Chapter 38

Role of Platelet Membrane Coated Nanoparticles to Treat Rheumatoid Arthritis

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ABSTRACT

Rheumatoid arthritis is a severe autoimmune condition marked by persistent joint inflammation that significantly impacts those affected by it. Traditional methods of treatment frequently have restrictions, requiring the investigation of new and creative healing approaches. Platelet-coated nanoparticles have become a hopeful method for treating rheumatoid arthritis, taking advantage of the special characteristics of platelets to improve focused drug delivery. This review offers a thorough examination of how platelet membrane-coated nanoparticles can help overcome the obstacles of treating rheumatoid arthritis. The platelet membranes' inherent biocompatibility and targeting capabilities, along with their composition and structure, make them a perfect choice for coating nanoparticles. This method mimics nature by using the innate ability of platelets to target inflamed joints, resulting in accurate and targeted drug delivery. The way in which nanoparticles work involves targeted interactions with synovial cells, modulation of the immune system, and continued release of medication in the inflamed area. In order to overcome these challenges, it is crucial to develop surface modification methods and incorporate them with additional therapeutic methods. In the future, improvements in designing nanoparticles, such as creating smart and versatile platforms, combined with personalized medicine approaches, offer the potential for customizing treatments for each patient. This new method represents a significant change in the way medicine is practiced, focusing on precision and customization. It provides optimism for improved and personalized therapies for those dealing with rheumatoid arthritis.

KEYWORDS
Rheumatoid arthritis; Platelet membrane-coated nanoparticles; Targeted drug delivery; Autoimmune disorder; Precision medicine; Inflammation modulation; Biomimetic Nanomedicine

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INTRODUCTION

Overview of Rheumatoid Arthritis (RA)

Rheumatoid arthritis is a long-term disease where the lining of our joints gets swollen and causes pain. It is caused by our immune system attacking our body. This condition causes pain, and swelling, and can damage the joints over time (Finckh et al., 2022). Rheumatoid arthritis can harm many joints, changing their shape and making it hard to live a normal life. We don't know exactly what causes RA, but it's related to the immune system attacking the body's tissues (Zou, 2020). Controlling RA usually means using different types of medicine like pain relievers, drugs that can change the course of the disease, and stronger medicine in severe cases. Although these treatments can help with symptoms and slow down the disease, they may not work completely, have bad side effects, and need to be taken for a long time (Akram et al., 2021). Also, some patients may not get better with current treatments, so we need new and better ways to treat them. Tiny particles used in medicine look hopeful for helping with the problems of regular RA treatments. Nanoparticles are very tiny and have special qualities (Gisbert-Garzarán et al., 2020). They can be used to send medicine to a specific place in the body, make medicines work better, and lower the side effects on the body. Platelets wrapped around tiny particles are a new and hopeful way to help in this situation.

Platelet Membrane Coated Nanoparticles for RA Treatment

Rationale for Platelet Membrane Coating

Platelets are very important for the body's defenses and responses to injury. The surface of their cells has special parts

that help them communicate with injured areas and places with inflammation (Portier & Campbell, 2021). Covering tiny particles with platelet membranes helps them act like natural cells, making them better at finding and treating inflamed joints (Hu et al., 2015). Platelet-covered nanoparticles can use the body's natural way of finding specific places. The proteins on the outside of platelets help the nanoparticles go to the swollen joints of people with rheumatoid arthritis. This method helps drugs work better and causes less harm to healthy tissues (Jiménez-Jiménez et al., 2020a).

Mechanisms of Action

Nanoparticles covered with platelet membranes might be able to help control the abnormal immune response seen in RA. These tiny particles can help calm down swelling in the joints by working with the body's immune cells. The platelet coating on nanoparticles helps them reduce inflammation and deliver medicine (Deng et al., 2022). This can help reduce swelling and pain in the joints for people with RA.

