ISSN No:-2456-2165

Enhancing Protein Coated Drug Delivery and their Preparation Techniques: A Review

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Abstract:- Nanoparticle coating have great potential in biochemistry and medical science. It can provide biocompatibility, prolonged blood circulation and possibly resolve the drug resistance cancer problem. This article delves into the intricate realm of protein corona formation on nanoparticles, nanoscale metal-organic frameworks (nMOFs) as drug delivery systems, and the challenges associated with nanomedicine. It explores the impact of preparation techniques on the precision and interpretation of biomolecular/protein corona, shedding light on methods, causes of methodological problems, and typical misunderstandings. Additionally, the article investigates the potential of genetically engineered biomimetic nanoparticles for altering intracellular localization and enhancing payload delivery. It discusses the importance of accurate characterization, stability, and controlled release of nanoparticles for effective drug delivery. Furthermore, it explores antibacterial coatings, silver nanoparticle coatings, and coatings made of magnetic nanoparticles, offering insights into their applications and biocompatibility. This holistic examination underscores the critical need for methodological precision in nanomedicine, with implications for diagnostics, therapeutics, and future research endeavor's.

Keywords:- *Nanoscale metal organic framework, protein corona, magnetic nanoparticles, antibacterial coating, silver nanoparticle coating, drug delivery.*

I. INTRODUCTION

The protein corona is an ever-evolving biomolecular shell that develops on the surface of nanoparticles (NPs) as a result of their interactions with biological fluids [1, 7]. Aside from enhancing the precision and reliability of procedures for creating the protein corona produced on NPs, boosting these attributes can also considerably enhance reproducibility and transparency in nanomedicine while reducing misunderstandings [4]. The approaches employed should, in turn, rely on the intended usage. In this section, let's concentrate on how preparation techniques affect the precision and interpretation of biomolecular/protein corona.

Among a variety of nonmaterial, nanoscale metal-organic frameworks (nMOFs) have shown promise as drug delivery systems [12, 14]. Nanoscale metal-organic frameworks are a relatively novel family of hybrid porous materials with organized pore structure, substantial specific surface area, and a profusion of modification sites [33]. They are made of metal ions or clusters connected by organic ligands. Because they can reach extraordinarily high drug loading capacities (LC) and interact with multiple molecules as required to perform varied activities, nMOFs have a lot of potential as drug transport carriers [39, 45]. Furthermore, the regulated release, biodegradability, low toxicity, and superior biocompatibility properties of the nMOFs are a result of the reversible coordination between the ligands and metal ions inside [216, 231].

The majority of therapeutic payloads must localize to subcellular compartments other than the endosomes in order to exhibit action, making effective endosomal escape following cellular uptake a significant problem in the field of Nano delivery [323]. By inducing membrane fusion during endocytosis, viruses can easily transfer their genetic material to the cytoplasm of host cells in nature. The hemagglutinin (HA) protein on the surface of the influenza A virus bonds the viral envelope with the surrounding membrane at endosomal pH levels [325, 342]. Here, endosomal escape-capable biomimetic nanoparticles were created employing a membrane coating made from cells that were made to produce HA on their surface. These virus-like nanoparticles demonstrated successful delivery of an mRNA payload to the cytosolic compartment of target cells during in vitro testing, leading to the production of the encoded protein. In both local and systemic administration situations, the mRNA-loaded nanoparticles considerably boosted the levels of protein expression when given in vivo [210]. Therefore, we draw the conclusion that expressing viral fusion proteins on the surface of nanoparticles coated in cell membranes via genetic engineering techniques is a workable method for modifying the intracellular localization of encapsulated payloads [325].

II. METHODS FREQUENTLY USED TO PRODUCE PROTEIN CORONA

The following steps make up the general procedure for creating a protein corona: gathering and preparing NPs; gathering biological fluids; combining NPs and fluids; incubating for a predetermined amount of time at a predetermined temperature; isolating protein corona-coated NPs; purifying to remove excess and loosely attached proteins; and characterizing the protein corona using proteomics methods [17 – 25]. The five basic techniques used to isolate protein-coated NPs are field flow fractionation, gradient centrifugation, size exclusion chromatography, and centrifugation based on centrifugation. The most often employed of these for the collection of corona-coated NPs is centrifugation [37, 40].

