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Review

Recent Advancements, Challenges, and Future Prospects in Usage of Nanoformulation as Theranostics in Inflammatory Diseases

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Abstract: As of today, chronic inflammatory diseases are a progressive cause of death worldwide, accounting for more than 50% of all fatalities. These inflammatory conditions are a major concern, ranging from heart disease to cancer, diabetes, to even neurodegenerative conditions. Conventional diagnosis and treatment for these problems are often challenging and limited due to complex pathophysiology. To improve upon current treatment and diagnostic strategies, theranostic nanomaterials have been developed. Theranostics is an amalgamation of diagnostic biomarkers and therapeutic medicines that have a shared target in damaged cells or tissues. Different theranostic nanoparticles generate enhanced imaging results for facilities such as MRI, PET scan, and CT scans depending on the site of inflammation in different organs. Furthermore, they can be treated with radiopharmaceuticals and/or medicine in nanoparticles. Following a brief discussion of conventional inflammatory diagnosis and therapeutic strategies, this review will cover the recent progress made in theranostic nanomaterials and nanomedicine tactics for managing inflammatory disorders, covering the preclinical and clinical stages of these advances from the past five years. Furthermore, present challenges with theranostic nanoparticles for inflammatory detection and treatment are discussed, as well as future research possibilities.

Keywords: inflammation; theranostics; MRI; PET; CT

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1. Introduction

Inflammation is a self-protecting system that is crucial for preventing negative stimuli and beginning in initiating the healing process [1]. These stimuli can be physical, chemical, biological, or environmental. There are various factors associated with these stimuli that affect the biological response, including trauma, heat, cold, radiation, toxins, acidic substances, irritants, infections, pollutants, allergens, and other environmental agents. Inflammatory response against these associated factors is typically self-healing; however, under uncontrolled conditions, it gives unwanted detriments to organs/the body. The inflammatory condition may be characterized by the duration of biological responses, i.e., acute or chronic. In acute inflammation, conditions are characterized by short-term and rapid changes in tissue response and microcirculation, i.e., leukocyte migration and interstitial leukocyte infiltration indicate acute inflammation. This condition is typically marked by red skin (erythema), heat effects (hyperemia), swelling of the area (exudation), painfulness (*via* nerves and chemical mediators), and loss of function (pain) [2]. However, the inflammatory feedback becomes sustained longer, characterized by a sustained release of cytokines, and can lead to tissue damage, bringing considerable harm to the tissue site/specific organ [3]. In fact, chronic inflammatory diseases, which include autoimmune and neurodegenerative conditions, coronary disease, stroke, tumor, diabetes, kidney disorder, and nonalcoholic fatty liver disease, have been named the world's leading cause of death, responsible for more than half of all fatalities [4].

Evidence has suggested that the emerging risk of instigating inflammation can be tracked down to earlier development, and its consequences, which are now known to last a lifetime, influencing adult health and the risk of death [5–7]. However, the source of inflammation is frequently unknown and, even if identified, becomes easy to eliminate or suppress. As a result, there is increasing interest in diagnosing and therapeutically improving inflammatory action to block and limit disease progression [8]. Because the inflammatory response is essential in the host homeostasis mechanism, the issues of overabundance, host remuneration, and the need for basic immune functionality often compromise the benefit–risk balance of anti-inflammatory drugs [9]. To understand the disease mechanism, theranostic medicine combines diagnostic and treatment to provide optimal illness management. Furthermore, the combination of nanomedicine has the potential to transform healthcare by delivering "the right diagnosis, the right therapy, at the right dose, and at the right time [10,11]." We present here the creation of a technology that accomplishes this targeted goal in order to face the problems of suppressing inflammatory disorders with a strategy that can be applied for specialized personalized therapy.

Nanotechnology is a branch of science dealing with influencing atoms and molecules in order to create materials in the nanometer (nm) scale, preferably less than 100 nm [12]. It comprises the formulation and execution of physical, chemical, and biological systems where properties change as the parameter size changes [13]. Nanomedicine is the most important area of nanotechnology today, with nanoparticles being used to detect, treat, diagnose, monitor, and control biological activity. Nanomedicine fundamentally deals with the delivery of therapeutic and diagnostic substances, as well as their effectiveness in treating and curing diseases [14]. Nanoparticles offer a new opportunity for treating inflammation through their ability to preferentially travel to the targeted tissue from the site of administration. This solves the traditional problem of therapies for inflammation causing target side effects and systemic toxicity [15,16]. The innumerous development of nanoparticles that can regulate the expression of anti-inflammatory chemicals, while also targeting inflammatory sensors or macrophages by cell eating, shows considerable potential for the effective management of illnesses associated with inflammation [15]. Furthermore, the ability to target effector cells passively (by adjusting the size, surface area, and surface charge of nanoparticles or by actively targeting antigen-presenting cells) using nanocarriers could be very helpful in increasing cellular response or immunological tolerance by coating nanoparticles with specific antibodies [16]. To overcome the negative effects of traditional medication such as nonspecific targeting, toxicity problems, excessive dose, and lengthy processing time, great emphasis has been placed on the development of more effective anti-inflammatory nanomedicines. Nanodrugs may provide potential hope in the removal of various chemical, anatomical, physiological, and clinical obstacles that reduce the efficacy of standard drugs. Nanotherapeutics have the potential to precisely target the infection site, avoid unwanted side effects, increase effectiveness, and improve patient compliance and prognosis. The enhanced permeation and retention (EPR) effect is a phenomenon where nanoparticles accumulate in inflamed tissues due to the increased permeability and retention of the blood vessels in the inflamed area. The small size of nanoparticles allows them to passively diffuse into inflamed tissues, where they can accumulate and exert their therapeutic effects. Further, nanoparticles can be engineered to have specific surface properties that allow them to selectively bind to biomolecules expressed on the surface of inflamed cells, such as activated endothelial cells or leukocytes. This can improve the biodistribution of the drug and increase its accumulation in the inflamed tissue. Nanotheranostics can be designed to release their therapeutic payload in response to specific stimuli, such as changes in pH or temperature in the inflamed tissue. This allows for the targeted delivery of the drug to the site of inflammation and can reduce the risk of systemic side effects. Last, biocompatible and biodegradable nanoparticles reduce the risk of toxicity associated with traditional therapies [17,18].

Nanotheranostics is a specialized area that integrates nanotechnology, diagnostics, and treatments. It is a relatively new and advanced sector of medicine and healthcare

with fascinating potential. It includes multifunctional nanostructures that perform drug detection, therapy, and continuous monitoring within the body [19,20]. This diagnostic and therapeutic approach improves the standard of care and enables the noninvasive real-time monitoring of the medication's response. There are numerous forms and architectures for theranostic nanomedicines [21]. Theranostic nanomedicine is a relatively new field that uses inorganic nanoparticles for both imaging and therapy. These nanoparticles can be made of gold, silver, silica, or magnetic materials. They can be used to entrap drugs or to deliver therapeutic substances such as drugs, ligands, or antibodies [22]. This dual delivery system enables both imaging and therapy to take place at the same time [23]. In the development of noninvasive nanomedical inflammatory therapy, the contrast agent must be adaptable to existing detection techniques such as X-ray, computed tomography (CT), MRI, and positron emission tomography (PET) or single-photon emission [24]. This study offers a summary of a few current advancements and developments in nanotheranostics, which are used to treat several inflammatory diseases. We also talk about the clinical translational potential and present issues with theranostic nanoparticles for inflammation. Finally, new study avenues are suggested.

