic drug may cause toxicity on various organs of the patient's body like gastrointestinal, kidney, skin, and immune suppression-mediated infection. For the treatment of RA, nanomedicine has developed as a potential therapeutic technique for efficiently localizing medicines in inflamed joints [109].

8.1. Delivery Strategies to Inflamed Joints. Antigen-presenting cells such as dendritic cells activate autoantigen-specific lymphocytes which infiltrate into joint tissues and cause an inflammatory response and leukocyte recruitment as a result of the inflammatory status increase. Normally, a lining in the synovial joint is formed by synovial cells but it abnormally proliferates and results in hypoxic and nutrient-deficient

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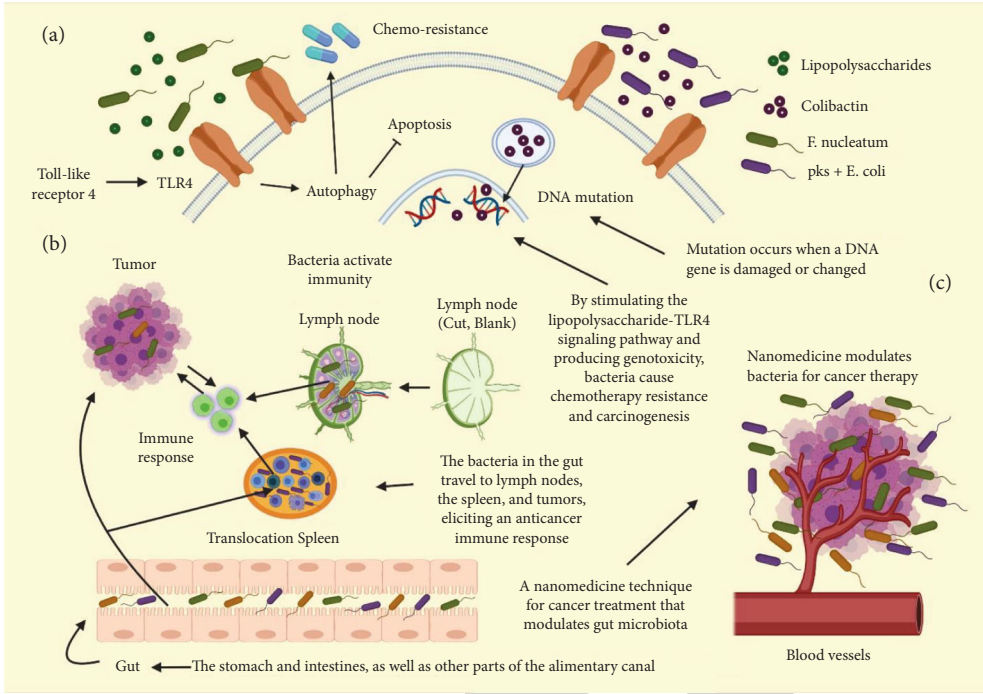

Figure 1: The link between the gut microbiota and cancer and cancer treatment strategies using nanotechnology. (a) Bacteria induce chemotherapy resistance and carcinogenesis by activating the lipopolysaccharide-TLR4 signaling pathway and causing genotoxicity material. (b) Gut microbiota migrates to the lymph nodes, spleen, and tumors and elicits an antitumor immune response. (c) A nanomedicine strategy that regulates gut bacteria for cancer treatment [93].

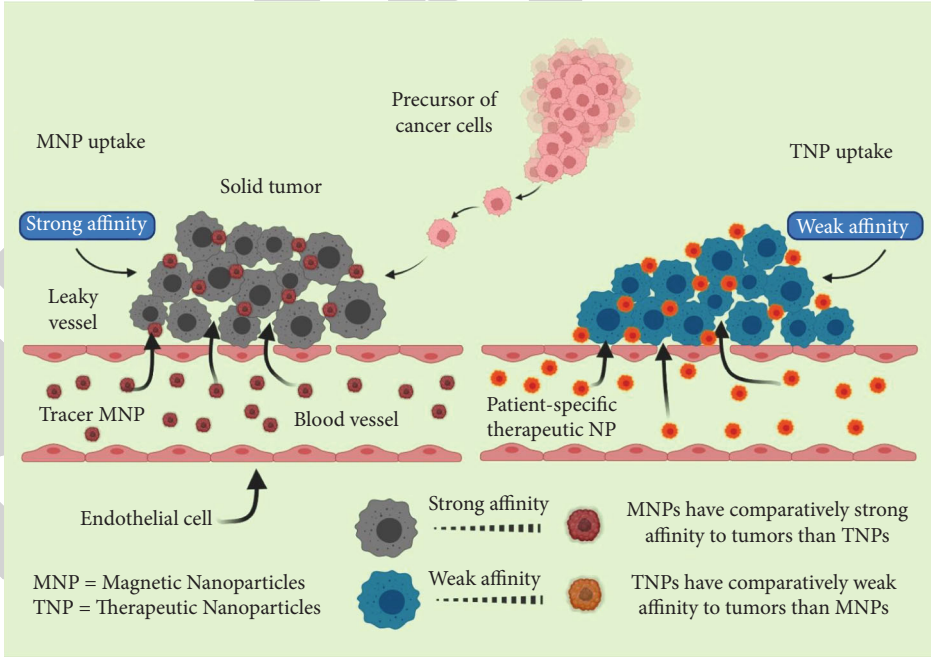

Figure 2: MNP can accumulate in tumors and be imaged in the same way that TNPs can, but not free medications [98].

microenvironments and angiogenesis [110, 111]. That makes the vasculature leaky with large fenestration up to 600 nm [112–114] and permits the diffusion of the macromolecules into the inflamed joint tissues. Selectively, accumulation of the intravenously administered nanomedicine is caused by this leaky vasculature by passive targeting. The delivery efficacy is significantly enhanced compared with intravenous injection of free drugs in that technique. The mononuclear phagocytic system (MPS) such as the liver and spleen also clears a significant amount of nanomedicine [115, 116]. It is also believed that the threshold for renal clearance is around 5 nm [117]. That is why the quick excretion of

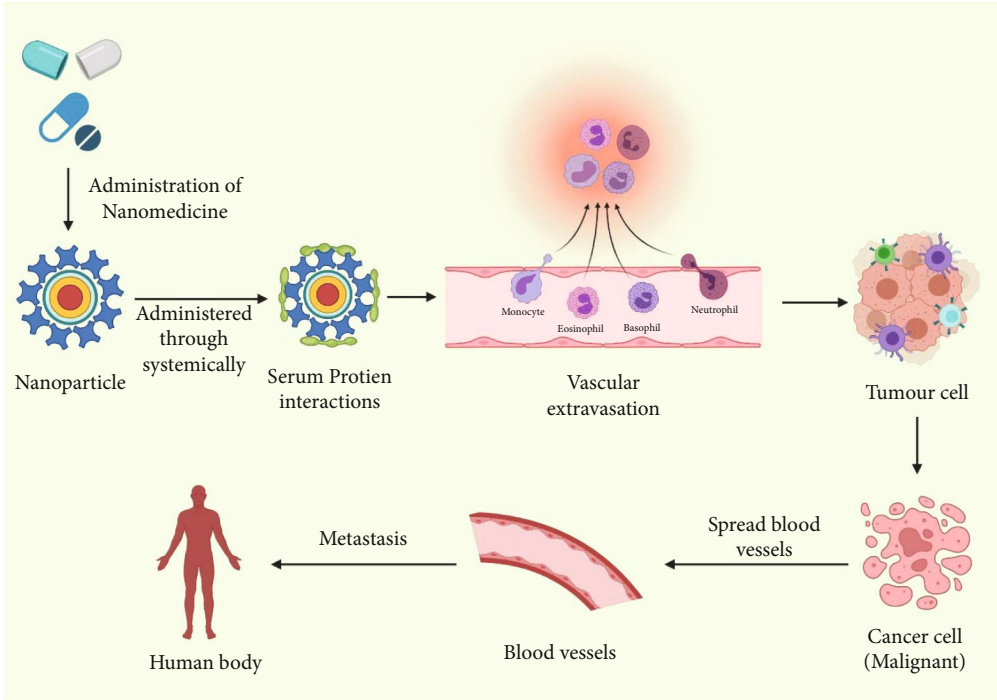

Figure 3: Nanoparticle (NP) properties can be affected by the interaction with serum protein. Extravasation intracellular peddling takes place into tumor tissue through leaky tumor vessels [100, 106].

nanotherapeutic delivery systems below this size limit can be achieved by this route after intravenous injection. The size and charge are considered to be key factors for nanomedicine generally to elude the MPS and renal clearance.

Efficient delivery of nanomedicine to the inflamed joints can be achieved by following the recommended optimal size range which is around 200 nm [118, 119], and for the minimization of the interaction between nanomedicine and macrophages, zwitterionic surface charge is preferred rather than negative or positive surfaces [120, 121]. A functional surface coating can also enhance the delivery of nanomedicine to the inflamed joints. For minimizing the macrophage uptake and prolonging of the blood circulation, coating of stealth polymers such as poly (ethylene glycol) (PEG) was used [121, 122]. Drugs like NSAIDs (indomethacin), [123], corticosteroids (prednisolone, methyl prednisolone, budesonide, dexamethasone, and betamethasone), DMARDs (methotrexate), siRNAs (NF-κB siRNA, TNFα siRNA, and Mcl-1 siRNA), therapeutic peptides, and other drugs (camptothecin) [109] are administered by that method to the inflamed joints. Corticosteroid derivatives which are water soluble like prednisolone phosphate [124, 125] and budesonide phosphate [126] were formulated with the PEGylated liposomal formulation where insoluble corticosteroids were formulated with PEGylated micelles [127, 128] or polymer-based NPs [129]. PEGylated liposomes [130, 131] or polymeric a hybrid nanoparticle [132, 133] was also used to administer methotrexate and in order to increase the therapeutic efficacy and reduce the systemic toxicity.

Particularly, the positively charged PEGylated lipid NPs were used for siRNA encapsulation for effective cytosolic delivery. PEG-free liposomes were developed to minimize the allergic reactions against PEG and prolong the therapeutic efficacy of dexamethasone in the inflamed joint [134, 135].

Coating of NPs with biological self-materials like albumin can also result in prolonged blood circulation as it will be recognized to the MPS system as self-material and blood clearance will be reduced. DMARDs, methotrexate, and IL-1 receptor agonist were coated with albumin to facilitate drug delivery efficiently to the inflamed joints [136–138]. Red blood cell membrane-coated nanoparticles were developed for increasing the blood residence time. Another way for increasing the accumulation of circulating drugs in the specific region of the body is the magnetic drug delivery system. An external magnetic field is used to localize the administered drugs in the specific region of the body in the magnetic drug delivery system.

8.2. Therapeutic Strategies. Although the accumulation of nanomedicine in the inflamed joints can be enhanced by passive delivery strategies via a leaky vasculature, the drugs release and diffuse to every cell in the articular cavity which tends to reduce the therapeutic efficacy of the drugs. That is why it was suggested to use targeted delivery of nanomedicine to the inflamed joint-associated molecules and cells for improving the therapeutic efficacy of the antirheumatic drugs. The proinflammatory cytokines and cells like macrophages and synoviocytes are the main therapeutic target in the arthritic joints as pathological progression of RA is strongly related to proinflammatory cells. For the therapeutic target, the proinflammatory cells including macrophages, T cells, and FLSs and their cytokines have been actively studied [109].