III. METHODOLOGICAL PROBLEMS IN PROTEIN CORONA

Protein corona data mistakes can initially be caused by inadequate knowledge of the procedures used to collect and store biological fluids (such as serum or plasma) [22, 45]. This is primarily because the stability of proteins and other macromolecules inside bodily fluids is affected by collection and storage techniques. The collection and storage process involves a variety of variables, all of which might alter the composition of the bio fluid. For instance, the anticoagulant agents employed with blood products can modify the protein corona composition by changing the biomolecular contents of plasma [51]. Another illustration is the long-term (multiyear) preservation of biological fluids, which can have a major impact on the quantity of several proteins, metabolomes, and lipids and alter the protein corona's composition [16, 49]. Therefore, strict biological fluid quality monitoring and reporting are crucial for protein corona analysis.

The accuracy of corona analysis and interpretations for both diagnostic and therapeutic reasons can be considerably impacted by preparation techniques. As a result, these techniques ought to reduce the introduction of protein contamination and contaminants [62]. The targeting/therapeutic efficacy or diagnostic capability of the protein corona may be harmed by failing to account for potential impurities and contamination. False-positive and/or false-negative results may also result from failing to account for potential impurities and contamination. For instance, recent research showed that protein contamination during size-exclusion chromatography for corona-coated NP collection is common due to coelution of unattached proteins [66 – 71].

Corona impurity is a further source of protein contamination. It has recently been shown that the protein corona layer may contain a large quantity of tiny, agglomerated contaminants unrelated to the corona composition using a combination of imaging and simulation. These contaminants may significantly skew the results of proteomics analysis, including different kinds of mass spectrometry [12, 72]. Additionally, it was stated that the NP concentration is critical in the development of these contaminants in the corona composition, indicating that lower NP concentrations would produce more reliable results. It is crucial to stress that each particle in a Nano-population may differ from the others according to its particular synthesis condition [76].