2. Conventional Diagnosis and Therapy for Various Inflammatory Diseases

2.1. Diagnosis

There is no single test that can identify diseases that cause inflammation or diagnose it. Instead, a diagnosis is made using a combination of tests and procedures that are recommended depending on the symptoms. (Table 1).

Table 1. Conventional diagnosis of inflammation.

S.No.	Diagnosis	Mechanism	Applications	Ref.
		Blood tests		
1.	C-reactive protein (CRP)	CRP protein produced by liver that increases in concentration in response to inflammation	Inflammation from bacteria or viruses, inflammatory intestinal problems, and autoimmune disorders	[25,26]
2.	Serum protein electrophoresis (SPE)	Separating proteins based on their net charge, size, and shape	Kidney inflammatory diseases (condition may be chronic or acute) and liver diseases	[27]
3.	Erythrocyte sedimentation rate (ESR)	Inflammation causes cells to clump. As clumps are denser than single cells, they subside to bottom more quickly	Conditions cause inflammation, including arthritis, vasculitis, infection, and inflammatory bowel disease	[28]
4.	Fibrinogen analyses	Fibrinogen is made in liver; higher levels of it in inflammation are indicated	Differentiate hyperfibrinogenemia due to inflammation	[29]
		Imaging techniques		
5.	Ultrasound	Uses high-frequency sound waves and create an image, used in showing inflammation of tendons and tissue	Synovitis, tenosynovitis, enthesitis, bone erosions, and crystal deposits	[30]
6.	Computed tomography (CT)	Cross-sectional imaging (slices) of bones, blood arteries, and soft tissues in combination with several X-ray plates	Fracture, inflammatory intestinal problems, brain, and spinal cord inflammation	[31]

Table 1. *Cont.*

S.No.	Diagnosis	Mechanism	Applications	Ref.
7.	Magnetic resonance imaging	Multiplanar viewing of bone and soft tissues in three dimensions	Synovitis, bone marrow edema, tenosynovitis, and erosions	[32]
8.	SPECT/PET	Radiotracer is injected into body, which is quantified in decided timeframe and then utilized to acquire knowledge regarding physiological, cellular, and molecular processes of interest	Stroke, Alzheimer's disease, atherosclerosis, and many autoimmune diseases	[33]
		Radiopharmaceuticals		
9.	^{99}mTc-hydroxymethylene diphosphonate and ^{99}mTc-methylene diphosphonate	Chemisorption causes ^{99}mTc to accumulate on surface of hydroxyapatite crystals in bone	Renal osteodystrophy, hyperparathyroidism, osteomalacia	[33]
10.	^{67}Ga-citrate	Lactoferrin-bound ^{67}Ga is delivered to site of inflammation, or it binds to lactoferrin that is produced after bacterial phagocytosis at sites of infection	Bronchogenic cancer, Hodgkin's disease, lymphoma, and several acute inflammatory diseases	[34]
11.	^{18}F-FDG PET	^{18}F-FDG imaging PET is utilized to describe and localize a variety of cancer forms as well as locate locations of impaired glucose metabolism	Differentiate between polyarteritis nodosa, Takayasu's arteritis, and giant-cell arteritis (GCA)	[34]
12.	^{111}In-labeled platelets	Lipid-soluble complex penetrates to platelet cell membrane where 111In detaches from complexes and becomes attached to cytoplasmic components	Inflammatory bowels disease, osteomyelitis infected joint and vascular prosthesis, endocarditis	[35]

2.1.1. Blood Tests

The identification of inflammation in the body can be aided by a number of signs. However, because these markers are nonspecific, elevated levels may suggest something is wrong without specifically identifying physiological problems [25]. For early detection of inflammation, analytical methods mostly include serum protein electrophoresis (SPE), C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and fibrinogen analyses [26].

2.1.2. Imaging Techniques

The manner of diagnosing an inflammatory disease is governed by the type of disease suspected, as well as the clinical presentation. Imaging is important for both infectious and noninfectious inflammatory diseases. Infectious diseases include osteomyelitis, vascular graft infection, and metastatic infectious disease. Noninfectious inflammatory diseases include rheumatoid arthritis (RA), vasculitis, inflammatory bowel disease (IBD), and sarcoidosis [27]. Ultrasound is a noninvasive, low-cost tool for evaluating many inflammatory conditions, such as synovitis, tenosynovitis, enthesitis, bone erosions, and crystal deposits, making it an efficient approach for identifying and differentiating the most frequent types of inflammatory disorders, including functional assessments [28]. Computed tomography (CT) has many advantages when compared to ultrasonography in visualizing inflammation. It can be used to diagnose conditions affecting the muscles and bones, including bone

tumors, fractures, and the positioning of malignancies, infections, or blood clots. It can be utilized further to direct approaches like operations, biopsies, and radiation therapy [29]. Magnetic resonance imaging (MRI) is often used to measure perfusion levels without exposure to ionizing radiation. Using this technique, perfusion maps are generated, offering a visual aid to assist in the clinical manifestation of inflammatory disorders. [30]. The typical endoscopic evaluation within the inflammatory gastrointestinal tract includes expanded mucosa, erythematous, vasculitis, and mucosal brittleness. SPECT/PET is changing the way in diagnosing patients with suspected or known infections and inflammation. This new technology is particularly useful for diagnosing infections and inflammation affecting the musculoskeletal system, as well as those located in various soft-tissue sites [31].

2.1.3. Radiopharmaceuticals

Radiopharmaceuticals should be extremely sensitive when utilized to scan inflammatory disorders (apart from having general characteristics such as effortless devising, widespread accessibility, and reasonable price). Various types of radiotracers have been examined to photo-detect many inflammatory illnesses for the attainment of required properties [32]. However, a handful of these medicines are presently in common use for imaging inflammation. These include ^{18}F-FDG, ^{99}mTc- or ^{111}In-labeled autologous WBCs, ^{67}Ga-citrate, ^{99}mTc-labeled nanocolloids, and ^{99}mTc- or ^{111}In-labeled proteins such as IgG or albumin. Nanotechnological approaches with radiopharmaceuticals provide better penetration, accuracy, and sensitivity compared to conventional approaches.