8.3. Nanomedicine and Osteoarthritis. Although, there are many advance technologies and ways in the cartilage biology for the better diagnosis and treatment of bone and joint decade, a new and advance way with the nanomedicine technology for the diagnosis and treatment of osteoarthritis (OA) has been developed.

8.3.1. Oxidative DNA Damage Contributes to Aging and Degeneration of Articular Cartilage. It has been found that at the time of development of OA, mechanical and chemical stresses on articular cartilage make the cellular activity of chondrocytes unstable and give rises to excess amounts of ROS and also proinflammatory cytokines and chemokines. Recent studies have shown that in degenerated articular cartilage, there is significant accumulation of ROS and chondrocyte aging. Studies have also disclosed that there is significant involvement of 8-oxyguanine (oxidative form of guanine) accumulation and impairment of mitochondrial DNA repair enzymes in the pathogenesis of OA and ROS is the major causative agent of 8-oxoguanine production in both DNA and nucleotide pools [139].

8.3.2. Application of Nanotechnology to Chondroprotection. According to a recent study, C60 fullerene which is water soluble has potential to work against the catabolic stress-induced degeneration of articular cartilage both *in vivo* and *in vitro* OA models. The study has also highlighted that C_{60} fullerene can also stimulate the expression of mitochondrial DNA repair enzymes and their functions in osteoarthritis. So, water-soluble fullerene nanoparticles can be used as potential therapeutic for the protection of articular cartilage in OA [139].

9. Nanomedicines for Treating Neurodegenerative Disorder

9.1. Alzheimer's Disease (AD). AD is defined clinically by a progressive deterioration in cognition and histologically by the development of intracellular neurofibrillary tangles and extracellular amyloid plaques in the brain [140, 141]. Currently, there is no efficient therapy for AD. More than 98% of available drugs cannot transfer from the blood to the brain, which is protected by a cellular fence, the blood-brain barrier (BBB) [142]. Currently, there are five drugs approved by the FDA for AD treatment and they are tacrine, donepezil, rivastigmine, galantamine, and memantine. One of the major problems for the drugs of AD treatment is the blood-brain barrier (BBB) crossing. NPs are being thought as a solution to overcome that problem. There are several types of NPs which can be used for AD treatment. They are polymer-based nanoparticles in which polymers like poly lactic acid (PLA) and poly glycolic acid (PGA) are used in polymer-based nanoparticles as they are biodegradable and biocompatible and have longer shelf life and stability during storage [143].

Polymer-based NP examples of drugs are curcumin, rivastigmine, estradiol, neuroprotective peptide, etc. Lipid-based nanoparticles are preferred due to high lipid solubility and high circulation and retention time, for example, aqueous phosphatidylcholines and solid lipid-based nanoparticles which are based on glyceride mixture. Solid lipid-based nanoparticles have advantages for the hydrophobic drugs as it has a suitable environment for the entrapment of drugs and release. Examples of liposomal or lipid-based NPs are curcumin, phosphatidic acid, cardiolipin, etc. Piperine is the example of solid lipid-based NPs. Tacrine is employed as a drug for various NPs such as albumin NPs, magnetic NPs, and chitosan NPs. And for gold NPs, Aβ-binding peptides are used [142]. In the amyloidogenic pathway, continuous cleaving of the amyloid precursor protein by β- and γ-secretases releasing amyloid beta (Aβ) peptide and aggregation of Aβ monomers leads to the formation of oligomers and fibrils. Oligomer formation is considered as the main toxic event in AD, which can cause neuronal dysfunction and death. Properly functionalized NPs can interfere in Aβ production or clearance. Moreover, properly functionalized NPs may also affect Aβ aggregation features or block its aggregation. Thus, NPs reduce Aβ levels [142].

Among all other NPs, liposomes and PEG-PLA NPs are being the mostly used NPs as they are known for the lack of toxicity, low immunogenicity, and full biodegradability [144, 145]. For example, curcumin, phosphatidic acid cardiolipin, and XO4 are used. PEGylated polymeric NPs are also used due to their ability to increase half-life which leads to increase interaction with the peptide [142].

9.2. Parkinson's Disease (PD). The capacity of a medication to penetrate the BBB and meet the target region, as well as the duration of drug delivery to prevent concentration changes, has been a major challenge in the development of successful treatments for PD. When compared to other therapeutic fields, medication development for the treatment of brain disorders has the lowest success rate [146]. Drug development for CNS disorders often takes significantly longer than drug development for non-CNS disorders. As a result, the creation of disposable nanoparticles that can readily pass across the BBB has been prioritized in the development of novel carriers for anti-Parkinsonian drugs [147, 148]. Dopamine is a chemical messenger in the brain that serves a variety of tasks in the body, and when dopamine levels in the body drop, the body is assaulted by PD [149].

Drug delivery into CNS has become a problem that has to be addressed, and polymeric NPs have proven to be a potential solution. Several studies have been conducted to see if polymer may be used to transport drugs to the brain. Bone marrow macrophages (BMM) are macrophage cells that are derived from bone marrow cells. Haney and colleagues synthesized BMM NP with a polymer composition (PEI-PEG) and catalyzed BMM NP to promote neuroprotection and reduce neuroinflammation. An NP with PEG corona and enzyme linked to a polyion complex is formed by the formulation. 1-Methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP), intoxication, and 6-OHPA were used to induce brain inflammation in C57BL/6 mice [150]. Investigators are considering developing NP-based formulation for PD patients to deliver DA to the brain. Yang and colleagues developed a sustained-release formulation comprising levodopa methyl ester (LDME) or benserazide-

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loaded polymeric (PLGA) NPs, which they tested on rats that had dyskinesia caused by levodopa (LD) injection. Dyskinesia in rats produced by LD is linked to the quantity of phosphorylated dopamine and cyclic adenosine monophosphate-regulated phosphoprotein (pDARPP-32), phosphorylated extracellular signal-regulated kinases 1/2 (p-ERK1/2), and fos protein. Furthermore, LD therapy caused rats to acquire aberrant involuntary reflexes [151].

Metallic NPs are widely utilized in the cure of different illnesses, such PD, cancer, and rheumatoid arthritis, to name a few. Magnetic NPs, gold NPs (AuNPs), silver NPs (AgNPs), and cerium oxide NPs (CeO_2NPs) are some of the metallic NPs that are utilized in the treatment of ailments [152]. Qiao et al. [153] synthesized Fe_3O_4 magnetic NPs and subsequently coupled them with lactoferrin, which functions as a brain MRI-guided delivery probe. Gao et al. [154] developed gold nanoclusters for the treatment of PD. Because of the two major features (particle size and redox properties), CeO_2NPs are also gaining increasing interest in the treatment or prevention of neurodegenerative disorders (Table 1) [23, 155–163]. Dillon et al. [164] synthesized CeO_2NPs and tested their antioxidant efficacy in a PD animal model caused by MPTP.

9.3. Huntington's Disease (HD). HD is a neurodegenerative disorder which is characterized by an autosomal dominant mutation in the Huntingtin gene (HTT) that produces CAG trinucleotide repetitions at the $5'$ end, leading to abnormal Huntingtin protein production and segmentation, which leads to neuronal damage and cytotoxicity [170]. This disease has a significant impact on the physical and psychological wellbeing of both the patients and health care providers and the socioeconomic level of the suffering persons and their families. HD strikes people primarily in their adulthood, when they are approximately 45 years old (on average), gradually overtaking the victim's motor and cognitive capabilities while also affecting their behavioral responses [171]. Its autosomal dominant character is both a benefit and a drawback, as it has the most phenotypic penetrance and is monogenic, making it possible to target effectively compared to other neurodegeneratives, which are caused by a complicated network of biochemical processes [172]. The sole licensed medicine for HD is tetrabenazine, and most contemporary therapy approaches are symptom based [173]. Targeted activation of the cAMP respond element binding protein, as well as the usage of coenzyme Q and Creatine, are among the other ways now being investigated. Grip force (Q motor), HD-CAB (cognitive), caudate volume (MRI), cortical activity electroencephalogram, amounts of neurofilament and mutant Huntingtin in cerebrospinal fluid (CSF), and other biomarkers are used in several clinical studies for the evaluation of HD [170].

Changes in neurochemical pathways including the dopamine, adenosine, and glutamate receptors, as well as oxidative damage and mitochondrial abnormalities, are all major contributors to HD pathophysiology. Sandhir et al. [174] employed solid-lipid NPs conjugated with curcumin to modify complex II activity in order to target mitochondrial abnormalities as a form of HD treatment. They also found that 3-nitropropionic acid increased the levels of Nrf2 mRNA. Bhatt et al. [175] tried every possible method, creating solid-lipid NPs conjugated with rosmarinic acid (RA) to target HD, relying on RA's high-brain-targeting efficacy. Cong et al. [176] recently demonstrated the use of selenium (Se) in a targeted delivery method for HD. Se and selenoproteins have been linked to brain malfunctioning, mutant Huntingtin aggregation, and elevated numbers of oxidized glutathione. Se insufficiency in the brain has been linked to brain abnormalities, mutant Huntingtin aggregation, and higher levels of oxidized glutathione. Se NPs have been proven to be the least hazardous and have the greatest potential to prevent oxidative damage of all the numerous therapeutic forms of Se that have been examined, even at concentrations lower than 0.5×10^{-3} M. The scientists also demonstrated that Se NPs can attenuate neurotoxicity and alleviate cognitive disruptions in a Caenorhabditis worm's model of HD, even at doses lower than 2×10^{6} M. Due to exceptional qualities like the ability to control HDAC (histone deacetylase) activity and diminish poly Q aggregation, which is one of the characteristics of HD pathophysiology, Se and its application represent significant potential in the potential implementation of anti-HD treatments.

9.4. Amyotrophic Lateral Sclerosis (ALS). People are diagnosed with ALS, a devastating category of NDs that causes the death of motor neurons in the spinal cord and brain. ALS is caused by genetic mutations in the superoxide dismutase 1 (SOD1) gene, which codes for the superoxide dismutase enzyme. SOD1 mutations generate harmful free radicals and inhibit proteasome and/or chaperone action, leading in protein misfolding and insufficient clearance [177]. Several clinical studies for the management of ALS have been unsuccessful in the past 10 years due to numerous limitations in traditional therapy techniques. The United States Food and Drug Administration (USFDA) has recognized riluzole as the only glutamate antagonist for the therapy of ALS. This eloquently demonstrates the critical desire for a new novel therapeutic strategy to the awful disease [178, 179]. To this purpose, nanomedicine, as we have shown, can represent a critical role in the development of innovative ALS treatment strategies. Bond et al. [180], for example, established riluzole administration utilizing solid-lipid NPs for the therapy of ALS with high drug encapsulation and improved clinical efficacy.