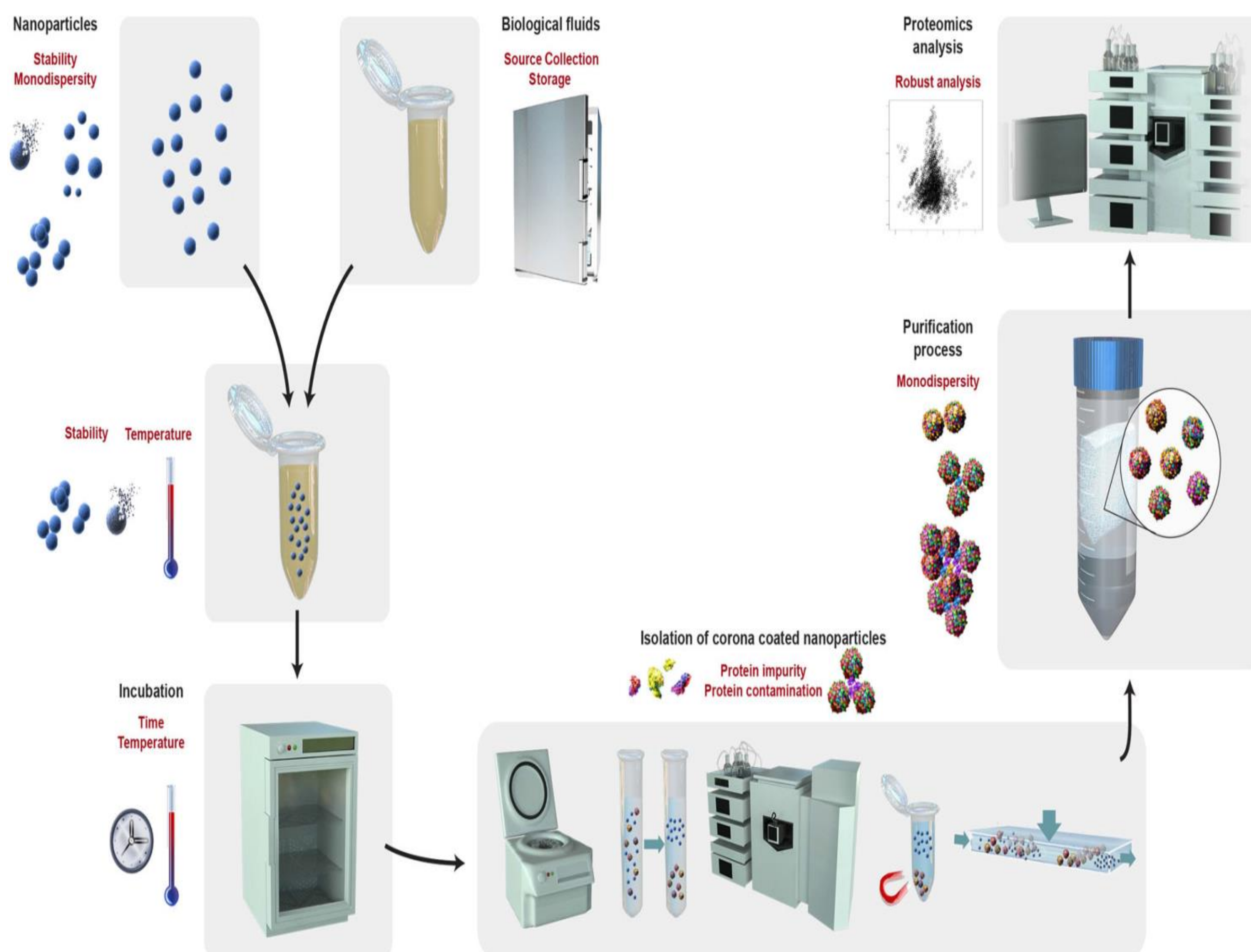

Fig. 1: General process of preparation of protein corona and common sources of errors and manipulation [80]

IV. MISUNDERSTANDINGSOURCES IN PROTEIN CORONA

In addition to the technological difficulties outlined above, there are other prevalent reasons that lead to variability in protein corona data and incorrect interpretation of proteomics results. For instance, using stable yet polydisperse NPs to prepare protein coronas can cause the results of proteomics to be misinterpreted [83]. The primary reason is that changes in NP size can have a big impact on how the protein corona is made up. Low polydispersity index (PDI) values, such as those between 0.2 and 0.3, are thought to be an appropriate homogeneous population for polymeric and lipid-based Nano carriers in order to prevent this type of misunderstanding [89].

One of the most effective ways to lessen the likelihood of incorrect interpretation of proteomics results is by careful assessment of the size and polydispersity of the NPs used to produce protein corona (particularly related mixture and purification procedures). For instance, after being put to the biological fluid, a perfectly stable and monodisperse NP could become unstable. Additionally, characterization of the size and polydispersity of the NPs after collection and purification of the protein corona and comparison to the NP's original characteristics (i.e., prior to mixture with biological fluids) are helpful in identifying potential errors in proteomics data, if appropriate techniques are available [91 – 102].

V. REDUCING METHODOLOGICAL ERRORS IN PROTEIN CORONA

Preparing protein corona-coated NPs without the common causes of scientific errors mentioned above can greatly increase reproducibility and transparency, making it easier to conduct future meta-analyses of protein corona results [105]. In order to guarantee the authenticity of proteomics results, the scientific community should pay more attention to the accuracy of the described procedures and characterizations of the various processes of protein corona creation. It is notable that successful clinical translation of nanomedicine products for both diagnostic and therapeutic uses depends critically on the validity and precision of proteomics analysis of the corona [23, 89]. The following suggestions are meant to reduce methodological mistakes made throughout various protein corona preparation procedures.

Before, during, and after the formation of the protein corona, NPs in solution should be characterized appropriately (e.g., by dynamic light scattering or differential centrifugal sedimentation), in accordance with their standard protocols [e.g., by the International Organization for Standardization (ISO) for dynamic light scattering]. This will ensure that the NPs remain stable and monodisperse throughout the experiment [108]. A simple method to reduce the likelihood of protein contamination through the creation of large aggregates is to compare the size and distribution of NPs before and after the formation of the protein corona. It is interesting that protein entrapment between NPs is facilitated by the fact that, from a physical perspective, nanoscale objects "experience" water-based solutions as highly viscous fluids (for example, molasses) [113 – 117]. The entrapped proteins will be read as data in the proteomics analysis if the size and polydispersity of the NPs are not accurately and properly characterized during the creation of the protein corona [120].

Protein impurities may be more likely to occur inside the corona shell when concentrated NPs (>0.5 mg/ml) are used to prepare protein coronas. When it is possible, new cutting-edge procedures that are appropriate for the NPs being used should be used because these types of contaminants are difficult to identify using standard methods. If high concentrations of NPs (>0.5 mg/ml) are employed, potential contaminants must be taken into account with controls and replication [122 – 128].