^{99}mTc-hydroxymethylene diphosphonate and ^{99}mTc-methylene diphosphonate reflect osteoblast activity as an active response to bone inflammation. Since the infectious process replaces bone marrow in osteomyelitis, bone marrow imaging is negative, but WBC scanning in the same area is positive. This multimodal imaging of inflammation with WBCs and nanocolloids will yield outstanding sensitivity and specificity of more than 90%. Next, the complex formed when ^{67}Ga binds to transferrin helps in detecting inflammatory areas due to enhanced vascular permeability, where it is subsequently transferred to lactoferrin within [33]. Further, a technique for detecting inflamed arterial walls that are incredibly sensitive is ^{18}F-FDG PET [34]. ^{111}In-labeled platelets have been employed in pancreatic and kidney transplants. In-labeled platelets accumulated in acute rejection of renal transplants; hence, it was possible to discriminate between acute tubular necrosis and cyclosporine nephrotoxicity [35]. Due to the method's complexity, it is currently utilized in a small number of situations, such as patients on hemodialysis with irreversibly nonfunctioning renal transplants, to help distinguish between infection and fever of immunological origin from the transplant.

2.2. Therapy

Inflammation is a natural part of the healing process. There are a few options that can help manage chronic inflammation and reduce the risk of long-term damage. Some of these options are outlined below.

2.2.1. NSAIDs

NSAIDs, salicylates, or cyclooxygenase-2 inhibitors are used as the first line of treatment for inflammation to reduce pain and swelling. These drugs have been used to treat various cardiovascular diseases, including atherosclerosis, as well as cancer [36]. Aspirin is the earliest and far-established example of utilizing an anti-inflammatory drug in treating cardiovascular disease. Aspirin is used as a cardioprotective medication to help prevent atherosclerosis. Additionally, NSAIDs have also been explored for the regulation of microRNA (miRNA) expression under several inflammatory conditions [37]. The signs of gastrointestinal side effects should always be kept an eye out for in cases of serious NSAID difficulties. Due to new investigations of potential harmful effects, cyclooxygenase-2 inhibitors should be used with caution.

2.2.2. Glucocorticoids

Glucocorticosteroids suppress inflammation in a number of circumstances, including autoimmune diseases, inflammatory bowel disease, rheumatoid arthritis, and allergy disorders. Our understanding of how glucocorticoids reduce inflammation has advanced significantly, which may open the door for the future development of enhanced glucocorticoids and more specific therapies. The great majority of glucocorticoids used worldwide are used to treat asthma, which is the most prevalent inflammatory illness. While short-term corticosteroid usage is associated with modest adverse effects, prolonged use can result in various serious adverse consequences, some of which may be irreversible [38]. Therefore, a collaborative novel approach to corticosteroid therapy and subsequent monitoring is required.

2.2.3. DMARDs

DMARDs are medications that inhibit the immune system and regulate immune function. They can be conventional or biologic in origin. Inflammatory arthritis conditions like rheumatoid arthritis (RA), psoriatic arthritis, and ankylosing spondylitis are treated with disease-modifying antirheumatic drugs (DMARDs). Examples of frequently used traditional DMARDs include methotrexate, leflunomide, hydroxychloroquine, and sulfasalazine. They can also be used to treat connective tissue disorders such as systemic sclerosis, systemic lupus erythematosus (SLE), and Sjogren syndrome, as well as inflammatory myositis, vasculitis, uveitis, inflammatory bowel disease, and a variety of cancers. According to new research, DMARD combinations may be more successful than single-drug regimens [39].

2.2.4. Biologics

Infliximab, adalimumab, etanercept, rituximab, abatacept, tocilizumab, and tofacitinib are some examples of biologic medications. Specialized biologic drugs work by specifically targeting a certain immune system process. These drugs come in a variety of forms, including small substances such as Janus kinase (JAK) inhibitors, receptors linked to fragments of human immunoglobulin, and monoclonal antibodies [40]. The TNF antagonist lowers TNF-alpha levels, which are higher in synovial fluid in people with rheumatoid arthritis. Leukopenia, skin irritation at the injection site, and an increased risk of infection are all potential negative effects. Rituximab (Rituxan), an antibody targeting a surface receptor on B cells, has shown promise in treating malignancies caused by inflammation.

2.2.5. Nanomedicines

There are many types of nanoparticles being studied for the treatment of inflammation, including liposomal, polymeric nanoparticles, micelles, dendrimers, and hydrogel formulations. These nanoparticles are at different stages of development, from preclinical to clinical studies. Liposomes are nanosized particles that have become increasingly popular in cancer research due to their ability to deliver drug payloads to tumors with minimal side effects. Anti-inflammatory liposomal nanoparticles are being actively researched in order to develop new and more effective treatments [41]. Moreover, nanocarriers are beneficial in augmenting cell response, as these can specifically interact with the antigen-antibody cells, enabling the effective delivery of the drug or therapeutic agent. Additionally, these particles can also be surface modified to further improve their targeting and therapeutic efficacy as shown in Figure 1. Studies have suggested that nanomedicines are more promising and alternative approaches compared to traditional practices. Table 1 lists many new nanomedicine systems used for the management of inflammatory diseases preclinically. Numerous nanomedicines have already been approved by the FDA, and several hundred new clinical trials are in progress. Three other nanomedicines, including Patisiran/ONPATTRO, VYXEOS, and NBTXR3/Hensify, have just received approval [42]. A lipid-based nanoparticle treatment called Patisiran/ONPATTRO, which delivers siRNA, is used to treat people with polyneuropathy brought on by hereditary transthyretin-mediated amyloidosis. Adults with recently discovered acute myeloid leukemia are treated with the liposomal anthracy-

cline chemotherapy known as VYXEOS. NBTXR3, a radioactive nanoparticle, is combined with Hensify, a high-intensity focused ultrasound, to specifically target and eradicate cancer cells while sparing healthy tissue.