9.5. Epilepsy. Epilepsy is a noncommunicable chronic condition caused by fast neuronal exoneration and uncontrolled electrical discharges in certain brain cells. These can be classified as status epilepticus; however, they may appear with few or no behavioral symptoms [181–184]. Epilepsy affects around fifty million people worldwide, according to the World Health Organization (WHO) estimates, making it the fourth most common neurodegenerative condition. Early death, wounds related with seizures and fractures, and greater grades of psychiatric problems such as depression and stress are all anticipated in individuals with this ailment [185–187]. Examining the patient's medical history, inspecting the nervous system, comprehensive blood

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Table 1: Therapeutic application of NPs in neurodegenerative disorders.

Nanoparticle	Therapeutic outcomes	Cell entry	Disease	Reference
Silver	Upregulation of hydrogen sulphide (H2S) and Ag2S reduces neurotoxicity	Silver's natural properties cross the BBB	PD	[165]
Silver	As a plant-based anti-Alzheimer medication, it has anticholinesterase and antioxidant action	Silver's natural properties cross the BBB	AD	[166]
Gold	Suppression of Aβ42 aggregation	Endocytosis of chiral nanoparticles across the BBB	AD	[167]
Gold	Apoptosis of dopaminergic neurons in the substantia nigra striatum is inhibited by PC12 cells	Nerve growth factor (NGF) endocytosis	PD	[168]
Selenium	In AD lesions, there is a reduction in amyloid plaques	Curcumin's capacity to form intermolecular hydrogen bonds with amyloid b and iron in plaques without the need for supplementary chemical linkers	AD	[169]

chemistries, thyroid function tests, an electroencephalogram, and a brain investigation are only a couple of minor basic methods for detecting epilepsy. In recent years, improved diagnostic methods including as magnetic resonance imaging (MRI), positron emission tomography (PET), and single-photon emission computed tomography (SPECT) have been used for epilepsy biological imaging and detection. There is no approved remedy for epilepsy at the moment, and only a few antiepileptic drugs (AEDs) are frequently used to control the condition [188, 189]. Drug delivery technologies based on nanomedicine provide a diverse framework for epilepsy treatment. Liposomes, dendrimers, polymeric NPs, carbon-based NPs, micelles, AuNPs, and other drug delivery systems are being employed to treat epilepsy [189–193]. Thyrotropin-releasing hormone (TRH) containing polymeric NPs, for example, has been injected into the amygdala of epilepsy-prone rats [194, 195]. In animal studies of seizures, Yusuf et al. [196] found that poly D-lactic acid (PLGA) NPs of the β-carotene surface coated with polysorbate-80 increased antioxidant and anticonvulsant effects. Furthermore, Musumeci et al. [197] found that oxcarbazepine-loaded PLGA NPs increased the action of parent oxcarbazepine in epileptic seizures in mice when compared to parent oxcarbazepine.

9.6. Neuro-Acquired Immunodeficiency Syndrome (NeuroAIDS). In the early stages of infection, human immunodeficiency virus 1(HIV 1) reaches the CNS, giving rise to NeuroAIDS, which encompasses both viral and neurological pathogenetic processes. About 15–30% of AIDS patients have neurological and neurocognitive problems, with dementia and encephalopathy affecting 7.3–11.3% and 30–60% of patients, respectively. BBB disturbance is not really the major cause of NeuroAIDS; activated endothelial cells with reduced barrier permeability, as well as CD 163, Glut5, and ISG15 genes, have been linked to the disease [198–202]. Because there are presently no viable vaccinations or specialized pharmacological therapies for NeuroAIDS, a significant advance to nanotechnology has offered light on new treatment options for HIV infection. In the management of NeuroAIDS, nanoformulated antiretroviral therapy (ART) was found to increase blood-brain penetration. In the HIV-1 encephalitis (HIVE) area of the brain, indinavir (IDV) NP-loaded murine bone marrow macrophages (BMM) promote lower HIV-1 replication [203, 204]. Their findings also showed that NP-loaded BMM can be used to explore targeted migration and antiviral reactions. Highly active antiretroviral therapy (HAART) based on nanotechnology also performed an important role in the treatment of psychosis. Polybutyl cyanoacrylate (PBCA), methyl methacrylate–sulfopropyl methacrylate (MMSPM), polylactide (PLA), and PLGA were nanoformulated with zidovudine, delavirdine, saquinavir, and lamivudine to raise BBP 10–20 times [205, 206]. In comparison to typical antiretroviral drug (ARV) medication treatment, liposome-loaded zalcitabine has been found to have enhanced efficacy and a longer half-life [207]. Solid lipid NP-loaded ARV medicines have recently gained attention. In NeuroAIDS, SLN-coated delavirdine and saquinavir ARV drugs replaced MMSPM-coated ARV drugs due to their large surface area and efficiency [203].

9.7. Stroke. Because it is hard to overcome the limitations of neuroregeneration in injured brain areas, stroke is the major cause of protracted impairment [208]. Angiogenesis and nerve proliferation are significantly suppressed with the development of ischemia, which is accompanied by an increased immune response, culminating in an ischemic cavity in the brain. Ischemia is responsible for roughly 87% of strokes, while hemorrhage is responsible for the rest [209, 210]. Ischemic stroke and behavioral abnormalities are caused by a lack of blood in the brain, which damages neurons and neuronal pathways. BBB breakdown and cerebral edema are linked to vascular endothelial growth factor levels [209]. The PEG NP-linked recombinant tissue plasminogen activator (rtPA) enhances the half-life of rtPA and reduces infarct volume during thrombosis [211]. Ceria NPs as antioxidants inhibit free radical proliferation in the initial stages of acute cerebral ischemia-reperfusion and so minimize the primary harm caused by ischemic stroke. When compared to free enzyme, solid polymer nanoparticles packed SOD as nanozyme lowers the volume of infarct

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Table 2: Latest clinical trials relating to the use of NPs in cancer and aging therapy.

Study title	NCT no.	Place of intended study	Phase	Reference
Curcumin in combination with 5FU for colon cancer	NCT02724202	Baylor Research Institute	Phase 1	[216]
Curcumin in preventing colorectal cancer in patients undergoing colorectal endoscopy or colorectal surgery	NCT00973869	University of Leicester	Phase 1	[217]
Nanocurcumin for prostate cancer patients undergoing radiotherapy (RT)	NCT02724618	Shahid Beheshti University of Medical Sciences	Phase 2	[218]
A clinical trial to study the effects of nanoparticle-based paclitaxel drug, which does not contain the solvent cremophor, in advanced breast cancer	NCT00915369	Fresenius Kabi Oncology Ltd.	Phase 1	[219]
Paclitaxel albumin-stabilized nanoparticle formulation in treating patients of different ages with metastatic breast cancer	NCT00609791	City of Hope Medical Center	Phase 2	[219]
Nanoparticle albumin-bound (Nab) paclitaxel/cyclophosphamide in early-stage breast cancer	NCT00629499	SCRI Development Innovations, LLC	Phase 2	[219]
Nab-paclitaxel and bevacizumab followed by bevacizumab and erlotinib in metastatic breast cancer	NCT00733408	University of Washington	Phase 2	[219]
31P-MRS imaging to assess the effects of CNM-Au8 on impaired neuronal redox state in multiple sclerosis (REPAIR-MS)	NCT03993171	Clene Nanomedicine	Phase 2	[220]
A phase 1 SAD and MAD clinical trial of CNM-Au8 in healthy male and female volunteers	NCT02755870	Clene Nanomedicine	Phase 1	[221]

Table 3: Latest patents relating to the use of NPs in cancer and aging therapy.

Patent no.	Title	Year	References
CN110841073	Preparation method of CPZ-coupled MS2 protein nanoparticles and application thereof in breast cancer resistance	2020	[222]
WO/2020/018049	Lipid nanoparticles loaded with ceranib-2 as anticancer agent	2020	[222]
US20190328677	Decreased adhesivity receptor-targeted nanoparticles for Fn14-positive tumors	2020	[222]
CN 106265624	Pharmaceutical composition for treating breast cancer, medicine transferring system, and preparation method thereof	2017	[223]
US20170258929A1	Cancer treatment combination compositions, methods, and uses	2017	[223]
WO 2020 023530A3	The invention claims effective administration of a composition comprising a therapeutically effective amount of anti-Aβ protofibril antibody for the treatment of AD. The focus of invention is to convert amyloid-positive subjects to negative in the early Alzheimer case	2019	[224]
WO 2018 081460A1	The novel antibody composition (at a dose ranging from 2.5 mg/kg to 10 mg/kg) is used for treating, preventing, and/or delaying the onset and/or development of AD	2018	[224]

regions in mouse models of stroke by over 50% [212, 213]. The sensor, which comprises of magnetic disks and a swellable hydrogel with high sensitivity to pH, has the potential to reduce the extent of ischemic stroke by improving brain tissue, protecting the BBB, and reducing neurotoxicity [214]. Biomimetic nanobubbles produced from platelet membranes can not only be used as a sensor to track the dynamic progression of a stroke using real-time contrast-enhanced ultrasound imaging but also be used for precise targeting and microvascular bioremodeling in the lesion [215].

10. Clinical Trials and Patent

The nanomedicine agency's prospects for cancer and aging therapy are still quite positive. It is commonly acknowledged and experimentally demonstrated that such formulations tend to improve the efficacy of anticancer as well as aging medications by allowing for more precise and selective drug distribution. Clinical studies and patents addressing the investigation of NPs for the treatment of cancer and aging are included in Tables 2 and 3.

11. Conclusion and Future Prospects

The therapeutic methods that integrate tumor-targeted nanomedicines with other clinical therapies have acquired a positive response. Furthermore, current research advances are focusing on the creation of systems that can respond to externally applied stimuli and can be activated to release their payload. These techniques are expected to be utilized

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to target medicines other than traditional antineoplastic drugs, such as anti-inflammatory medications to suppress tumor-associated inflammation or siRNA to lower the expression of proteins that are important for tumor growth. Because of the growing incidence and mortality of cancer, additional research is needed to discover innovative diagnostic and therapeutic approaches for treating this cancer successfully. The majority of neurological diseases, such as brain tumors, degenerative AD, PD, and those with an inflammatory component, have a significant impact on human health. Because of the BBB's strict protection, conventional therapeutics have limited access and so are therapeutically ineffective. NPs might be a promising technique for enhancing cancer prognosis and treatment choices. Imaging, efficient transport, and administration of medicines to particular target locations are both possible with NPs. As a result, NPs can be used as delivery vehicles to improve the therapeutic and pharmacological properties of cancer-fighting drugs. The incorporation of NPs into therapeutic molecules helps preserve the medication against degradation while also ensuring consistent targeting and release. NPs have the capacity to cross the BBB and influence drug reactions at the cellular level due to their small size.

However, addressing the challenge of how nanotechnology can be used industrially while maintaining health, safety, and environmental protection remains a key challenge. Efforts have been made to create techniques that will allow many industrial processes to scale up, with new ways becoming safer and easier to maintain. The industry may anticipate a variety of new products for both enterprises and consumers, which will create doors for other industries where the relationship between strength and weight balance is important. We explored the possible applications of NPs for cancer and aging treatment in this article. Therapeutic studies will be needed to assess the clinical effectiveness of these NP solutions in the treatment of cancer and aging.

Data Availability

Available data are presented in the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

Authors' Contributions

Md. Mominur Rahman and Fahadul Islam equally contributed to this work.