VI. TF-COATED (TRANSFERRIN)ACID-RESISTANT MOFS

Although the initial in vitro release test produced encouraging results, the issue of poor protein permeability in the intestinal epithelial cell layer needed to be resolved, and there was still a lack of in vivo study evidence to demonstrate whether successful INS (insulin subcutaneous injection) absorption was possible [131]. As far as we are aware, there hasn't been any research on MOF (Metal organic frameworks) -based nanosystems safeguarding INS from a harsh environment while enhancing INS penetration efficacy to finally produce a superior hypoglycemic impact [134].

Additionally, the Tf-coated acid-resistant MOFs oral delivery nanosystem may quickly enter intestinal cells, escape from lysosomes for deeper penetration, which is sufficient for quick and effective intestinal transportation and finally delivering a positive therapeutic impact [138]. Additionally, the creation of such a nanosystem is straightforward, inexpensive, and scalable because it is based on a single-step solvothermal reaction using accessible starting materials. This study demonstrated the significant potential of effective oral protein delivery by using the targeted protein-coated acid-resistant nMOFs for oral INS injection [140, 143].

VII. CREATION AND EVALUATION OF PROTEIN DELIVERY NANOSYSTEMS BASED ON NMOF

The simple one-step solvothermal approach produced nanoparticles with consistent, regular octahedron forms. After loading the INS, the NPs' shape and particle size saw minimal alteration. The regular octahedron has relatively acute hydrodynamic diameters and angles. The angles of NPs became blunted when varied amounts of Tf were painted on the surface by physical adhesion [146 – 151].

Following Tf coating, the morphology of NPs gradually transformed from a conventional octahedron to a spherical, and their size grew. After loading with INS and additional decorating with Tf, the zeta potentials of NPs increased from +25 to +35 mV and almost reached +40 mV. UV-visible (UV-vis) spectroscopy was used to confirm that the rhodamine B isothiocyanate (RITC)-labeled INS was

ISSN No:-2456-2165

successfully immobilized in NPs. Additionally, the optical images and confocal laser scanning microscopy (CLSM) results showed that the RITC-labeled INS was dispersed across the crystals [154, 155]. Due to the positively charged nature of NPs and INS in the acidic loading process (pH 4), hydrophobic interactions rather than electrostatic interactions were primarily responsible for the INS encapsulation [160].

VIII. TF-COATED NMOFS' IN VITRO STABILITY AND PROTEIN PROTECTIVE ABILITIES

By observing the changes in size and morphology under various conditions and over varying time periods, it is possible to assess the in vitro stability of the nanosystems. Due to the excellent acid-proof stability of the nanoparticle, no discernible change in particle size was seen when various formulations were distributed in a simulated stomach pH environment [164]. In contrast, the nanoparticle started to cluster together and dissolve if the particle size increased significantly under physiological conditions. The deconstruction was significantly delayed after Tf decoration, proving that Tf decoration gave the nanosystem slow-release performance under physiological settings [166].

IX. SUSTAINED AND CONTROLLED INS RELEASE KINETICS

As a successful oral delivery Nano carrier, has demonstrated that it is capable of providing enough protection for INS against challenging circumstances. In addition, it was necessary for the acid-resistant nMOFs to release INS steadily under physiological circumstances. Effective release kinetics has been provided by the release profiles of INS in simulated GI environment and simulated physiological circumstances [168 – 174].

To mimic the state of medications taken orally, the continuous release of INS in various conditions was also assessed. Under acidic to neutral pH conditions in the stomach and intestine, hardly any INS was released. However, started to disassemble and release INS after being incubated in a neutral PBS environment [177]. While the percentage of released INS was only about 80% in PBS, the INS was virtually entirely released within 10 hours. In line with the stability finding, Tf marginally reduced the rate of INS release and hampered the disintegration [178]. The aforementioned findings showed that phosphate in PBS, as opposed to pH, specifically stimulated the release of INS from Tf-coated nMOFs, which had a significant sensitivity to the environment.

X. ANALYSIS OF BIOCOMPATIBILITY AND LONG-TERM SAFETY

Live/dead imaging was used to examine the biocompatibility of the nanosystems in vitro [181]. Even at concentrations of 500 g/ml, all samples showed low cytotoxicity (cell viability >85%) on three separate cell lines, which was further supported by live/dead labeling. NP was incubated with erythrocytes for 4 hours to test for possible cell membrane breakdown; however there was no sign of hemolysis. When the concentration reached 1 mg/ml, the hemolysis rate was 3.23%, demonstrating that NP seldom damaged cell membranes [183 -185].