Current Research and Future Prospects

Many tests in animals have shown that coating nanoparticles with platelet membranes could help treat rheumatoid arthritis. These studies have found that treatment works better, has fewer side effects, and can get to swollen joints more easily (Kunde and Wairkar, 2021). Platelet-coated nanoparticles show potential, but we need to figure out how to make them in large quantities, make sure they are safe for a long time, and follow the rules before we can use them in medicine (Adhalrao et al., 2024). Current research is working to make these tiny particles better and check how they affect animals over a long time (Sekhon et al., 2022). The creation of tiny particles covered in platelet membranes for treating rheumatoid arthritis is a new and interesting area of study in medicine using very small particles (Gisbert-Garzarán et al., 2020). More study is needed to make sure that this new treatment works well, is safe, and is made in the best way. If they work, platelet-coated nanoparticles could change the way doctors treat rheumatoid arthritis. They would be a precise, effective, and well-tolerated treatment for patients with this serious autoimmune disease.

Platelet Membrane-Coated Nanoparticles

A. Platelet Membrane Structure and composition

Platelets are tiny, round blood cells that are important for stopping bleeding and fighting off infections. Covering very tiny particles with the outer layer of cells to make them look like cells. The structure of a platelet membrane is made up of two layers of fats with proteins and receptors in them. These things are like bricks that make up the membrane. They come together in two layers to make the membrane strong. The surface of platelet membranes has glycoproteins that help them stick to other cells and tissues and send signals to them. Platelet walls have receptors that help them stick to other things and respond to signals (Robier, 2020). Different proteins on the outside of platelets help them do their job in fighting off germs, reducing swelling, and healing cuts and injuries. Covering tiny particles with platelet membranes uses the natural abilities of these components to stick to and target inflamed tissues, like the synovium in rheumatoid arthritis.

Table 1: Role of platelet membrane coated nanoparticles Core Materials

Sr.No	Platelet Membrane-Coated Nanoparticles	Nanoparticle Core Material	Target Site	Benefits	References
1	Platelet Membrane	Lipids, Polymers	Inflamed Joints, Synovial Tissue, Inflammatory Sites	Biocompatibility, Enhanced Targeting, Prolonged Circulation Time, Reduced Immune Response	(Y. Song et al., 2019)
2	Platelet Membrane	Inorganic Nanoparticles	Inflamed Joints, Synovial Tissue, Inflammatory Sites	Biocompatibility Enhanced Targeting, Reduced Immune Response, Prolonged Circulation Time	(W. Song et al., 2022)
3	Platelet Membrane	Hybrid Materials	Inflamed Joints, Synovial Tissue, Inflammatory Sites	Prolonged Circulation Time, Reduced Immune Response, Enhanced Targeting, Biocompatibility	(Chen et al., 2020)

Nanoparticle Core Material

Nanoparticles have a middle part that holds the medicine. Choosing the right materials is very important for making sure the medicine is delivered properly. Some commonly used materials for the small particles in the center include (Joseph et al., 2023). Lipid-based tiny particles like liposomes or lipid nanoparticles are commonly used as the main material. These fats can trap drugs that don't dissolve in water inside their fatty layers (García-Pinel et al., 2019). Polymer materials that are safe for the body, like PLGA or chitosan, are often used for the center of the material. These substances can wrap up both water-fearing and water-loving medications (Liu et al., 2021). Silica or gold particles can be used as the center. Inorganic tiny particles have special abilities and can be designed to release medicine in a planned way (Moreira et al., 2018) Mixing different materials together can make tiny particles that are really strong because each material brings its own strengths.

Advantages of Platelet Membrane Coating

Platelet-coated nanoparticles are very safe and work well in the body because they are made from platelet membranes. Platelets are a part of blood that works with the body without causing any problems. Covering tiny particles with platelet