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References

[1] R. Duncan, "Polymer therapeutics as nanomedicines: new perspectives," *Current Opinion in Biotechnology*, vol. 22, no. 4, pp. 492–501, 2011.

[2] R. Sharma and P. K. Prajapati, "Nanotechnology in medicine: Leads from Ayurveda," *Journal of Pharmacy and Bioallied Sciences*, vol. 8, no. 1, pp. 80-81, 2016.

[3] D. P. De la Ossa, "Quality aspects of nano-based medicines," in *Proceedings of the SME Workshop: Focus on Quality for Medicines Containing Chemical Entities*, London, UK, 2014.

[4] J. A. Damasco, S. Ravi, J. D. Perez, D. E. Hagaman, and M. P. Melancon, "Understanding nanoparticle toxicity to direct a safe-by-design approach in cancer nanomedicine," *Nanomaterials*, vol. 10, no. 11, p. 2186, 2020.

[5] S. M. Janib, A. S. Moses, and J. A. MacKay, "Imaging and drug delivery using theranostic nanoparticles," *Advanced Drug Delivery Reviews*, vol. 62, no. 11, pp. 1052–1063, 2010.

[6] P. Couvreur, "Nanoparticles in drug delivery: past, present and future," *Advanced Drug Delivery Reviews*, vol. 65, no. 1, pp. 21–23, 2013.

[7] S. Ganta, H. Devalapally, A. Shahiwala, and M. Amiji, "A review of stimuli-responsive nanocarriers for drug and gene delivery," *Journal of Controlled Release*, vol. 126, no. 3, pp. 187–204, 2008.

[8] S. K. Patel and J. M. Janjic, "Macrophage targeted theranostics as personalized nanomedicine strategies for inflammatory diseases," *Theranostics*, vol. 5, no. 2, pp. 150–172, 2015.

[9] D. Shah, M. Gandhi, A. Kumar, N. Cruz-Martins, R. Sharma, and S. Nair, "Current insights into epigenetics, noncoding RNA interactome and clinical pharmacokinetics of dietary polyphenols in cancer chemoprevention," *Critical Reviews in Food Science and Nutrition*, vol. 16, pp. 1–37, 2021.

[10] S. G. Patel, F. P. May, J. C. Anderson et al., "Updates on Age to Start and Stop Colorectal Cancer Screening: Recommendations From the U.S. Multi-Society Task Force on Colorectal Cancer," *Gastroenterology*, vol. 162, no. 1, pp. 285–299, 2022.

[11] I. Fernandez-Piñeiro, I. Badiola, and A. Sanchez, "Nanocarriers for microRNA delivery in cancer medicine," *Biotechnology Advances*, vol. 35, no. 3, pp. 350–360, 2017.

[12] G. P. Nagaraju, G. Srivani, B. Dariya et al., "Nanoparticles guided drug delivery and imaging in gastric cancer," *Seminars in Cancer Biology*, vol. 69, pp. 69–76, 2021.

[13] P. Aneja, M. Rahman, S. Beg, S. Aneja, V. Dhingra, and R. Chugh, "Cancer targeted magic bullets for effective treatment of cancer," *Recent Patents on Anti-Infective Drug Discovery*, vol. 9, no. 2, pp. 121–135, 2015.

[14] R. Li, B. Liu, and J. Gao, "The application of nanoparticles in diagnosis and theranostics of gastric cancer," *Cancer Letters*, vol. 386, pp. 123–130, 2017.

[15] T. Sun, Y. Shrike Zhang, P. Bo, D. C. Hyun, M. Yang, and Y. Xia, "Engineered nanoparticles for drug delivery in cancer therapy," *Nanomaterials and Neoplasms*, vol. 22, pp. 31–142, 2021.

[16] K. Resort and S. Hp, "Impact of nanotechnology on drug delivery," *ACS Nano*, vol. 3, no. 1, pp. 16–20, 2009.

[17] P. Tagde, P. Tagde, F. Islam et al., "The multifaceted role of curcumin in advanced nanocurcumin form in the treatment and management of chronic disorders," *Molecules*, vol. 26, no. 23, p. 7109, 2021.

RETRACTED

[18] D. Carradori, A. Gaudin, D. Brambilla, and K. Andrieux, "Application of nanomedicine to the CNS diseases," *International Review of Neurobiology*, vol. 130, pp. 73–113, 2016.

[19] R. Sharma, N. Garg, D. Verma et al., "Indian medicinal plants as drug leads in neurodegenerative disorders," in *Nutraceuticals Brain Health Beyond*, pp. 31–45, Academic Press, 2021.

[20] V. Sharma, H. Rai, D. N. S. Gautam, P. K. Prajapati, and R. Sharma, "Emerging evidence on Omicron (B.1.1.529) SARS-CoV-2 variant," *Journal of Medical Virology*, vol. 94, 2022.

[21] R. Sharma, K. Kuca, E. Nepovimova, A. Kabra, M. M. Rao, and P. K. Prajapati, "Traditional ayurvedic and herbal remedies for Alzheimer's disease: from bench to bedside," *Expert review of Neurotherapeutics*, vol. 19, no. 5, pp. 359–374, 2019.

[22] M. Rahman, F. Islam, M. Saidur Rahaman, N. A. Sultana, N. F. Fahim, and M. Ahmed, "Studies on the prevalence of HIV/AIDS in Bangladesh including other developing countries," *Advances in Traditional Medicine*, vol. 21, pp. 1–12, 2021.

[23] F. Islam, S. Bibi, A. F. Meem et al., "Natural bioactive molecules: an alternative approach to the treatment and control of COVID-19," *International Journal of Molecular Sciences*, vol. 22, no. 23, p. 12638, 2021.

[24] A. V. Kabanov and H. E. Gendelman, "Nanomedicine in the diagnosis and therapy of neurodegenerative disorders," *Progress in Polymer Science*, vol. 32, no. 8–9, pp. 1054–1082, 2007.

[25] A. Adak, G. Das, S. Barman et al., "Biodegradable neurocompatible peptide hydrogel promotes neurite outgrowth, shows significant neuroprotection, and delivers anti-Alzheimer drug," *ACS Applied Materials & Interfaces*, vol. 9, no. 6, pp. 5067–5076, 2017.

[26] W. Zhang, Y. Wang, X. Sun, W. Wang, and L. Chen, "Mesoporous titania based yolk-shell nanoparticles as multifunctional theranostic platforms for SERS imaging and chemo-photothermal treatment," *Nanoscale*, vol. 6, no. 23, pp. 14514–14522, 2014.

[27] W. Ran and X. Xue, "Theranostical application of nanomedicine for treating central nervous system disorders," *Science China. Life Sciences*, vol. 61, no. 4, pp. 392–399, 2018.

[28] J. Yoo, E. Lee, H. Y. Kim et al., "Electromagnetized gold nanoparticles mediate direct lineage reprogramming into induced dopamine neurons *in vivo* for Parkinson's disease therapy," *Nature Nanotechnology*, vol. 12, no. 10, pp. 1006–1014, 2017.

[29] X. Xue, L. R. Wang, Y. Sato et al., "Single-Walled carbon nanotubes alleviate autophagic/lysosomal defects in primary glia from a mouse model of Alzheimer's disease," *Nano Letters*, vol. 14, no. 9, pp. 5110–5117, 2014.

[30] H. Kouyoumdjian, D. C. Zhu, M. H. El-Dakdouki et al., "Glyconanoparticle aided detection of β-amyloid by magnetic resonance imaging and attenuation of β-amyloid induced cytotoxicity," *ACS Chemical Neuroscience*, vol. 4, no. 4, pp. 575–584, 2013.

[31] C. C. Yang, S. Y. Yang, J. J. Chieh et al., "Biofunctionalized magnetic nanoparticles for specifically detecting biomarkers of Alzheimer's disease in vitro," *ACS Chemical Neuroscience*, vol. 2, no. 9, pp. 500–505, 2011.

[32] M. M. Rahman, F. Islam, M. A. Anwar Parvez, G. M. Ashraf, M. F. Ullah, and M. Ahmed, "Citrus limon L.(lemon) seed extract shows neuro-modulatory activity in an in vivo thiopental-sodium sleep model by reducing the sleep onset and enhancing the sleep duration," *Journal of Integrative Neuroscience*, vol. 21, no. 1, pp. 042–049, 2022.

[33] N. Martinez-Gonzalez, A. Miguel, and Martin-Calvo, "Current opinion in clinical nutrition & metabolic care," vol. 19, no. 6, pp. 1-2, 2016.

[34] E. Cevenini, C. Caruso, G. Candore et al., "Age-related inflammation: the contribution of different organs, tissues and systems. How to face it for therapeutic approaches," *Current Pharmaceutical Design*, vol. 16, no. 6, pp. 609–618, 2010.

[35] G. C. Leonardi, G. Accardi, R. Monastero, F. Nicoletti, and M. Libra, "Ageing: from inflammation to cancer," *Immunity & Ageing*, vol. 15, no. 1, p. 1, 2018.

[36] R. Sharma and N. Martins, "Telomeres, DNA damage and ageing: potential leads from ayurvedic rasayana (anti-ageing) drugs," *Journal of Clinical Medicine*, vol. 9, no. 8, pp. 2544–2547, 2020.

[37] C. Caruso, G. Accardi, C. Virruso, and G. Candore, "Sex, gender and immunosenescence: a key to understand the different lifespan between men and women?," *Immunity & Ageing*, vol. 10, no. 1, 2013.

[38] D. Muñoz-Espín and M. Serrano, "Cellular senescence: from physiology to pathology," *Nature Reviews. Molecular Cell Biology*, vol. 15, no. 7, pp. 482–496, 2014.

[39] J. Campisi and F. D. A. di Fagagna, "Cellular senescence: when bad things happen to good cells," *Nature Reviews. Molecular Cell Biology*, vol. 8, no. 9, pp. 729–740, 2007.

[40] A. Krtolica, S. Parrinello, S. Lockett, P. Y. Desprez, and J. Campisi, "Senescent fibroblasts promote epithelial cell growth and tumorigenesis: A link between cancer and aging," *Proceedings of the National Academy of Sciences of the United States of America*, vol. 98, no. 21, pp. 12072–12077, 2001.

[41] F. Rodier, J. P. Coppé, C. K. Patil et al., "Persistent DNA damage signalling triggers senescence-associated inflammatory cytokine secretion," *Nature Cell Biology*, vol. 11, no. 8, pp. 973–979, 2009.

[42] T. Kuilman and D. S. Peeper, "Senescence-messaging secretome: SMS-ing cellular stress," *Nature Reviews. Cancer*, vol. 9, no. 2, pp. 81–94, 2009.

[43] A. Pribluda, E. Elyada, Z. Wiener et al., "A senescence-inflammatory switch from cancer-inhibitory to cancer-promoting mechanism," *Cancer Cell*, vol. 27, no. 6, pp. 877-878, 2015.

[44] F. Dall'Olio, V. Vanhooren, C. C. Chen, P. E. Slagboom, M. Wuhrer, and C. Franceschi, "N-Glycomic biomarkers of biological aging and longevity: a link with inflammaging," *Ageing Research Reviews*, vol. 12, no. 2, pp. 685–698, 2013.