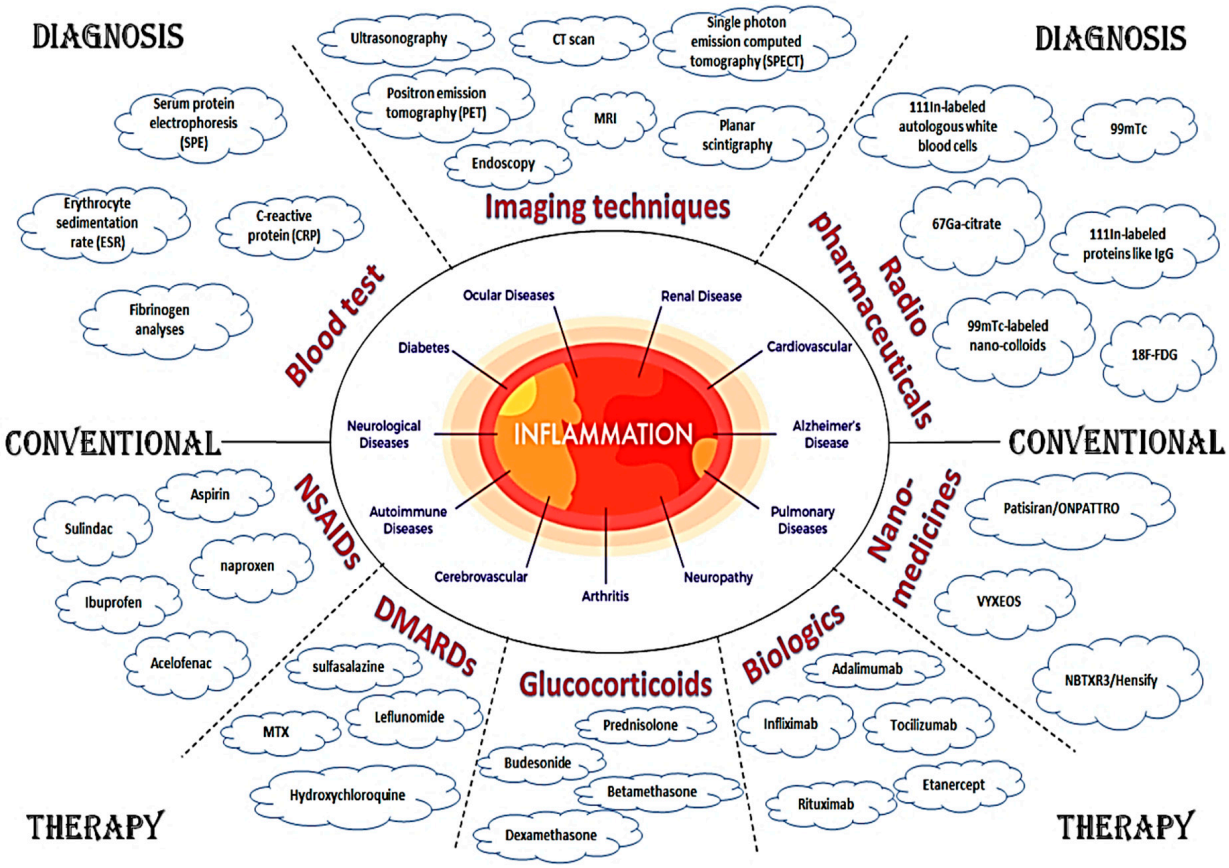

Figure 1. Conventional diagnosis and treatment of inflammatory diseases.

3. Nanomaterials for Theranostics: Recent Advances in Inflammation

Nanotheranostics have the ability to act as exosomes in TME maturation and, in combination with the fact that they are stable in biofluids, have proved these nanovesicles as promising agents to be utilized for oncological therapy. Numerous research works aimed at the usage of gold nanoparticles for treatment and detection purposes have been published (nanotheranostics). Au clusters of nanoscale in graphene oxide combination were developed to form a nanotheranostics platform in the conjugation of hyaluronic acid, 5-fluorouracil. Enzyme degeneration of hyaluronic acid at the tumor microenvironment through hyaluronidases allows the release of 5-fluorouracil, which improves antitumor efficacy when combined with laser irradiation [43–45].

3.1. Rheumatoid Arthritis

Kalshnikova et al. investigated the theranostic potential of albumin-ceria-ICG formulations, showing promising results in regard to the image-guided treatment of rheumatoid arthritis, with the goal of assessing delivery and efficacy via imaging. Nanotheranostics based on bovine serum albumin and indocyanine green dyes were developed for the effective delivery of cerium oxide nanoparticles to inflamed joints for rheumatoid arthritis (RA) therapy, as well as the creation of novel ceria-based theranostic nanoparticles for the therapeutics of rheumatoid arthritis. The development of nanotheranostics is simple and requires following a simple study methodology [46].

3.2. Cardiovascular

McCarthy et al. created magnetic fluorescent nanoparticles for atherosclerosis accompanied by inflammation theranostics. Dextran-coated iron oxide nanomaterials were redesigned for near-infrared fluorescence with AlexaFluor 750 and phototoxic treatment of inflammatory macrophages with meso-tetra(mhydroxyphenyl) chlorin (THPC). Experiments with near-infrared imaging in C57/BL6 mice revealed that THPC-based nanomaterials were capable of forming aggregates in specific regions with an abundance of macrophages and foam cells. According to the findings, this therapeutic nanomaterial could be used to treat atherosclerotic vascular diseases. Novel hydrophilic photosensitizers based on 5-(4-carboxyphenyl)10,15,20-triphenyl 2,3-dihydroxychlorin (TPC) and magnetic nanoparticles have been developed for the treatment of atherosclerosis through the induction of macrophage lysis. In vitro experiments revealed that TPC nanoparticles are capable of causing human macrophages to die at a rate of up to 100% [47,48].

Bagalkot and fellow researchers created a lipid latex (LiLa) nanoparticle system of phosphatidylserine along with the oxidized cholesterol ester derivative cholesterol-9-carboxynonanoate, as well as gadolinium (Gd) and fluorescein isothiocyanate (FITC), making possible the selective targeting of M1 inflammatory macrophages through the implementation of MRI and optical selection techniques. The nanoparticle combination Gd-FITC-LiLa enabled the noninvasive MR scanning of atherosclerotic plaques in subject animals, the selective deposition of which can also be achieved in macrophages of affected adipose tissues and used as a messenger of druggable compounds. This nanocarrier is filled with rosiglitazone (Rosi) to provide an anti-inflammatory therapeutic effect. It is a theranostic nanosystem with potential applications in atherosclerosis imaging and therapy [49].

Qin and fellow researchers created Au-nanorods as a base for inflammatory macrophage theranostics. Micro-CT imaging of macrophages revealed that an increment in concentration intensifies the signal. After intravenous injection of the formulation, in vivo thermal therapy in Apo E knockout mice showed a minute increment in CT potency in a swollen femoral artery. This formulation has been shown as a potential nontoxic, novel atherosclerosis theranostic base. Gold computed tomography agents demonstrated the potential to diagnose atherosclerosis [50].

3.3. Cancer Theranostics

Jianrong Wu et al. synthesized a new nanotheranostic agent built on Hsp 90 inhibitor-encapsulated biodegradable hollow mesoporous organosilica nanoparticles (HMONs), following being gated with bovine serum albumin–iridium oxide nanoparticles (AHBIPs) of nanoscale range, with the goal of reducing flaws in traditional photothermal therapy (PTT) research and improving the therapeutic efficacy of oncological theranostics. 17AAG-loaded nanoparticles were reduced in thermal resistance by inhibiting Hsp90, which could induce effective apoptosis [51].

CXCR4 expression imaging in oncology, CXCR4-directed ERT, and especially imaging are all gaining popularity at a few academic centers. CXCR4 articulation dynamics (e.g., chemotherapy-induced) present a novel opportunity for the potential modulation of CXCR4 expression and functionality. Higher sensitivities may benefit CXCR4 upregulation and downregulation, and anticancer therapeutics may find more targets on the cellular plane for more powerful results. Furthermore, labeling a CXCR4 ligand with an alpha-emitter for ERT could be groundbreaking for hematologic malignant problems, as increased energy transfer will have an effect on the annihilation of cancer and supportive oncological cells [52–54].

In addition, theranostic cells of mammals have been formulated for a variety of other ailments. Although yet to be developed for clinical purposes, preclinical studies gave good results [55–58]. TNF and IL-22 are cytokines associated with psoriasis, but HEK293 cells only show a part of the IL-22 receptor endogenously. The endogenous TNF-responsive pathway was developed to control the formulation of the other part of the IL-22 receptor

in order to endow HEK293 cells with the capability to recognize IL-22. This pathway was reprogrammed to regulate the making of the anti-inflammatory cytokines IL-4 and IL-10. When the cells detect the psoriatic phenotype, they successfully reduce inflammation, and in mice models, they stop the upstart of psoriatic flares and attenuate acute psoriasis [59,60].