membranes reduces the chance of our bodies reacting to them, so they can be used for medical treatments. Platelet membrane-coated nanoparticles can hit their target better. Platelets are good at finding their way to areas of the body that are inflamed. The proteins and receptors on the outside of platelets help the nanoparticles find and go to specific inflamed tissues, like the synovium in people with rheumatoid arthritis(Iqbal, Altaf, Salma, et al., 2024). This special delivery helps drugs work better in certain places and reduces their side effects in other areas. The covering on the outside of platelets helps them stay in the bloodstream longer. Platelets can avoid being cleared by the immune system, and they pass this ability on to the nanoparticles they coat. The stealth effect makes it harder for the body to remove the nanoparticles quickly, so they can stay in the body for longer. The nanoparticles stay in the body longer, which makes it more likely they will reach and build up at the inflamed areas we want to target. Covering tiny particles with platelet membranes can help reduce the body's reaction to the particles. The platelet membrane acts like a shield that makes it harder for the immune system to notice the nanoparticles (C.-M. J. Hu et al., 2015). This is really helpful for long-term conditions like rheumatoid arthritis, where people often need to take medicine regularly. Reducing the body's reactions to the treatment makes it safer and more effective, which helps patients get better results (He et al., n.d.).

Mechanisms of Action

Targeting Inflamed Joints and Platelet Membrane Interaction with Inflammatory Sites

Platelet-covered nanoparticles go to inflamed joints in conditions like rheumatoid arthritis by interacting with the inflamed areas in a specific way. Platelets have special parts on their surface that help them stick to inflamed cells in blood vessels near sore joints. These parts are called adhesion molecules and receptors. This recognition is increased because adhesion molecules are turned up when there is inflammation. Platelets can react to signals released when the body is inflamed(Altaf & Iqbal, 2023). The platelet membrane-coated nanoparticles can use the signals released in the synovium of rheumatoid joints. When the swollen joints are nearby, tiny particles covered with platelets stick to them and go through the body's barrier. This process, called extravasation, lets the tiny particles get into the synovial tissue and reach the inflamed area. When platelets interact with nanoparticles, they gather in rheumatoid joints using special methods. The EPR effect means nanoparticles collect in areas with leaky blood vessels, like inflamed tissues. In rheumatoid arthritis, the blood vessels and synovial membrane in the joints are not working well. This allows platelet-coated nanoparticles to build up in the affected joints. The outside of platelet-covered nanoparticles can attach specifically to cells in swollen joints. Platelet receptors connect with molecules on the surface of cells that cause inflammation or are found in joint tissues. This particular attachment helps nanoparticles get inside the right cells and release the medicine they contain. After entering the swollen joints, the tiny particles slowly let out the enclosed medicine. The slow release of the medicine makes it last a long time, which helps with the long-term treatment of rheumatoid arthritis(Iqbal & Altaf, 2024). This special way of giving medicine to the body helps to lower the amount of medicine in the whole body and reduces the side effects of treatment (He et al., n.d.).

Modulation of Immune Response and Inhibition of Inflammatory Cytokines

Platelet-covered particles can help control the immune response in rheumatoid arthritis by stopping the production and activity of harmful substances. Tiny particles covered in platelet membranes can capture inflammatory molecules like TNF-α, IL-1β, and IL-6. The platelet membrane's ability to attract these cytokines allows the nanoparticles to attach to and stop them from causing harm during inflammation. Platelet parts on tiny particles can stop inflammation signals. This problem might make important signals in the body slow down, which can reduce inflammation in the joints. Platelet membrane-coated nanoparticles have anti-inflammatory drugs inside them. These medicines stop the production or action of inflammation-causing substances in the affected area, which reduces the immune system's reaction. Tiny particles covered with platelet membranes also help control immune cells that cause rheumatoid arthritis. Macrophages are a key part of the body's inflammatory response in RA. Tiny particles covered with platelet membranes can change the way certain immune cells behave, making them less inflamed and more helpful (Muhammad et al., 2020). This change helps make a setting that is not good for ongoing swelling. T cells, especially T helper cells, play a part in the autoimmune reaction in rheumatoid arthritis. Tiny particles covered with platelet membranes can affect T cells, changing how they work and develop. This rule can stop the too-strong immune response that causes harm to the joints. Abnormal activation of certain cells in the joints makes rheumatoid arthritis more damaging and aggressive. Platelet-covered tiny particles might stop synovial fibroblasts from causing harm to joint tissues (Lin et al., 2023).