[45] N. Feldman, A. Rotter-Maskowitz, and E. Okun, "DAMPs as mediators of sterile inflammation in aging-related pathologies," *Ageing Research Reviews*, vol. 24, Part A, pp. 29–39, 2015.

[46] C. Franceschi and J. Campisi, "Chronic inflammation (Inflammaging) and its potential contribution to age-associated diseases," *Journals of Gerontology Series A: Biomedical Sciences and Medical Sciences*, vol. 69, Supplement 1, pp. S4–S9, 2014.

[47] A. M. O'Hara and F. Shanahan, "The gut flora as a forgotten organ," *EMBO Reports*, vol. 7, no. 7, pp. 688–693, 2006.

[48] M. E. Icaza-Chávez, "Gut microbiota in health and disease," *Revista de Gastroenterología de México*, vol. 78, no. 4, pp. 240–248, 2013.

RETRACTED

[49] M. C. Noverr and G. B. Huffnagle, "Does the microbiota regulate immune responses outside the gut?," *Trends in Microbiology*, vol. 12, no. 12, pp. 562–568, 2004.

[50] D. A. Kashtanova, O. N. Tkacheva, I. D. Strazhesko et al., "Gut microbiota and aging," pp. 263–278, 2019.

[51] M. J. Claesson, I. B. Jeffery, S. Conde et al., "Gut microbiota composition correlates with diet and health in the elderly," *Nature*, vol. 600, no. 178, pp. 1–12, 2016.

[52] A. Ticinesi, C. Milani, F. Lauretani et al., "Gut microbiota composition is associated with polypharmacy in elderly hospitalized patients," *Scientific reports*, vol. 7, no. 1, p. 11102, 2017.

[53] L. B. Lovat, "Age related changes in gut physiology and nutritional status," *Gut*, vol. 38, no. 3, pp. 306–309, 1996.

[54] A. G. Renehan, M. Tyson, M. Egger, R. F. Heller, and M. Zwahlen, "Body-mass index and incidence of cancer: a systematic review and meta-analysis of prospective observational studies," *Lancet*, vol. 371, no. 9612, pp. 569–578, 2008.

[55] G. S. Hotamisligil, "Inflammation and metabolic disorders," *Nature*, vol. 444, no. 7121, pp. 860–867, 2006.

[56] R. Medzhitov, "Origin and physiological roles of inflammation," *Nature*, vol. 454, no. 7203, pp. 428–435, 2008.

[57] M. F. Gregor and G. S. Hotamisligil, "Inflammatory mechanisms in obesity," *Annual Review of Immunology*, vol. 29, no. 1, pp. 415–445, 2011.

[58] T. Fulop, J. McElhaney, G. Pawelec et al., "Frailty, inflammation and immunosenescence," *Frailty in Aging*, vol. 41, pp. 26–40, 2015.

[59] E. Montecino-Rodriguez, B. Berent-Maoz, and K. Dorshkind, "Causes, consequences, and reversal of immune system aging," *The Journal of Clinical Investigation*, vol. 123, no. 3, pp. 958–965, 2013.

[60] L. Ziegler-Heitbrock, P. Ancuta, S. Crowe et al., "Nomenclature of monocytes and dendritic cells in blood," *Blood*, vol. 116, no. 16, pp. e74–e80, 2010.

[61] B. Bottazzi, E. Riboli, and A. Mantovani, "Aging, inflammation and cancer," *Seminars in Immunology*, vol. 40, pp. 74–82, 2018.

[62] A. Mantovani, P. Allavena, A. Sica, and F. Balkwill, "Cancer-related inflammation," *Nature*, vol. 454, no. 7203, pp. 436–444, 2008.

[63] F. Balkwill, K. A. Charles, and A. Mantovani, "Smoldering and polarized inflammation in the initiation and promotion of malignant disease," *Cancer Cell*, vol. 7, no. 3, pp. 211–217, 2005.

[64] T. Gutschner and S. Diederichs, "The hallmarks of cancer: a long non-coding RNA point of view," *RNA Biology*, vol. 9, no. 6, pp. 703–719, 2012.

[65] A. Mantovani, "Inflaming metastasis," *Nature*, vol. 457, no. 7225, pp. 36-37, 2009.

[66] A. Mantovani, F. Marchesi, A. Malesci, L. Laghi, and P. Allavena, "Tumour-associated macrophages as treatment targets in oncology," *Nature Reviews. Clinical Oncology*, vol. 14, no. 7, pp. 399–416, 2017.

[67] "bcc Research. INTRODUCTION," https://www.bccresearch.com/market-research/nanotechnology/NAN029A.html#:~:text=Nanotechnology%20tools%20and%20instruments%20are.

[68] S. Abeer, "Future medicine: nanomedicine," *Journal International Medical Sciences Academy*, vol. 25, no. 3, pp. 187–192, 2012.

[69] S. M. Nimjee, C. P. Rusconi, and B. A. Sullenger, "Aptamers: an emerging class of therapeutics," *Annual Review of Medicine*, vol. 56, no. 1, pp. 555–583, 2005.

[70] D. H. Bunka and P. G. Stockley, "Aptamers come of age–at last," *Nature Reviews Microbiology*, vol. 4, no. 8, pp. 588–596, 2006.

[71] R. Stoltenburg, C. Reinemann, and B. Strehlitz, "SELEX–A (r)evolutionary method to generate high-affinity nucleic acid ligands," *Biomolecular Engineering*, vol. 24, no. 4, pp. 381–403, 2007.

[72] D. H. Bunka, O. Platonova, and P. G. Stockley, "Development of aptamer therapeutics," *Current Opinion in Pharmacology*, vol. 10, no. 5, pp. 557–562, 2010.

[73] T. R. Friberg, M. Tolentino, LEVEL Study Group et al., "Pegaptanib sodium as maintenance therapy in neovascular age-related macular degeneration: the LEVEL study," *The British Journal of Ophthalmology*, vol. 94, no. 12, pp. 1611–1617, 2010.

[74] D. H. Anderson, M. J. Radeke, N. B. Gallo et al., "The pivotal role of the complement system in aging and age-related macular degeneration: Hypothesis re-visited," *Progress in Retinal and Eye Research*, vol. 29, no. 2, pp. 95–112, 2010.

[75] Y.-H. Lao, K. K. L. Phua, and K. W. Leong, "Aptamer nanomedicine for cancer therapeutics: barriers and potential for translation," *ACS Nano*, vol. 9, no. 3, pp. 2235–2254, 2015.

[76] C. Cheng, Y. H. Chen, K. A. Lennox, M. A. Behlke, and B. L. Davidson, "*In vivo* SELEX for Identification of Brain-penetrating Aptamers," *Molecular Therapy-Nucleic Acids*, vol. 2, article e67, 2013.

[77] R. B. Shah and M. A. Khan, "Nanopharmaceuticals: challenges and regulatory perspective," in *Nanotechnology in Drug Delivery*, pp. 621–646, Springer, New York, NY, 2009.

[78] D. A. Slatter, C. L. Percy, K. Allen-Redpath et al., "Enzymatically oxidized phospholipids restore thrombin generation in coagulation factor deficiencies," *JCI Insight*, vol. 3, no. 6, 2018.

[79] H. Bergmann and H. Sinzinger, *Radioactive Isotopes in Clinical Medicine and Research*, Birkhäuser, 1995.

[80] Y. Namiki, T. Fuchigami, N. Tada et al., "Nanomedicine for cancer: lipid-based nanostructures for drug delivery and monitoring," *Accounts of Chemical Research*, vol. 44, no. 10, pp. 1080–1093, 2011.

[81] R. M. Ferreira, J. Pereira-Marques, I. Pinto-Ribeiro et al., "Gastric microbial community profiling reveals a dysbiotic cancer-associated microbiota," *Gut*, vol. 67, no. 2, pp. 226–236, 2018.

[82] D. Nejman, I. Livyatan, G. Fuks et al., "The human tumor microbiome is composed of tumor type–specific intracellular bacteria," *Science*, vol. 53, no. 9, pp. 1689–1699, 2019.

[83] T. O. Tollefsbol, "Dietary epigenetics in cancer and aging," *Cancer Treatment and Research*, vol. 159, pp. 257–267, 2014.

[84] N. Iida, A. Dzutsev, C. A. Stewart et al., "Commensal bacteria control cancer response to therapy by modulating the tumor microenvironment," *Science*, vol. 342, no. 6161, pp. 967–970, 2013.

[85] T. C. Yu, F. Guo, Y. Yu et al., "_Fusobacterium nucleatum_ Promotes Chemoresistance to Colorectal Cancer by Modulating Autophagy," *Cell*, vol. 170, no. 3, pp. 548–563.e16, 2017.

[86] C. Pleguezuelos-Manzano, J. Puschhof, A. Rosendahl Huber et al., "Mutational signature in colorectal cancer caused by

RETRACTED

genotoxic _pks_ $^{+}$ _E. coli_," *Nature*, vol. 580, no. 7802, pp. 269–273, 2020.

[87] M. R. Wilson, Y. Jiang, P. W. Villalta et al., "The human gut bacterial genotoxin colibactin alkylates DNA," *Science*, vol. 363, no. 6428, 2019.

[88] D. H. Dapito, A. Mencin, G. Y. Gwak et al., "Promotion of hepatocellular carcinoma by the intestinal microbiota and TLR4," *Cancer Cell*, vol. 21, no. 4, pp. 504–516, 2012.

[89] W. A. Al-Soud, U. Stenram, Å. Ljungh, K. G. Tranberg, H. O. Nilsson, and T. Wadström, "DNA of *Helicobacter* spp. and common gut bacteria in primary liver carcinoma," *Digestive and Liver Disease*, vol. 40, no. 2, pp. 126–131, 2008.

[90] J. M. Ridlon, S. C. Harris, S. Bhowmik, D. J. Kang, and P. B. Hylemon, "Consequences of bile salt biotransformations by intestinal bacteria," *Gut Microbes*, vol. 7, no. 1, pp. 22–39, 2016.

[91] X. Cui, L. Bao, X. Wang, and C. Chen, "The nano–intestine interaction: understanding the location-oriented effects of engineered nanomaterials in the intestine," *Small*, vol. 16, no. 21, p. 1907665, 2020.

[92] W. Song, K. Tiruthani, Y. Wang et al., "Trapping of lipopolysaccharide to promote immunotherapy against colorectal cancer and attenuate liver metastasis," *Advanced Materials*, vol. 30, no. 52, article 1805007, 2018.

[93] I. Javed, X. Cui, X. Wang et al., "Implications of the human gut-brain and gut-cancer axes for future nanomedicine," *ACS Nano*, vol. 14, no. 11, pp. 14391–14416, 2020.

[94] M. E. Davis, J. E. Zuckerman, C. H. J. Choi et al., "Evidence of RNAi in humans from systemically administered siRNA via targeted nanoparticles," *Nature*, vol. 464, no. 7291, pp. 1067–1070, 2010.

[95] P. Singh, U. Gupta, A. Asthana, and N. K. Jain, "Folate and folate-PEG-PAMAM dendrimers: synthesis, characterization, and targeted anticancer drug delivery potential in tumor bearing mice," *Bioconjugate Chemistry*, vol. 19, no. 11, pp. 2239–2252, 2008.