Cheng et al. (2014) characterized doxorubicin-loaded liposomes with respect to their distribution of size, zeta potential, drug entrapment efficiency, and morphology by exploiting the EGFR binding affinity of a novel peptide GE11. In A549 cytotoxicity, optimal GE11 density was found to be 10%. Cellular uptake experiments also revealed a significant role in the clathrin-mediated endocytosis pathway. They discovered that the gathering up and reservation of GE-11-modified liposomes were higher than unmodified liposomes using a near-infrared (NIR) fluorescence imaging system [61].

Lin et al. designed, synthesized, and characterized dual-ligand (anticarbonic anhydrase IX (anti-CA IX) antibody and CPP33)-modified triptolide-loaded liposomes (dl-TPL-lip) for the efficient transportation of triptolide (TPL) to NSCLC. An apoptosis assay was used to assess cell-killing ability. Importantly, the liposomes have superior tumor penetration and tumor growth inhibition efficacy [62,63].

CXCR4 and its natural ligand, the chemokine CXCL12, are responsible for tumor growth and metastasis and have the crucial role of a psychological perspective in embryonic growth. CXCR4 is overexpressed on the cell surface of a variety of different cancers. Several therapeutics have been developed that target CXCR4 or its ligand CXCL12. Several CXCR4-directed imaging tracers have been formulated, and the most common example that is used today is the positron-emitting PET tracer [^{68}Ga]Pentixafor. CXCR4 imaging with [^{68}Ga] Pentixafor was successfully undertaken in a variety of cancers, as well as in cardiovascular disease and contaminations. CXCR4-directed imaging and radionuclide therapy research is brisk, and novel approaches are expected in the coming years [64–68].

Pediatric oncology currently shows that [$^{123/131}$I]mIBG is currently the sole theranostic presently in hand for systematic medicinal usage for the imaging and treatment of neuroblastoma tumors, which expresses the norepinephrine transporter (NET). [^{123}I]mIBG SPECT image-taking is now the gold standard for diagnosing primary tumors and distant metastases in neuroblastoma, as well as staging and assessing disease response after therapy. Although [^{123}I]mIBG SPECT is highly specific and sensitive, it comes with several drawbacks, which include poor resolution of images, lengthy scans, and iodine-induced thyroid toxicity. [^{131}I]mIBG, when combined with imaging, initially demonstrated therapeutic efficacy in bulky tumors [69–73]. Two systematic reviews, however, found no survival benefit for [^{131}I]mIBG-treated patients [74]. Pandit-Taskar et al. showed a biodistribution and dosimetry study in neuroblastoma patients with comparative outcomes with [^{123}I]mIBG. [^{18}F]mFBG outperformed [^{123}I]mIBG in all test cases. These encouraging results prompted further clinical trials for [^{18}F]mFBG as an alternative to the present standard product, [^{123}I]mIBG. Aside from improved imaging, researchers are now working on developing a better alternative to [^{131}I]mIBG therapy. ^{131}I is an emitter with a longer half-life [75].

3.4. Liver

Magnetic nanoparticles play crucial roles in four important nonexhaustive areas. The first important concept is the use of a magnetic field to capture binding-related cells. Cancer treatment has been greatly improved by the use of chimeric antigen receptor (CAR) T cells, which are formed by genetically engineering isolated T cells for developing autologous donors that aim at specified antigens. Although the technology is currently approved for the treatment of B-cell lymphoma, different clinical studies supported its potential for the treatment of hepatic cancer. The role of macrophages in the modulation of the worst actions of CAR T cell-based therapeutics is crucial. Other immune cells, such as natural killer cells, were also manipulated [76–78].

According to Wang et al. [78], the second area of application for MNPs is mechanical cell control. The rigidity of biological molecules and intracellular organelles could be measured in the coming times. Magnetic tweezers could be utilized for measuring biomolecular

mechanical force in this context. Low-frequency magnetic fields can cause directed cell apoptosis [79]. The principle of controlling cells mechanically previously regulated the modification of stem cells and behaviors, such as the divergence of a single cell [80].

A third application of MNPs is drug delivery. Aside from the innate poisonous effects of MNPs and their thermomagnetic effects, targeted drug delivery using these particles may be a viable method of eliminating injured or infected cells [81]. The use of magnetism in drug delivery has several advantages, including increased drug release from a unicarrier made of porous materials, azo-functionalized MNP-based remotely manipulated release of dosage, and enhanced release of drugs from magnetically controlled carriers of nanoscale [82].

Magnetism's fourth application is its edge in photoimaging approaches [83]. Although there are no specified markers of fibrosis in the early stages, early prognosis of hepatic fibrosis is associated with the premature prognosis of the ailment. Liquid biopsy using the identification of the N-terminal propeptide of type-III collagen (Pro-C3) may be useful in the speedy detection of hepatic fibrosis [84]. Another intriguing methodology could be the utilization of MNPs in the form of biosensors. Furthermore, MPI can straight away image the distribution of MNPs. This technology was first showcased around the early 2000s [85,86]. Because MPI has a higher temporal and spatial resolution than magnetic resonance imaging, it could be an encouraging system for detecting hepatic diseases [87].

Regarding hepatocellular cancer (HCC), Vaughan et al. developed a targeted therapeutic approach to cancer killing that does not cause toxicity or liver failure. PBAE nanoparticles (NPs) were utilized for delivering a CpG-free plasmid containing mutant herpes simplex virus type 1 sr39 thymidine kinase (sr39) DNA to human HCC cells. Transfection with sr39 allows oncological cells to be killed with the prodrug ganciclovir while also accumulating 9-(4-18F-fluoro-3-hydroxymethylbutyl)guanine (18F-FHBG) for in vivo imaging. A CpG-free human alpha-fetoprotein (AFP) promoter was used to achieve targeting (CpGf-AFP-sr39). The treatment reduced tumor size by 62%, and therapeutic genetic expressions were detected using positron emission tomography [88].

By formulating galactosylated-carboxymethyl chitosan-magnetic iron oxide nanoparticles, Wan-JiangXue et al. created a nanovector with dual aiming qualities for the systematic transport of the tumor suppressor gene RASSF1A exclusively into hepatocellular carcinoma (HCC) cells (Gal-CMCS-Fe_3O_4-NPs). It was discovered that Gal-CMCS-Fe_3O_4-NPs were rounded with a comparatively steady zeta potential after their conjugation with galactose and CMCS to the plane of Fe_3O_4-Nanoparticles. In pH 7 solution, Gal-CMCS-Fe_3O_4-NPs had high DNA condensing capability and were nontoxic at large. Experiments in vitro revealed that Gal-CMCS-Fe_3O_4-NPs were discriminative for HCC and hepatic cells. In vivo experiments revealed the specified amassing of Gal-CMCS-Fe_3O_4-NPs in HCC tissue, particularly when an external magnetic field was applied. The Gal-CMCS-Fe_3O_4-NPs/pcDNA3.1(+)RASSF1A compound and mitomycin were administered intravenously to naked mice with orthotopically transplanted HCC. In comparison with a group of mice that received treatment, these mice showed the tiniest tumors, the highest number of TUNEL-positive cells, and elevated levels of caspase-3 expression in tumor cells. These findings point to the probable use and deliverance of Gal-CMCS-Fe3O4-NPs for the RASSF1A gene in HCC therapy [89].