Experimental Studies

In vitro Studies and Interaction with Synovial Cells

Scientists have done experiments in a lab on platelet membrane-coated nanoparticles interacting with synovial cells. This helps us understand how these nanoparticles could be used to treat rheumatoid arthritis. They used special nanoparticles that glow to the cells and take them in. These studies want to learn how well nanoparticles get inside cells, especially how receptors and mechanisms on platelets and synovial cells work together. Scientists studied what happens to nanoparticles covered with platelet membranes inside synovial cells. By watching the tiny particles for a while, they can see if the covered particles stay in certain parts of the cell, like endosomes or lysosomes, and check if the medicine keeps coming out for a long time. In lab research, scientists are also testing if platelet membrane-coated nanoparticles are harmful to synovial cells (Zhou et al., 2023). We test the nanoparticles to make sure they won't harm cells. We check if the cells are alive if they're dying, and for other signs of their health.

Evaluation of Anti-Inflammatory Effects

In the lab, we are studying platelet-covered nanoparticles can reduce inflammation. Scientists are checking that certain chemicals in joints change when they are treated with tiny particles covered in platelet membranes. These chemicals are important in causing inflammation. This shows nanoparticles can change the levels of inflammation in rheumatoid arthritis. Laboratory tests are looking at tiny particles covered with platelet membranes that affect certain enzymes and substances that cause inflammation in the body. This includes looking at the effects on enzymes like COX-2 and MMPs. These studies are trying to figure out how nanoparticles help reduce inflammation(Umair et al., 2022). Scientists study platelet membrane-coated nanoparticles affect the body's inflammation pathways within cells. This involves studying proteins are changed, how a factor called NF-κB becomes active, and other signals that control the way genes that because inflammation is turned on.

In vivo Studies and Animal Models of Rheumatoid Arthritis

Studying animals with arthritis is important for testing if platelet-coated nanoparticles can help treat the disease and if they are safe to use. Animal models that are often used include. CIA is a common way to imitate many parts of human rheumatoid arthritis in research. In this model, animals like mice or rats are given collagen to make their immune system attack their own body and cause joint swelling. Doctors will check how bad the arthritis is and examine the damage to the joints as time goes on (Floris et al., 2020). AIA models use adjuvants like complete Freund's adjuvant to make animals show symptoms similar to arthritis (Jones et al., 2018). This model is often used to study how arthritis develops and how new treatments might work. This model includes taking serum from mice with arthritis and giving it to other mice, which causes joint inflammation. Researchers can use it to learn about how arthritis affects the whole body and to see if treatments work.

Therapeutic Efficacy of Platelet Membrane-Coated Nanoparticles

In live animal tests, researchers are studying if platelet membrane-coated nanoparticles can be effective in treating rheumatoid arthritis (Deng et al., 2022). Scientists are coating tiny particles with platelet membranes can help make arthritis symptoms and joint damage less severe. This assessment looks at the joints by looking at them, using special pictures, and examining their tissues under a microscope. We are checking the levels of certain substances in the blood and joint fluid to see if platelet-coated nanoparticles can help reduce inflammation in the joints. Scientists are studying how platelet membrane-coated nanoparticles affect the immune cells in the joints (Zhu et al., 2021). This involves immune cell change and reaction in rheumatoid arthritis. This means looking at how certain types of immune cells are affected in the disease. In vivo studies also look at how platelet-covered nanoparticles move through the body as long they stay in the bloodstream (Zhu et al., 2021), where they go into the body, and are removed from the body. It is important to carefully study the possible negative effects and long-term safety of using platelet membrane-coated nanoparticles to make sure they are a good treatment option (Han et al., 2022). This includes checking organs are working, evaluating whether the body is being harmed, and looking for any signs of immune system reactions.