[96] D. C. Drummond, C. O. Noble, Z. Guo et al., "Development of a highly stable and targetable nanoliposomal formulation of topotecan," *Journal of Controlled Release*, vol. 141, no. 1, pp. 13–21, 2010.

[97] A. Schroeder, R. Honen, K. Turjeman, A. Gabizon, J. Kost, and Y. Barenholz, "Ultrasound triggered release of cisplatin from liposomes in murine tumors," *Journal of Controlled Release*, vol. 137, no. 1, pp. 63–68, 2009.

[98] M. A. Miller, S. Gadde, C. Pfirschke et al., "Predicting therapeutic nanomedicine efficacy using a companion magnetic resonance imaging nanoparticle," *Science Translational Medicine*, vol. 7, no. 314, article 314ra183, 2015.

[99] J. Kreuter, "Drug delivery to the central nervous system by polymeric nanoparticles: what do we know?," *Advanced Drug Delivery Reviews*, vol. 71, pp. 2–14, 2014.

[100] J. Hrkach, D. Von Hoff, M. M. Ali et al., "Preclinical development and clinical translation of a PSMA-targeted docetaxel nanoparticle with a differentiated pharmacological profile," *Science Translational Medicine*, vol. 4, no. 128, article 128ra39, 2012.

[101] S. Eliasof, D. Lazarus, C. G. Peters et al., "Correlating preclinical animal studies and human clinical trials of a multifunctional, polymeric nanoparticle," *Proceedings of the National Academy of Sciences of the United States of America*, vol. 110, no. 37, pp. 15127–15132, 2013.

[102] T. Cedervall, I. Lynch, S. Lindman et al., "Understanding the nanoparticle-protein corona using methods to quantify exchange rates and affinities of proteins for nanoparticles," *Proceedings of the National Academy of Sciences of the United States of America*, vol. 104, no. 7, pp. 2050–2055, 2007.

[103] A. E. Nel, L. Mädler, D. Velegol et al., "Understanding biophysicochemical interactions at the nano-bio interface," *Nature Materials*, vol. 8, no. 7, pp. 543–557, 2009.

[104] M. Mahmoudi, I. Lynch, M. R. Ejtehadi, M. P. Monopoli, F. B. Bombelli, and S. Laurent, "Protein−nanoparticle interactions: opportunities and challenges," *Chemical Reviews*, vol. 111, no. 9, pp. 5610–5637, 2011.

[105] M. P. Monopoli, C. Åberg, A. Salvati, and K. A. Dawson, "Biomolecular coronas provide the biological identity of nanosized materials," *Nature Nanotechnology*, vol. 7, no. 12, pp. 779–786, 2012.

[106] J. Shi, P. W. Kantoff, R. Wooster, and O. C. Farokhzad, "Cancer nanomedicine: progress, challenges and opportunities," *Nature Reviews. Cancer*, vol. 17, no. 1, pp. 20–37, 2017.

[107] J. S. Smolen, D. Aletaha, A. Barton et al., "Rheumatoid arthritis," *Nature Reviews Disease Primers*, vol. 4, no. 1, 2018.

[108] I. McInnes and G. Schett, "Cytokines in the pathogenesis of rheumatoid arthritis," *Nature Reviews. Immunology*, vol. 7, no. 6, pp. 429–442, 2007.

[109] M. Jeong and J. H. Park, "Nanomedicine for the treatment of rheumatoid arthritis," *Molecular Pharmaceutics*, vol. 18, no. 2, pp. 539–549, 2021.

[110] U. Müller-Ladner, C. Ospelt, S. Gay, O. Distler, and T. Pap, "Cells of the synovium in rheumatoid arthritis. Synovial fibroblasts," *Arthritis Research & Therapy*, vol. 9, no. 6, p. 223, 2007.

[111] S. Konisti, S. Kiriakidis, and E. M. Paleolog, "Angiogenesis in rheumatoid arthritis," in *Angiogenesis and Vascularisation*, pp. 339–365, Springer, Vienna, 2013.

[112] L. K. Prasad, H. O'Mary, and Z. Cui, "Nanomedicine delivers promising treatments for rheumatoid arthritis," *Nanomedicine*, vol. 10, no. 13, pp. 2063–2074, 2015.

[113] H. Maeda, "The enhanced permeability and retention (EPR) effect in tumor vasculature: The key role of tumor-selective macromolecular drug targeting," *Advances in Enzyme Regulation*, vol. 41, no. 1, pp. 189–207, 2001.

[114] M. Dellian, F. Yuan, V. S. Trubetskoy, V. P. Torchilin, and R. K. Jain, "Vascular permeability in a human tumour xenograft: Molecular charge dependence," *British Journal of Cancer*, vol. 82, no. 9, pp. 1513–1518, 2000.

[115] Y. Mengxiao and J. Zheng, "Clearance pathways and tumor targeting of imaging nanoparticles," *ACS Nano*, vol. 28, pp. 1181–1225, 2020.

[116] W. H. De Jong, W. I. Hagens, P. Krystek, M. C. Burger, A. J. Sips, and R. E. Geertsma, "Particle size-dependent organ distribution of gold nanoparticles after intravenous administration," *Biomaterials*, vol. 29, no. 12, pp. 1912–1919, 2008.

[117] H. Soo Choi, W. Liu, P. Misra et al., "Renal clearance of quantum dots," *Nature Biotechnology*, vol. 25, no. 10, pp. 1165–1170, 2007.

[118] S. Zhang, L. Wu, J. Cao et al., "Effect of magnetic nanoparticles size on rheumatoid arthritis targeting and photothermal therapy," *Colloids Surfaces B Biointerfaces*, vol. 170, pp. 224–232, 2018.

[119] D. Van Haute and J. M. Berlin, "Challenges in realizing selectivity for nanoparticle biodistribution and clearance: lessons

RETRACTED

from gold nanoparticles," *Therapeutic Delivery*, vol. 8, no. 9, pp. 763–774, 2017.

[120] W. Xiao, J. Lin, M. Li et al., "Prolonged in vivo circulation time by zwitterionic modification of magnetite nanoparticles for blood pool contrast agents," *Contrast Media & Molecular Imaging*, vol. 7, no. 3, pp. 320–327, 2012.

[121] J. Zhao, Z. Qin, J. Wu, L. Li, Q. Jin, and J. Ji, "Zwitterionic stealth peptide-protected gold nanoparticles enable long circulation without the accelerated blood clearance phenomenon," *Biomaterials Science*, vol. 6, no. 1, pp. 200–206, 2018.

[122] J. S. Suk, Q. Xu, N. Kim, J. Hanes, and L. M. Ensign, "PEGylation as a strategy for improving nanoparticle-based drug and gene delivery," *Advanced Drug Delivery Reviews*, vol. 99, no. Part A, pp. 28–51, 2016.

[123] P. Srinath, M. G. Chary, S. P. Vyas, and P. V. Diwan, "Long-circulating liposomes of indomethacin in arthritic rats – a biodisposition study," *Pharmaceutica Acta Helvetiae*, vol. 74, no. 4, pp. 399–404, 2000.

[124] W. Hofkens, L. C. Grevers, B. Walgreen et al., "Intravenously delivered glucocorticoid liposomes inhibit osteoclast activity and bone erosion in murine antigen-induced arthritis," *Journal of Controlled Release*, vol. 152, no. 3, pp. 363–369, 2011.

[125] W. Hofkens, G. Storm, W. B. Van Den Berg, and P. L. Van Lent, "Liposomal targeting of glucocorticoids to the inflamed synovium inhibits cartilage matrix destruction during murine antigen-induced arthritis," *International Journal of Pharmaceutics*, vol. 416, no. 2, pp. 486–492, 2011.

[126] W. Hofkens, J. M. van den Hoven, G. J. Pesman et al., "Safety of glucocorticoids can be improved by lower yet still effective dosages of liposomal steroid formulations in murine antigen-induced arthritis: comparison of prednisolone with budesonide," *International Journal of Pharmaceutics*, vol. 416, no. 2, pp. 493–498, 2011.

[127] Q. Wang, H. Jiang, Y. Li et al., "Targeting NF-kB signaling with polymeric hybrid micelles that co-deliver siRNA and dexamethasone for arthritis therapy," *Biomaterials*, vol. 122, pp. 10–22, 2017.

[128] Q. Wang, J. Jiang, W. Chen, H. Jiang, Z. Zhang, and X. Sun, "Targeted delivery of low-dose dexamethasone using PCL-PEG micelles for effective treatment of rheumatoid arthritis," *Journal of Controlled Release*, vol. 230, pp. 64–72, 2016.

[129] T. Ishihara, T. Kubota, T. Choi, and M. Higaki, "Treatment of experimental arthritis with stealth-type polymeric nanoparticles encapsulating betamethasone phosphate," *The Journal of Pharmacology and Experimental Therapeutics*, vol. 329, no. 2, pp. 412–417, 2009.

[130] A. Williams, R. Goodfellow, N. Topley, N. Amos, and B. Williams, "The suppression of rat collagen-induced arthritis and inhibition of macrophage derived mediator release by liposomal methotrexate formulations," *Inflammation Research*, vol. 49, no. 4, pp. 155–161, 2000.

[131] P. Prabhu, R. Shetty, M. Koland et al., "Investigation of nano lipid vesicles of methotrexate for anti-rheumatoid activity," *International Journal of Nanomedicine*, vol. 7, pp. 177–186, 2012.

[132] H. J. Kim, S. M. Lee, K. H. Park, C. H. Mun, Y. B. Park, and K. H. Yoo, "Drug-loaded gold/iron/gold plasmonic nanoparticles for magnetic targeted chemo-photothermal treatment of rheumatoid arthritis," *Biomaterials*, vol. 61, pp. 95–102, 2015.

[133] S. M. Lee, H. J. Kim, Y. J. Ha et al., "Targeted chemo-photothermal treatments of rheumatoid arthritis using gold half-shell multifunctional nanoparticles," *ACS Nano*, vol. 7, no. 1, pp. 50–57, 2013.

[134] U. Rauchhaus, F. W. Schwaiger, and S. Panzner, "Separating therapeutic efficacy from glucocorticoid side-effects in rodent arthritis using novel, liposomal delivery of dexamethasone phosphate: long-term suppression of arthritis facilitates interval treatment," *Arthritis Research & Therapy*, vol. 11, no. 6, p. R190, 2009.

[135] R. Anderson, A. Franch, M. Castell et al., "Liposomal encapsulation enhances and prolongs the anti-inflammatory effects of water-soluble dexamethasone phosphate in experimental adjuvant arthritis," *Arthritis Research & Therapy*, vol. 12, no. 4, 2010.

[136] M. Liu, Y. Huang, L. Hu et al., "Selective delivery of interleukine-1 receptor antagonist to inflamed joint by albumin fusion," *BMC Biotechnology*, vol. 12, no. 1, 2012.

[137] C. Fiehn, U. Müller-Ladner, S. Gay et al., "Albumin-coupled methotrexate (MTX-HSA) is a new anti-arthritic drug which acts synergistically to MTX," *Rheumatology*, vol. 43, no. 9, pp. 1097–1105, 2004.

[138] C. Fiehn, E. Neumann, A. Wunder, S. Krienke, S. Gay, and U. Mueller-Ladner, "Methotrexate (MTX) and albumin coupled with MTX (MTX-HSA) suppress synovial fibroblast invasion and cartilage degradation in vivo," *Annals of the Rheumatic Diseases*, vol. 63, no. 7, pp. 884–886, 2004.