While this was going on, when the cell monolayer was exposed to NP, there was no noticeable drop in transepithelial electrical resistance (TEER), which supported the integrity of the tight connections. Examine the possible long-term toxicity of the nanosystem by an extensive in vivo experiment, which is motivated by the low toxicity of single-dose [188]. After receiving treatment twice daily for seven days straight, the mice's small intestinal tissue showed finger-like villi, demonstrating the intestine's structural integrity. In addition, the organs and small intestine tissue showed no obvious structural damage [192]. The aforementioned findings supported the nanosystem's strong biocompatibility.

XI. TF-MEDIATED INCREASED CELLULAR INTERNALIZATION AND TRANSEPITHELIAL ACTIVITY

Human colon adenocarcinoma (Caco-2) cells are currently being used to research the transportability of drugs across the intestinal barrier to forecast drug absorption. These cells have a structure and function that is comparable to small intestinal epithelial cells [195 – 198]. This study investigated whether Tf-coated nMOFs could cross the intestinal epithelium by TfR-mediated endocytosis and successfully evade the lysosome for deeper penetration using Caco-2 cells as an in vitro model [200].

XII. IMPROVED PENETRATION EFFICIENCY

After the Tf-coated nMOFs were discovered to be efficient at the cellular level in previous in vitro experiments, this research further validated the ability to transport across the small intestinal ex vivo since the intestinal epithelium layer has been considered the most difficult barrier to the oral absorption of Nano carriers [202, 204].

XIII. CELL MEMBRANE-COATED NANOPARTICLES

To maximize the therapeutic potential of drug payloads, it is critical to achieve the correct subcellular localization [206]. Delivery of Nano therapeutics to the cytosol, which contains cellular machinery that is the target of many treatments, has long been a significant obstacle. Notably, the endolysosomal pathway, which cells frequently use to trap and destroy foreign particles, presents a challenge for Nano delivery vehicles. After merging with lysosomes, where nanoparticles can be destroyed by acids and enzymes, endosomes go from being weakly acidic early endosomes to being more acidic late endosomes. The proton sponge strategy, in which nanoparticles are made with buffering properties that enable them to break endosomes via osmotic swelling, is one option to avoid this process [34, 209].

Alternately, you may create leaky endosomes by destabilizing the cell's plasma membrane during endocytosis and before it forms. Using nanoparticles that can move directly over the plasma membrane and into the cytosol due

to their structure and charge allows for the complete avoidance of the endosomal pathway [211 -215]. Unfortunately, many of these traditional methods of cytosolic administration have a history of cytotoxicity, making clinical application challenging [217].

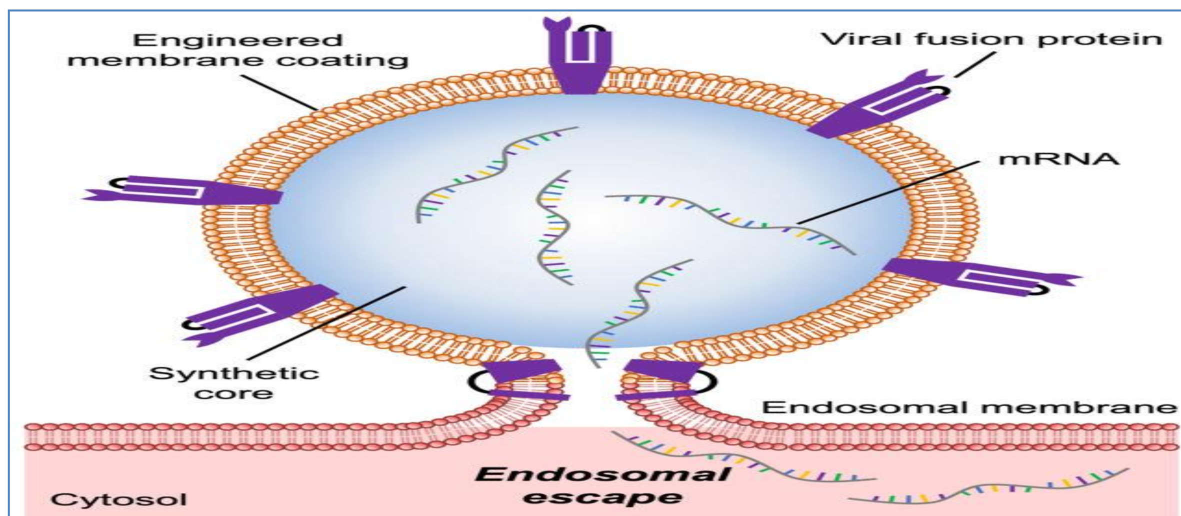

Fig. 2: Cell membrane coated nanoparticle [220]