Challenges and Solutions

Potential Obstacles in Clinical Translation and Immunogenicity Concerns

Nanomaterials, like platelet membrane-coated nanoparticles, could cause they might affect the immune system. The immune system might see these tiny particles as invaders and launch an attack, which could make them less effective or safe for medical treatment. We need to do careful tests before using platelet membrane-coated nanoparticles they affect the immune system. This means checking to see if the body's immune system reacts to the nanoparticles by making antibodies or activating specific pathways(Iqbal, Altaf, Fatima, et al., 2024). We can look at changing the surface or adding a coating to reduce the body's immune response. Careful watching during medical trials will help find and deal with any unexpected immune reactions in people (Ernst et al., 2021). Moving from making a small amount of something in a laboratory to making a lot of it for use in hospitals and clinics can be difficult. It is important to keep the platelet membrane-coated nanoparticles consistent and reliable when making them in large amounts for medical use. It is very important to have strong manufacturing methods and good checks to control quality. Using advanced technology to make things in a better and faster way can help make more of them. "Working with industry partners are familiar with making lots of tiny particles can give us helpful information. " Furthermore, following the rules for making things well and the government's guidelines is very important to make sure nanoparticles for medical use are consistent and high-quality (Isaac et al., 2022).

Strategies to Overcome Challenges and Surface Modification Techniques

Addressing Immunogenicity

Using stealth coatings like polyethylene glycol (PEG) on the surface of platelet membrane-coated nanoparticles can make them less likely to cause an immune response. PEGylation makes nanoparticles hard for the immune system to notice and helps them stay in the body for longer (Fam et al., 2020). Modifying the surface of platelet membrane-coated nanoparticles to make them more like natural membranes can help them avoid detection by the immune system. This means making the coating better so it works well with the body and doesn't cause a bad reaction (Wang et al., 2020). Using cross-linking techniques to make the platelet membrane coating stronger can make nanoparticles more stable. Cross-linking agents help make the membrane components stronger, so the coated nanoparticles can last longer when they are moving around in the body or being stored (C. Hu et al., 2020). Adding specific molecules to the outside of platelet-covered

nanoparticles can help them stick better to inflamed tissues. This change makes sure that medicine goes to the right place in the body better (Pires et al., 2021).

Integration with other Therapeutic Approaches and Combination Therapies

Combining different treatments and putting them inside platelet capsules helps in delivering multiple therapies at once (Wilkins et al., 2024). This method can work together to target many different parts of rheumatoid arthritis, making the treatment work better. Platelet membrane-coated nanoparticles can be created to help improve current treatments for rheumatoid arthritis. Mixing these tiny particles with regular DMARDs or biologics may lead to a better and more powerful treatment plan (Radu & Bungau, 2021). Adding imaging dyes to platelet-covered nanoparticles lets us see where they go in the body and how well they hit their target. This combination helps doctors make special treatment plans by giving them information about the disease and how well the treatment is working. Creating tiny particles covered in platelet membranes that release medicine in a certain way when they sense certain signals like pH or inflammation (Jiménez-Jiménez et al., 2020b). This makes it easier to deliver medicine to the right place and reduces any unwanted effects.

Future Directions

Emerging Technologies, Innovations and Advancements in Nanoparticle Design

Future studies might look at making tiny particles that can release drugs in response to something. These tiny particles can be made to release medicine when certain things happen in the body, like a change in pH or temperature, or when there are signs of inflammation in the joints. This would make delivering drugs more accurate and controlled (Mitchell et al., 2021). Developments in making tiny particles could mean creating versatile platforms that can carry several treatments at once. Combining different medicines or treatments into one tiny particle could help treat different parts of rheumatoid arthritis, and make the treatment work better. In the future, tiny particles could be made with other biological parts like enzymes or proteins to make medicines work better (Pandit et al., 2022). Nano-biohybrids could use the combined effects of man-made tiny particles and natural molecules to better target specific areas and help the immune system (Guo et al., 2020).