[139] K. Yudoh, R. Karasawa, K. Masuko et al., "I-18 Nanomedicine and osteoarthritis:what can we expect for the future?," *Osteoarthritis and Cartilage*, vol. 18, p. S7, 2010.

[140] L. Götz and J. Ittner, "Amyloid-β and tau – a toxic _pas de deux_ in Alzheimer's disease," *Nature Reviews. Neuroscience*, vol. 12, no. 2, pp. 67–72, 2011.

[141] M. Rahman, S. Majumder, F. Akter, F. Islam, M. Shahriar, and J. Alam, "Pre-clinical investigation of analgesic, antidiarrheal and CNS depressant effect of Pterocarpus indicus in Swiss albino mice," *Jordan Journal of Pharmaceutical Sciences*, vol. 14, no. 1, 2021.

[142] B. Formicola, A. Cox, R. Dal Magro, M. Masserini, and F. Re, "Nanomedicine for the treatment of Alzheimer's disease," *Journal of Biomedical Nanotechnology*, vol. 15, no. 10, pp. 1997–2024, 2019.

[143] A. Binda, C. Murano, and I. Rivolta, "Innovative Therapies and Nanomedicine Applications for the Treatment of Alzheimer's Disease: A State-of-the-Art (2017–2020)," *International Journal of Nanomedicine*, vol. Volume 15, pp. 6113–6135, 2020.

[144] S. G. Antimisiaris, P. Kallinteri, and D. G. Fatouros, "Liposomes and drug delivery," in *Pharmaceutical Manufacturing Handbook Production and Processes*, pp. 443–507, John Wiley & Sons, 2008.

[145] R. Z. Xiao, Z. W. Zeng, G. L. Zhou, J. J. Wang, F. Z. Li, and A. M. Wang, "Recent advances in PEG-PLA block copolymer nanoparticles," *International Journal of Nanomedicine*, vol. 5, no. 1, pp. 1057–1065, 2010.

[146] K. R. Chaudhuri, M. A. Qamar, T. Rajah et al., "Non-oral dopaminergic therapies for Parkinson's disease: current treatments and the future," *npj Parkinson's Disease*, vol. 2, no. 1, 2016.

[147] S. Kumar, S. Dang, K. Nigam, J. Ali, and S. Baboota, "Selegiline nanoformulation in attenuation of oxidative stress and

RETRACTED

upregulation of dopamine in the brain for the treatment of Parkinson's disease," *Rejuvenation Research*, vol. 21, no. 5, pp. 464–476, 2018.

[148] S. Setya, T. Madaan, M. Tariq, B. K. Razdan, and S. Talegaonkar, "Appraisal of transdermal water-in-oil nanoemulgel of selegiline HCl for the effective management of Parkinson's disease: pharmacodynamic, pharmacokinetic, and biochemical investigations," *AAPS PharmSciTech*, vol. 19, no. 2, pp. 573–589, 2018.

[149] L. Nayak and C. Henchcliffe, "Rasagiline in treatment of Parkinson's disease," *Neuropsychiatric Disease and Treatment*, vol. 4, no. 1, pp. 11–20, 2008.

[150] M. J. Haney, Y. Zhao, S. Li et al., "Cell-mediated transfer of catalase nanoparticles from macrophages to brain endothelial, glial and neuronal cells," *Nanomedicine*, vol. 6, no. 7, pp. 1215–1230, 2011.

[151] N. B. Bolshette, K. K. Thakur, A. P. Bidkar, C. Trandafir, P. Kumar, and R. Gogoi, "Protein folding and misfolding in the neurodegenerative disorders: a review," *Revue Neurologique (Paris)*, vol. 170, no. 3, pp. 151–161, 2014.

[152] O. Veiseh, J. W. Gunn, and M. Zhang, "Design and fabrication of magnetic nanoparticles for targeted drug delivery and imaging," *Advanced Drug Delivery Reviews*, vol. 62, no. 3, pp. 284–304, 2010.

[153] R. Qiao, Q. Jia, S. Hüwel et al., "Receptor-mediated delivery of magnetic nanoparticles across the blood-brain barrier," *ACS Nano*, vol. 6, no. 4, pp. 3304–3310, 2012.

[154] G. Gao, R. Chen, M. He, J. Li, L. Wang, and T. Sun, "Gold nanoclusters for Parkinson's disease treatment," *Biomaterials*, vol. 194, pp. 36–46, 2019.

[155] M. M. Rahman, M. R. Islam, M. T. Islam et al., "Stem cell transplantation therapy and neurological disorders: current status and future perspectives," *Biology*, vol. 11, no. 1, p. 147, 2022.

[156] M. M. Rahman, K. S. Ferdous, and M. Ahmed, "Emerging promise of nanoparticle-based treatment for Parkinson's disease," *Biointerface Research in Applied Chemistry*, vol. 10, pp. 7135–7151, 2020.

[157] M. M. Rahman, K. S. Ferdous, M. Ahmed et al., "Hutchinson-Gilford progeria syndrome: an overview of the molecular mechanism, pathophysiology and therapeutic approach," *Current Gene Therapy*, vol. 21, no. 3, pp. 216–229, 2021.

[158] M. M. Rahman, M. S. Rahaman, M. R. Islam et al., "Multifunctional therapeutic potential of phytocomplexes and natural extracts for antimicrobial properties," *Antibiotics*, vol. 10, p. 1076, 2021.

[159] H. Chopra, S. Bibi, F. Islam et al., "Emerging Trends in the Delivery of Resveratrol by Nanostructures: Applications of Nanotechnology in Life Sciences," *Journal of Nanomaterials*, vol. 4, p. 13, 2022.

[160] M. M. Rahman, M. S. Rahaman, M. R. Islam et al., "Role of phenolic compounds in human disease: current knowledge and future prospects," *Molecules*, vol. 27, no. 1, p. 233, 2021.

[161] A. Rauf, T. Abu-Izneid, A. A. Khalil et al., "Berberine as a potential anticancer agent: a comprehensive review," *Molecules*, vol. 26, no. 23, p. 7368, 2021.

[162] T. Bhattacharya, G. A. B. E. Soares, H. Chopra et al., "Applications of phyto-nanotechnology for the treatment of neurodegenerative disorders," *Materials*, vol. 15, no. 3, p. 804, 2022.

[163] S. Naz, J. Beach, B. Heckert et al., "Cerium oxide nanoparticles: a 'radical' approach to neurodegenerative disease treatment," *Nanomedicine*, vol. 12, no. 5, pp. 545–553, 2017.

[164] C. E. Dillon, M. Billings, K. S. Hockey, L. DeLaGarza, and B. A. Rzigalinski, "Cerium oxide nanoparticles protect against MPTP-induced dopaminergic neurodegeneration in a mouse model for Parkinson's disease," *Nanotechnology*, vol. 3, pp. 451–454, 2011.

[165] D. A. Gonzalez-Carter, B. F. Leo, P. Ruenraroengsak et al., "Silver nanoparticles reduce brain inflammation and related neurotoxicity through induction of H 2 S-synthesizing enzymes," *Scientific Reports*, vol. 7, 2017.

[166] K. A. Youssif, E. G. Haggag, A. M. Elshamy et al., "Anti-Alzheimer potential, metabolomic profiling and molecular docking of green synthesized silver nanoparticles of Lampranthus coccineus and Malephora lutea aqueous extracts," *PLoS One*, vol. 14, no. 11, 2019.

[167] K. Hou, J. Zhao, H. Wang et al., "Chiral gold nanoparticles enantioselectively rescue memory deficits in a mouse model of Alzheimer's disease," *Nature Communications*, vol. 11, no. 1, 2020.

[168] K. Hu, X. Chen, W. Chen et al., "Neuroprotective effect of gold nanoparticles composites in Parkinson's disease model," *Nanomedicine Nanotechnology, Biologie et Médecine*, vol. 14, no. 4, pp. 1123–1136, 2018.

[169] X. Huo, Y. Zhang, X. Jin, Y. Li, and L. Zhang, "A novel synthesis of selenium nanoparticles encapsulated PLGA nanospheres with curcumin molecules for the inhibition of amyloid β aggregation in Alzheimer's disease," *Journal of Photochemistry and Photobiology B: Biology*, vol. 190, pp. 98–102, 2019.

[170] G. P. Bates, R. Dorsey, J. F. Gusella et al., "Huntington disease," *Nature Reviews Disease Primers*, vol. 1, pp. 1–21, 2015.

[171] C. Ross, E. Aylward, E. Wild et al., "Huntington disease: natural history, biomarkers and prospects for therapeutics," *Nature Reviews. Neurology*, vol. 10, no. 4, pp. 204–216, 2014.

[172] E. J. Wild and S. J. Tabrizi, "Therapies targeting DNA and RNA in Huntington's disease," *Lancet Neurology*, vol. 16, no. 10, pp. 837–847, 2017.

[173] P. McColgan and S. J. Tabrizi, "Huntington's disease: a clinical review," *European Journal of Neurology*, vol. 25, no. 1, pp. 24–34, 2018.

[174] R. Sandhir, A. Yadav, A. Mehrotra, A. Sunkaria, A. Singh, and S. Sharma, "Curcumin nanoparticles attenuate neurochemical and neurobehavioral deficits in experimental model of Huntington's disease," *Neuromolecular Medicine*, vol. 16, no. 1, pp. 106–118, 2014.

[175] R. Bhatt, D. Singh, A. Prakash, and N. Mishra, "Development, characterization and nasal delivery of rosmarinic acid-loaded solid lipid nanoparticles for the effective management of Huntingtons disease," *Drug Delivery*, vol. 22, no. 7, pp. 931–939, 2015.

[176] W. Cong, R. Bai, Y. F. Li, L. Wang, and C. Chen, "Selenium nanoparticles as an efficient nanomedicine for the therapy of Huntington's disease," *ACS Applied Materials & Interfaces*, vol. 11, no. 38, pp. 34725–34735, 2019.

[177] R. M. Ahmed, E. Mioshi, J. Caga et al., "Body mass index delineates ALS from FTD: implications for metabolic health," *Journal of Neurology*, vol. 261, no. 9, pp. 1774–1780, 2014.

[178] S. M. Haake, J. D. Weyandt, and W. Kimryn Rathmell, "Insights into the genetic basis of the renal cell carcinomas

RETRACTED

from the Cancer Genome Atlas," *Molecular Cancer Research*, vol. 14, no. 7, pp. 589–598, 2016.

[179] G. Siciliano, C. Carlesi, L. Pasquali et al., "Clinical trials for neuroprotection in ALS," *CNS & Neurological Disorders-Drug Targets (Formerly Current Drug Targets-CNS & Neurological Disorders)*, vol. 9, no. 3, pp. 305–313, 2012.

[180] M. L. Bondì, E. F. Craparo, G. Giammona, and F. Drago, "Brain-targeted solid lipid nanoparticles containing riluzole: preparation, characterization and biodistribution," *Nanomedicine*, vol. 5, no. 1, pp. 25–32, 2010.