Hu et al. used folate (FA)-modified chitosan nanoparticles, a nonviral vector with the capability of targeting tumor cells with better FA receptor expression. FA-chitosan particles were utilized here as biological delivery agents for a plasmid expressing the mice interferon-induced protein-10 (mIP-10) gene, which is a powerful chemotherapeutic attracting agent for cytotoxic T cells. The mix of FA-chitosan/mIP-10 and DC/tumor cell fusion vaccines targeting hepatocellular carcinoma (HCC) proved to be a potent tumor growth inhibitor with extended mouse survival. In the mouse spleen, the combination regimen notably reduced myeloid-derived suppressor cells (MDSCs). The numbers show that mIP-10 improves the antitumor effectiveness of a DC/tumor cell fusion parenteral dosage form by reducing the immunosuppressive tumor surrounding [90].

Cheng et al. used target-specified nanomedication, enabling the in vivo repair of tissues, photographing, and localized enrichment through cells and not using cells directly. A magnetic bifunctional cell engager is created when the conjugation of Fe- particles of nanoscale is achieved with two types of antibodies (out of two, a part is directed towards the antigens of therapeutic cellular regions and other affected cells). The antibodies connect therapeutic cells and the affected cell, while MagBICE's Fe-core allows for physicality enhancement and photographing. Treatment of acute MI was carried out through the targeting of injured cardiomyocytes with exterior bone-marrow-derived stem cells (expression of CD45) or interior CD34-positive cells. MagBICE has minimal cytotoxicity in vitro. Finally, magnetic-antibody-linked nanomatchmakers allow for molecule-level aiming, physical advancement, and noninvasive imaging in a single effortlessly synthesized compound [91].

Van der Valk et al. investigated the medicinal utility of a liposomal nanoparticle with a longer circulation time enclosing prednisolone phosphate (LN-PLP) atherosclerosis-affected people. Firstly, they profiled the pharmacokinetics of liposomal prednisolone in people by calculating the deliverance towards plaque-forming microbes extracted from the iliofemoral plaques of cases referred for vascular surgery. Following that, they utilized noninvasive multimodal imaging to assess LN-anti-inflammatory PLP's effectiveness in atherosclerosis-affected people. We show that intravenously administered LN-PLP can be delivered locally into macrophages extracted from the atherosclerosis plaques of humans. Short-term LN-PLP usage failed to cope with expectations, as effective anti-inflammatory atherosclerosis medication in patients suffering from the same. Nonetheless, we highlight nanomedicine's potential as a new regimen of therapy for people suffering from atherosclerosis [92].

Ahn et al. created nanoparticulates that are photosensitive (dubbed Glu/Ce6 nanocomplexes) in aqueous conditions through hydrophobic chlorin e6 (Ce6) encapsulation in a triple-helical Glu structure. When exposed to a laser, Glu/Ce6 nanocomposites produce singular oxygen. These composites formulated were internalized by foam cells, delivering Ce6 molecules inside their cytoplasm. They caused remarkable damage to membranes, also causing apoptosis in foam cells after exposing them to laser light. These findings imply that the complex thus developed could find its utility as materials activated by light to treat atherogenic foam cells [93]. The developments made in recent and past years are given below in Figure 2, which gives a schematic representation of what can be delivered through nantheranostics agents and their composition. Table 2 describes the nanotheranostics approaches applied in past and current scenarios.

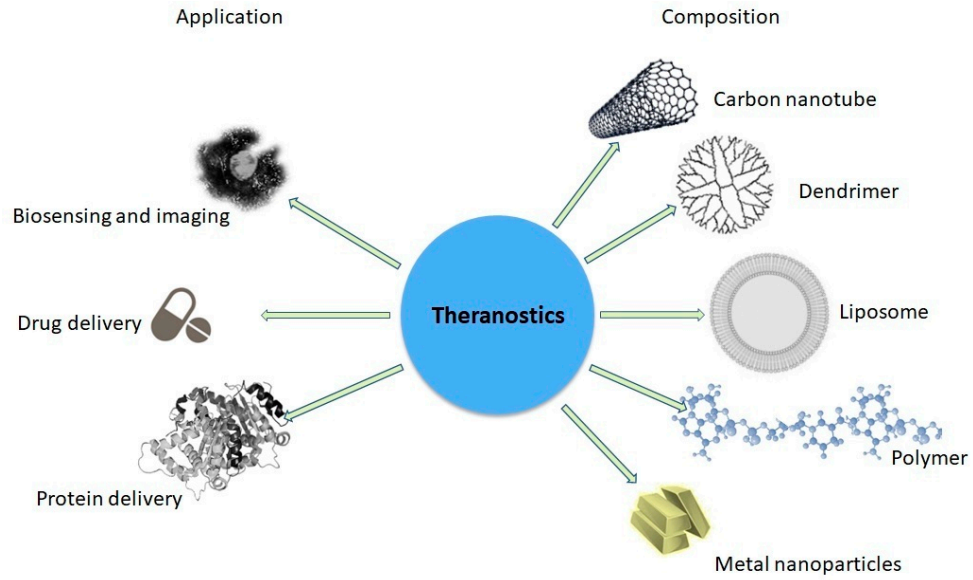

Figure 2. Schematic representation of items delivered through nantheranostics agents and their composition.

Table 2. Nanotheranostics approaches applied in past and current scenarios.

S. No.	Nanoformulation	Type	Loading Drug	Outcome	Ref.
1.	Gold nanoparticle clustered with graphene oxide in conjugation with 5-fluorouracil	Detection and imaging and phototherapy	Fluorouracil	Multifaceted theranostic unit was developed successfully, furthering into bioimaging-assisted cancer therapy	[43]
2.	Albumin-nanoceria-conjugated nanoparticles.	Inflammation control with guided imaging	Ceria	Inflammation targeting with contrast imaging and therapy shows potential as systemic arthritis treatment	[46]
3.	Dextran-coated magnetic fluorescent nanoparticle	Imaging and therapy of atherosclerosis	Meso-tetra(myhydroxyphenyl) chlorin	Highly efficacious and sensitive imaging proved to be potent therapeutic platform	[47]
4.	Lipid latex nanoparticle system	Imaging of atherosclerotic plaques and therapy	Rosiglitazone	Preferable signal interception and therapeutic efficacy shown on models, leaving room for future clinical applications to be worked upon	[49]
5.	Gold nanorods	Inflammatory macrophage theranostics	NA	Provided platform for phototherapy and developing biosensors for detection of cholesterol, phosphate, etc.	[50]
6.	Hollow mesoporous organosilica nanoparticle-based biodegradable nanotheranostics	HMONs gated with bovine serum albumin nanoparticles. Provides edge over traditional photothermal therapy	NA	Compound shows promising outcomes as multimodal image-guided combinatorial therapeutic platform.	[51]
7.	Modified liposomes of dual-ligand (anticarbonic anhydrase IX (anti-CA IX) antibody and CPP33)	Tumor penetration and tumor growth inhibition	Triptolide	Dual-ligand system has potential use as modified lipid vehicle for local targeted cancer drug delivery	[62]
8.	CXCR4 ligand Ga-Pentixafor PET/CT	Imaging of chronic bone infection	Ga-Pentixafor	Outcome is suitable alternative to established therapeutics, showing better diagnostic and imaging of bone infections	[65]
9.	^{18}F-meta-fluorobenzylguanidine (^{18}F-MFBG) PET/CT	Imaging and targeting of tumor	^{18}F-MFBG	Compounds have safer imaging and better biodistribution and targeting of lesions, giving better alternative to therapy of children	[75]
10.	Multipole magnetic tweezer system	Intracellular physical micromanipulations and measurements.	NA	System showed longer stay for imaging and better diagnosis over its counterparts	[79]