Integration with Personalized Medicine Approaches and Patient-specific Formulations

Personalized medicine means making tiny particles that are coated with material from a patient's blood cells (Vaz & Kumar, 2021). These particles can be customized based on each patient's specific traits. Many things, like sick someone is, their genes, they react to treatment, can affect how nanoparticles are made to help each patient the most. Discoveries in finding markers in the body could help create tiny particles covered with platelet membranes. These particles would be made to seek out and treat the specific signs of rheumatoid arthritis in each patient (Alghamdi et al., 2022). This precise targeting can make the treatment work better and reduce the side effects. In the future, new ideas may include adding tests to platelet-covered nanoparticles(Altaf et al., 2023). This could help doctors keep track of how a disease is developing and how the treatment is working. It would allow them to change the treatment plan if the patient's condition changes. New tiny particles that can give both treatment and diagnostic images might become more common (Yu et al., 2021). These combined systems can give important information about the disease and also give the right treatment. This helps to make treatments personalized and more effective.

Clinical Implications

Potential for Patient-specific Treatment and Tailored Nanoparticle Therapeutics

Using platelet membrane-coated nanoparticles in hospitals could help make personalized medicine for patients (Zhu et al., 2021). This method might mean changing the makeup, size, and amount of medication in tiny particles to fit each patient's needs and reactions. Tailoring small particle therapies to the individual needs of a patient with rheumatoid arthritis, taking into account the severity and progression of the disease, may enhance the effectiveness of the treatment (An et al., 2024). Customized medicines can change to match the disease, making sure that patients get the best and most personalized treatments. Customized medicine using platelet-coated nanoparticles could have benefits beyond just the nanoparticles (Yaman et al., 2020). Working together with other customized treatments, like special medications or biologics, could provide complete treatment plans that take into account all the different aspects of a person's rheumatoid arthritis.

Predictive Biomarkers for Treatment Response

Using platelet membrane-coated nanoparticles in patients may require finding biomarkers that can show if the patient will respond well to this treatment (Jiménez-Jiménez et al., 2020b). Molecular or genetic signs linked to how bad a disease is and how well the body responds to nanoparticles could help doctors decide on the best treatment. Predictive biomarkers can help the treatment work and change the treatment plan if necessary (Mahler et al., 2020). Regularly checking these markers while receiving treatment might help identify who is responding well and who is not. This would allow us to make changes to the treatment plan earlier to try to improve results. Using platelet membrane-coated nanoparticles in personalized treatment for rheumatoid arthritis could become a common practice. These computer programs would look at each patient's information, like their biomarker status, to help doctors choose the best treatment(Iqbal et al., 2023). Using predictive biomarkers can help improve long-term results by allowing for a more personalized and proactive treatment approach (Tufail et al., 2024). This might help people with rheumatoid arthritis to control their disease better, have fewer side effects, and have a better quality of life.

Conclusion

Research into the use of platelet membrane-coated nanoparticles as a potential therapeutic approach for rheumatoid arthritis has resulted in encouraging findings. Rheumatoid arthritis is a persistent autoimmune condition typified by inflammation of the joints, with existing treatment modalities encountering difficulties related to insufficient effectiveness and the occurrence of adverse reactions. The utilization of nanoparticle-based therapeutics, in particular platelet membrane-coated nanoparticles, offers an innovative strategy with potential benefits for precise drug delivery. Platelet membrane coating is a technique that harnesses the inherent properties of platelets to augment the performance of nanoparticles. The nanoparticles exhibit a high degree of biocompatibility, improved localization to inflamed joints, extended circulation within the body, and decreased immune reactivity. The modulation of the immune response occurs through the inhibition of inflammatory cytokines and the regulation of immune cells that contribute to the pathology of rheumatoid arthritis. The identification of challenges, such as immunogenicity concerns and scale-up production challenges has been reported in the literature. Various strategies incorporating surface modification techniques and integration with other therapeutic approaches have been suggested as a means to address these challenges. Recent developments in technology encompass innovations in the design of nanoparticles, demonstrating the emergence of smart nanoparticles and multifunctional platforms. The potential for future treatments of rheumatoid arthritis may involve the incorporation of platelet membrane-coated nanoparticles into current therapeutic modalities, which could provide complementary and synergistic effects. The identification of predictive biomarkers linked to the responsiveness of platelet membrane-coated nanoparticles holds promise for improved patient monitoring and personalized treatment adjustments in the future.

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