[181] D. Sone, I. Beheshti, N. Maikusa et al., "Neuroimaging-based brain-age prediction in diverse forms of epilepsy: a signature of psychosis and beyond," *Molecular Psychiatry*, vol. 26, no. 3, pp. 825–834, 2021.

[182] P. Perucca, "Genetics of focal epilepsies: What do we know and where are we heading?," *Epilepsy Currents*, vol. 18, no. 6, pp. 356–362, 2018.

[183] V. Villanueva, A. Gutiérrez, M. García et al., "ILAE official report: a practical clinical definition of epilepsy," *Epilepsia*, vol. 55, no. 4, pp. 475–482, 2014.

[184] D. Boison, "Adenosine kinase, epilepsy and stroke: mechanisms and therapies," *Trends in Pharmacological Sciences*, vol. 27, no. 12, pp. 652–658, 2006.

[185] E. B. Gonçalves, T. A. M. de Oliveira Cardoso, C. L. Yasuda, and F. Cendes, "Depressive disorders in patients with pharmaco-resistant mesial temporal lobe epilepsy," *The Journal of International Medical Research*, vol. 46, no. 2, pp. 752–760, 2018.

[186] M. H. Nogueira, C. L. Yasuda, A. C. Coan, A. M. Kanner, and F. Cendes, "Concurrent mood and anxiety disorders are associated with pharmacoresistant seizures in patients with MTLE," *Epilepsia*, vol. 58, no. 7, pp. 1268–1276, 2017.

[187] R. H. Thomas and S. F. Berkovic, "The hidden genetics of epilepsy - a clinically important new paradigm," *Nature Reviews. Neurology*, vol. 10, no. 5, pp. 283–292, 2014.

[188] A. Vezzani, S. Balosso, and T. Ravizza, "Neuroinflammatory pathways as treatment targets and biomarkers in epilepsy," *Nature Reviews. Neurology*, vol. 15, no. 8, pp. 459–472, 2019.

[189] W. Löscher, H. Klitgaard, R. E. Twyman, and D. Schmidt, "New avenues for anti-epileptic drug discovery and development," *Nature Reviews. Drug Discovery*, vol. 12, no. 10, pp. 757–776, 2013.

[190] M. F. Bennewitz and W. M. Saltzman, "Nanotechnology for delivery of drugs to the brain for epilepsy," *Neurotherapeutics*, vol. 6, no. 2, pp. 323–336, 2009.

[191] T. Musumeci, A. Bonaccorso, and G. Puglisi, "Epilepsy disease and nose-to-brain delivery of polymeric nanoparticles: an overview," *Pharmaceutics*, vol. 11, no. 3, 2019.

[192] A. R. de La Torre, G. Luna-Bárcenas, S. Orozco-Suárez et al., "Pharmacoresistant epilepsy and nanotechnology," *Frontiers in Bioscience-Elite*, vol. 6E, no. 2, pp. 329–340, 2014.

[193] M. C. Bonferoni, S. Rossi, G. Sandri et al., "Nanoemulsions for 'nose-to-brain' drug delivery," *Pharmaceutics*, vol. 11, no. 2, p. 84, 2019.

[194] M. J. Kubek, D. Liang, K. E. Byrd, and A. J. Domb, "Prolonged seizure suppression by a single implantable polymeric-TRH microdisk preparation," *Brain Research*, vol. 809, no. 2, pp. 189–197, 1998.

[195] M. C. Veronesi, Y. Aldouby, A. J. Domb, and M. J. Kubek, "Thyrotropin-releasing hormone d,l polylactide nanoparticles (TRH-NPs) protect against glutamate toxicity in vitro and kindling development in vivo," *Brain Research*, vol. 1303, pp. 151–160, 2009.

[196] M. Yusuf, R. A. Khan, M. Khan, and B. Ahmed, "Plausible antioxidant biomechanics and anticonvulsant pharmacological activity of brain-targeted β-carotene nanoparticles," *International Journal of Nanomedicine*, vol. 7, pp. 4311–4322, 2012.

[197] T. Musumeci, M. F. Serapide, R. Pellitteri et al., "Oxcarbazepine free or loaded PLGA nanoparticles as effective intranasal approach to control epileptic seizures in rodents," *European Journal of Pharmaceutics and Biopharmaceutics*, vol. 133, pp. 309–320, 2018.

[198] P. Shapshak, F. Chiappelli, D. Commins et al., "Molecular epigenetics, chromatin, and NeuroAIDS/HIV: translational implications," *Bioinformation*, vol. 3, no. 1, pp. 53–57, 2008.

[199] M. Mintz, "Clinical comparison of adult and pediatric NeuroAIDS," *Advances in Neuroimmunology*, vol. 4, no. 3, pp. 207–221, 1994.

[200] F. E. Bloom and D. M. Rausch, "HIV in the brain: pathology and neurobehavioral consequences," *Journal of Neurovirology*, vol. 3, no. 2, pp. 102–109, 1997.

[201] W. Banks, N. Ercal, and T. Otamis Price, "The blood-brain barrier in NeuroAIDS," *Current HIV Research*, vol. 4, no. 3, pp. 259–266, 2006.

[202] E. S. Roberts, M. A. Zandonatti, D. D. Watry et al., "Induction of pathogenic sets of genes in macrophages and neurons in neuroAIDS," *The American Journal of Pathology*, vol. 162, no. 6, pp. 2041–2057, 2003.

[203] F. Doualla-Bell, D. Turner, H. Loemba, M. Petrella, B. Brenner, and M. A. Wainberg, "HIV drug resistance and optimization of antiviral treatment in resource-poor countries," *Médecine Sciences*, vol. 20, no. 10, pp. 882–886, 2004.

[204] S. Soni, R. K. Ruhela, and B. Medhi, "Nanomedicine in central nervous system (CNS) disorders: a present and future prospective," *Advanced Pharmaceutical Bulletin*, vol. 6, no. 3, pp. 319–335, 2016.

[205] V. Sagar, S. Pilakka-Kanthikeel, R. Pottathil, S. K. Saxena, and M. Nair, "Towards nanomedicines for neuroAIDS," *Reviews in Medical Virology*, vol. 24, no. 2, pp. 103–124, 2014.

[206] R. F. Omar, N. Dusserre, A. Desormeaux et al., "Liposomal encapsulation of foscarnet protects against hypocalcemia induced by free foscarnet," *Antimicrobial Agents and Chemotherapy*, vol. 39, no. 9, pp. 1973–1978, 1995.

[207] Y. C. Kuo and F. L. Su, "Transport of stavudine, delavirdine, and saquinavir across the blood-brain barrier by polybutylcyanoacrylate, methylmethacrylate-sulfopropylmethacrylate, and solid lipid nanoparticles," *International Journal of Pharmaceutics*, vol. 340, no. 1–2, pp. 143–152, 2007.

[208] S. Niu, L. K. Zhang, L. Zhang et al., "Inhibition by multifunctional magnetic nanoparticles loaded with alpha-synuclein RNAi plasmid in a Parkinson's disease model," *Theranostics*, vol. 7, no. 2, pp. 344–356, 2017.

[209] L. R. Nih, E. Sideris, S. T. Carmichael, and T. Segura, "Injection of microporous annealing particle (MAP) hydrogels in the stroke cavity reduces gliosis and inflammation and promotes NPC migration to the lesion," *Advanced Materials*, vol. 29, no. 32, 2017.

[210] L. R. Nih, S. Gojgini, S. T. Carmichael, and T. Segura, "Dual-function injectable angiogenic biomaterial for the repair of brain tissue following stroke," *Nature Materials*, vol. 17, no. 7, pp. 642–651, 2018.

RETRACTED

[211] M. Machado-Pereira, T. Santos, L. Ferreira, L. Bernardino, and R. Ferreira, "Intravenous administration of retinoic acid-loaded polymeric nanoparticles prevents ischemic injury in the immature brain," *Neuroscience Letters*, vol. 673, pp. 116–121, 2018.

[212] Y. Gao, X. Chen, and H. Liu, "A facile approach for synthesis of nano-CeO2 particles loaded co-polymer matrix and their colossal role for blood-brain barrier permeability in cerebral ischemia," *Journal of Photochemistry and Photobiology B: Biology*, vol. 187, pp. 184–189, 2018.

[213] T. Zhang, C. Y. Li, J. J. Jia et al., "Combination therapy with LXW7 and ceria nanoparticles protects against acute cerebral ischemia/reperfusion injury in rats," *Current Medical Science*, vol. 38, no. 1, pp. 144–152, 2018.

[214] D. S. Manickam, A. M. Brynskikh, J. L. Kopanic et al., "Well-defined cross-linked antioxidant nanozymes for treatment of ischemic brain injury," *Journal of Controlled Release*, vol. 162, no. 3, pp. 636–645, 2012.

[215] G. Zabow, S. J. Dodd, and A. P. Koretsky, "Shape-changing magnetic assemblies as high-sensitivity NMR-readable nanoprobes," *Nature*, vol. 520, no. 7545, pp. 73–77, 2015.

[216] M. Shakibaei, C. Buhrmann, P. Kraehe, P. Shayan, C. Lueders, and A. Goel, "Curcumin chemosensitizes 5-fluorouracil resistant MMR-deficient human colon cancer cells in high density cultures," *PLoS One*, vol. 9, no. 1, article e85397, 2014.

[217] ClinicalTrials gov, "Curcumin in preventing colorectal cancer in patients undergoing colorectal endoscopy or colorectal surgery," September 2021, https://clinicaltrials.gov/ct2/show/NCT00973869.

[218] ClinicalTrials gov, "Nanocurcumin for prostate cancer patients undergoing radiotherapy (RT)," September 2021, https://clinicaltrials.gov/ct2/show/NCT02724618.

[219] I. K. Grewal, S. Singh, S. Arora, and N. Sharma, "Polymeric nanoparticles for breast cancer therapy: Aa comprehensive review," *Biointerface Research in Applied Chemistry*, vol. 11, no. 4, pp. 11151–11171, 2021.

[220] ClinicalTrials gov, "31P-MRS Imaging to Assess the Effects of CNM-Au8 on Impaired Neuronal Redox State in Multiple Sclerosis," September 202, https://clinicaltrials.gov/ct2/show/NCT03993171.

[221] S. Gingele and M. Stangel, "Emerging myelin repair agents in preclinical and early clinical development for the treatment of multiple sclerosis," *Expert Opinion on Investigational Drugs*, vol. 29, no. 6, pp. 583–594, 2020.

[222] I. Grewal, S. Singh, S. Arora, and N. Sharma, "Polymeric nanoparticles for breast cancer therapy: a comprehensive review," *Biointerface Research in Applied Chemistry*, vol. 11, pp. 11151–11171, 2021.

[223] K. Doello, R. Ortiz, P. J. Alvarez, C. Melguizo, L. Cabeza, and J. Prados, "Latest in vitro and in vivo assay, clinical trials and patents in cancer treatment using curcumin: a literature review," *Nutrition and Cancer*, vol. 70, no. 4, pp. 569–578, 2018.

[224] K. Pathak, S. K. Mishra, A. Porwal, and S. Bahadur, "Nano-carriers for Alzheimer's disease: research and patent update," *Journal of Applied Pharmaceutical Science*, vol. 11, no. 3, pp. 1–21, 2021.

RETRACTED