Table 2. *Cont.*

S. No.	Nanoformulation	Type	Loading Drug	Outcome	Ref.
11.	Ultrasensitive nanomagnetic labels	Nonlinear magnetization for biosensing and imaging	NA	Potential for biomedical applications as tunable, highly sensitive, and scalable magnetic tag	[86]
12.	Chitosan-magnetic iron oxide nanoparticles for hepatocellular carcinoma therapy	Systematic transporting of tumor suppressor gene	RASSF1A compound and mitomycin	Potential use in delivery of suppressor gene and drug for hepatocellular carcinoma	[89]
13.	Folate (FA)-modified chitosan nanoparticles	Growth inhibition of hepatocellular carcinoma cells	MIP-10	Promising combinatorial therapy showing results leading to further research in carcinoma treatment	[90]
14.	Antibody-linked magnetic nanoparticles	In vivo repair of tissues, photographing and localized enrichment	NA	Nonspecific binding capability of MagBICE requires further study	[91]
15.	Photosensitive nanoparticulates	Biomarking for targeted imaging of inflammatory disease	Glucan and Chlorin E6	Showing potential as photoactivated therapeutic. Further study required for development atherosclerotic therapy	[93]

4. Clinical Potential of Nanoformulation-Based Theranostics

Due to the specificity and effectiveness of theranostics in the treatment and therapy of various diseases, here we try to shed light on the development of nanotheranostics in recent years. A virion genetic carrier was recently used in gene therapy for treating infarctions of the myocardium, finding its usage as a transporter of genetic materials to the zone of the infarction, as well as transporting stem cells to cardiomyocytes for regenerating and repairing [94].

In atherosclerotic subjects, a clinical study that involved several interventions and plasmonic light and heat-sensitive theranostic therapy was observed. Each group of subjects received one therapeutic serving of silica gold nanoparticles bioengineered onto an artery patch or a silica-Au Fe-bearing nanocomplex affixed with microbubbles as a targeted delivery mechanism [95]. Finally, magnetic steering and stent implantation methods were used to compare stem cells. The year-long trial showed promising results, and a regressive graph can be seen of the size of the atheroma under silica-Au plasmonic photothermal regimen [96].

An [18F]meta fluorobenzylguanidine ([18F]mFBG]), an 18F-labeled analog of [123I]mIBG has been proposed to be used as a PET substitute for photographing norepinephrine transporter (NET)-positive neuroblastoma tumors [97,98]. The radionuclide 18F is a cyclotron-produced b+-emitter with a small in vivo range that produces higher-resolution images. Additionally, PET-CT (or PET-MRI) images can be quantitatively analyzed for tracer distribution. As a result, 18F-labeled radiotherapeuticals are perfect for higher-resolution prognosis and rapid accession, along with a lower burden of radiation. However, until recently, developing an [18F]mFBG was difficult [99]. Recent breakthroughs and nuovo radiofluorination reactions nowadays allow for the development and medicinal utilization of [18F]mFBG [100,101].

Kim et al. developed Theranostic Agent 1 (TA1) for the selective delivery of an NSAID, indomethacin, to the inflammatory region to visualize the inflammation zone by employing fluorescent off–on imaging of Rhodol-TPP by triggering H2Sn while working on a new H2Sn-moderated anti-inflammatory theranostic agent. In this study, we discovered that

TA1 prefers H2Sn to others, such as amino acids and other reactive oxygen species, and that TA1's fluorescence signal is markedly improved not only in interior and exterior H2Sn environments, but also in LPS-induced RAW264.7 cells. Furthermore, TA1 demonstrated two-photon excited fluorescence imaging, finding its usage in in vivo and in vitro experiments. As a result, the findings strongly suggest that the newly discovered TA1 has the potential to be a new theranostic agent because it is better applied to in vivo modeled therapeutics for inflammatory diseases [102].

Song et al. created a macrophage mannose receptor (MMR)-targeting theranostic drug of nanoscale, namely (mannose–polyethylene glycol–glycol chitosan–deoxycholic acid–cyanine 7-lobeglitazone; MMR-Lobe-Cy), which was developed for the detection of inflammatory activities and for the delivery of the PPAR agonist lobeglitazone specifically to alarmingly risky plaques. This novel theranostic regimen targeting red-flagged coronary plaques offers a promising theranostic strategy [103]. Further data on some ongoing clinical trials of theranostics, along with their stages of development, are noted in Table 3.

Table 3. Nanotheranostics targeting inflammation along with their stages of development.

S. No.	Clinical Trial	Ailment	Target	Phases	Ref.
1.	NCT04589234	Metastatic pancreatic cancer	Salmonella typhimurium expressing human IL-2 in mixture of FOLFIRINOX or gemcitabine	2nd	[104]
2.	NCT03751007	Type 1 diabetes mellitus	Lactococcus lactis mixed alongside teplizumab	1st/2nd	[60]
3.	NCT04633148	Transitional cell cancer of the renal pelvis and ureter, prostate cancer	Modular, uniCART cells combined with recombinant antibody derivate aimed at PSMA peptide	1st	[60]
4.	NCT04167137	Metastatic neoplasm, lymphoma	Escherichia coli Nissle modified into expressing STING agonist when combined along with atezolizumab	1st	[60]
5.	NCT04377932	Relapsed or refractory GPC3+ solid tumors	GPC3 CAR T cells "shielded" with impression of IL-15, which in addition expresses a suicide gene (iCasp9) to allow CAR T cell dissipation after rimiducid regimen	1st	[60]
6.	NCT03896568	Glioblastoma	Mesenchymal stem cells which produces oncolytic adenovirus	1st	[60]
7.	NCT04040088	Neuroblastoma	Somatostatin Receptor 2A	1st/2nd	[105,106]
8.	NCT02348749	Neuroblastoma	Norepinephrine Transporter	1st/2nd	[75]

5. Challenges Faced with Theranostic Regimen

The translation of theranostic nanomedicine to clinics has significant **biological challenges** due to the nano-bio interaction [107–109]. When a nanomedicine interacts with biological material, the possible toxicity or incompatibility of the nanomedicine can result in diseases such as immunoreaction and inflammatory conditions. A "protein corona" is created on the surface of a biological system when nanoparticles interact with its proteins. This protein adsorption changes the stability, size, dispersibility, pharmacometrics, biodistribution, and toxicity profile of the nanoparticles. Given that each patient responds differently to treatment, theranostic nanomedicine may have difficulty in obtaining regulatory approval if **safety** is viewed as a single size, leading to the fitness of all [110]. Many experiments suggested nanotheranostics with high therapeutic potential have low or no

diagnosing signals. Gold nanoparticles coated with anti-EGFR 20 nm in size exhibited the highest tumor uptake, while those with a 50 nm size provided the highest CT imaging. According to the studies mentioned above, the utilization of theranostic nanomedicines as theranostic agents is constrained by their size-dependent dispersion in tumors. Therefore, continuous monitoring of patients is essential for theranostics. Another remarkable barrier to the **scalable and cost-effective** clinical translation of theranostics nanomedicines is troublesome controlling and reproducing synthesis processes [111]. The viability of large-scale economic manufacturing is one of the most difficult obstacles for translation. Theranostics have many active functions and typically require several preparation, purification, and processing stages, which provide scale-up issues. As a result, the majority of developed theranostics are limited to laboratory and preclinical research. A fourth big issue that needs addressing is the widened gap between the research community and **regulation bodies** [108]. Many government policies are being implemented to supervise the commodification of nanomedicine based on regulatory criteria such as quality control, formulation methodology, safety profile, and patent. The absence of clear regulatory and safety requirements has a major impact on the timely and efficient introduction of theranostics to the market. Nanoparticles introduced into sales have gone through set ordinances; nevertheless, these standards may be insufficient and require additional adjustment to validate the quality, dependency, and potency of further nanotheranostics for utilization by humans. Most of the theranostics used optical imaging, which has limited clinical relevance due to light penetration. PET and SPECT can be utilized for research in both preclinical and clinical subjects, but regular use of these modalities for diagnosis and therapeutic monitoring is hindered by **radiation exposure**. Despite being in its early phases of research, 19F MRI has a lot of potential because its near-zero background enables quantitative identification. Because MRI has limited sensitivity and uses a lot of imaging agents, its biocompatibility, elimination, and toxicity must be considered carefully [112]. The **sensitivity and specificity** of the prognostic techniques (planar scintigraphy, SPECT, and PET) are restricted compared to other detection modalities, therefore having a tendency of leading to incorrect patient selections once in a while. If imaging-based selection criteria are used, this could lead to barring of sufferers who might respond to a certain therapy. These constraints are mostly based on imaging system factors such as spatial resolution and contrast resolution.

6. Future Aspects

Overall, nanotheranostics has demonstrated considerable promise in the detection and management of inflammation. Although functional nanosystems have made significant advances in the detection, treatment, and prevention of inflammation, this research area is still in its early stages and demands multidisciplinary collaboration, as well as the combination of chemistry.

The development of numerous diseases is linked to inflammation, which is driven by oxidative stress and is a major contributing factor to many diseases. In order to treat inflammatory conditions, antioxidants are employed as medication. Polyphenols are known to have antioxidant, anti-inflammatory, and anticarcinogenic properties, making them ideal for use in theranostic treatments. They have also been shown effective at targeting specific molecular targets, such as enzymes, receptors, and proteins, which can be used to identify and target disease-causing cells. Additionally, polyphenols can be used to deliver therapeutic agents and to monitor therapeutic response. RosA is one such phenolic molecule that contributes to its anti-inflammatory effect by interfering with the ROS-inflammation link through pathways such as ROS scavenging and ROS detoxification. Therefore, more research into potential antioxidant modulations by theranostics is necessary [113].

Cytokines are immune system signaling molecules, playing an important role in regulating and modulating immunological and inflammatory responses. Inflammation, cytokines, and adaptive, innate responses interact synergistically to maintain healthy homeostasis. To dynamically monitor inflammation, it becomes critical to advance precise

and sensitive methods for measuring cytokines in actual time, and such measures can serve as a crucial foundation for the effective treatment of emerging and chronic diseases. According to a study, redox probes with a positive charge (ruthenium hexamine) were used as signaling molecules and inserted into structure-switch aptamers. Redox probes are released when interferons (IFNs) are present, creating an electrochemical signal that may be used to measure the IFN concentration. This global theranostic platform has enormous potential for personalized therapy and the effective treatment of a wide range of inflammatory disorders [114].

As an alternative, small-molecule anti-inflammatory medications with well-known efficacy, toxicity, and safety profiles can also be used for theranostic research. Among these medications, NSAIDs have been effective in inflammatory disease models, but it is unclear how they affect macrophage regulation. For instance, celecoxib lowers inflammation by preventing COX-2 synthesis, yet it has been demonstrated that in cancer, it increases TAMs' proinflammatory activity by transforming their phenotype to M1-like. Future research could focus on using theranostics to elucidate the mechanism of action of such medicines on macrophage activity. In this approach, theranostics could aid in the visualization of macrophages in an inflammatory state, while the inserted medication controls their activity [36].

The development of a multifunctional polymeric vesicle made of poly(ethylene glycol) and poly(lactic-co-glycolic acid) and poly(lactic-co-glycolic acid) (PLGAPEG) for the simultaneous delivery of COPD/CF medications (corticosteroids, prednisone, anti-inflammatory bronchodilators, theophylline, DF508-CF correctors, etc.) and molecular probes used for theranostic application in obstructive lung diseases. Utilizing noninvasive imaging techniques to track the biodistribution and anti-inflammatory consequences of the probe/drug-loaded nanocarriers in actual time will be made into a possibility by the implementation of such nanocarriers in clinics in the future, enabling theranostics for CF and COPD [115].

A P-selectin-based theranostic is being developed in targeting the PLGANP nanodelivery system to transfer natural chemicals BA and resin under the inflammation site of the colon. In vitro study of NPs containing the BA/Res/NP-PBP system showed effective nanoparticle size, size distribution, zeta potential, and prolonged release. Additionally, the targeting action assisted by P-selectin boosted the assimilation of NPs in the site of the inflammatory colon region, and the polymer-encapsulated codelivery system successfully amplified the anti-inflammatory action of independent BA or Res. This technology offers a noninvasive and extremely sensitive tool for precisely imaging inflammatory disorders, as well as the potential for combined delivery of natural nanodrug delivery systems for therapy.

7. Conclusions

Theranostics has unrivaled value in the diagnosis and treatment of various ailments. Many novel theranostic are being developed and will be available for clinical trials and care soon. Molecular imaging can aid in diagnosis, staging, treatment planning, and predicting response to targeted therapy. Many of the studies discussed here have made significant contributions to the investigation of novel imaging and therapeutic strategies for inflammatory diseases. A number of new targets have been identified as potentially useful for overcoming resistance to standard-of-care treatments. These new studies are encouraging in preclinical studies. We hope to see more studies progress to clinical trials in the near future.

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