XIV. CYSTOLIC DELIVERY OF MRNA

The majority of viruses need their genetic material to be delivered into the cytosol in order to replicate. In order to avoid being destroyed, several viruses have developed ways to get out of the endosomal compartment [222]. The hemagglutinin (HA) protein found on the surface of the influenza virus aids in this function. After being expressed, HA undergoes proteolytic cleavage to transform into its mature form, yielding two subunits. The HA1 component enables the virus to bind to the target cells' plasma membrane and start endocytosis [225, 227]. Following endocytic absorption, the HA2 component goes through a conformational change brought on by a drop in pH that makes it easier for the viral envelope and endosomal membrane to fuse.

XV. CELL MEMBRANE COATING

Cell membrane coating is a newly developed top-down strategy for improving the bio interfacing properties of Nano carriers [230]. For instance, erythrocyte membranes have been exploited to increase the time that nanoparticles spend in the bloodstream, while cancer cell and platelet membranes have been used to deliver drugs to specific targets [232]. In more recent years, genetic engineering techniques have been used to create cell membranes that are enhanced with a particular surface marking, allowing researchers to specifically alter the functionality of cell membrane-coated Nano formulations. Complex surface proteins that would be impossible to include using standard synthetic techniques can be added to these designed nanoparticles [235 – 242].

In this study, we designed a cell membrane-coated nanoparticle to show HA, resulting in a Nano carrier with increased cytosolic transport and endosomal escape capabilities that match those of a virus [236]. We chose to test our Nano formulation’s capacity to deliver model mRNA payloads both in vitro and in vivo given the growing interest in mRNA-based vaccinations [243]. Overall, the disclosed method is a strong method for increasing the usefulness of cell membrane-coated Nano carriers, especially for the administration of medications that need to be localized in the cytosol [245].

XVI. MODEL VIRAL PROTEIN FOR EXPRESSION

Due of its potent ability to promote fusion, HA subtype H7 was selected as a model viral protein for expression. Furthermore, as H7 specifically targets 2, 3-linked sialic acid, we were able to test our platform in vivo using mouse models [245, 247]. The H7 expression plasmid was transfected into wild-type B16F10 cells (referred to as "B16-WT") to create engineered cells (referred to as "B16-HA") that have a lot of the viral fusion protein on their surface. The functioning of the HA transgene was assessed in vitro using a cell-cell fusion investigation because B16-WT is known to express 2, 3-linked sialic acid.Two aliquots of B16-HA cells were divided, and each aliquot was stained with either Cell Trace Far Red or Cell Trace Violet [248 – 253].

The two dye-labeled aliquots were combined, the cell mixture was treated with L-(tosylamido-2-phenyl) ethyl chloromethyl ketone (TPCK) to induce HA maturation, and then endosomal pH was applied to encourage fusion activity. The cells were examined by flow cytometry after 2 hours of incubation, and the results showed a sizable population of cells that were positive for both Cell Trace Violet and Cell Trace Far Red [251 – 257]. This demonstrated that the HA on the modified cells' surfaces was functional and capable of encouraging cell-cell fusion. In contrast, B16-WT cells exposed to the same experimental technique and examined using flow cytometry revealed a minimal proportion of double-positive cells [259, 261]. Please be aware that our research was unable to discriminate between fusion events between cells that were labeled with different dyes or detect events between three or more cells [265].

XVII. NANOPARTICLES WITH MRNA LOADED

The engineered B16-HA cells were harvested once HA expression was verified to have been successful, and their membrane was extracted as previously explained. Then, using a sonication procedure, the pure cell membrane was coated onto prefabricated poly (lactic-co-glycolic acid) (PLGA) nanoparticle cores. mRNA was added to the PLGA nanoparticle cores using a twofold emulsion technique with the help of the cationic lipid-like molecule G0-C14 [268 – 272].

The resulting mRNA-loaded nanoparticles coated with B16-WT and B16-HA membranes, referred to as "WT-mRNA-NP" and "HA-mRNA-NP," respectively, had average diameters of around 185 nm and zeta potentials of about 20 mV. Negatively stained HA-mRNA-NP by transmission electron microscopy proved that the membrane was adequately deposited onto the polymeric cores [274 – 278]. Western blotting analysis was used to check for the presence of HA on the isolated cell membrane and on the Nano formulations. Both the final HA-mRNA-NP formulation and the membrane made from B16-HA were visibly covered in HA [280, 281].

XVIII. EXPRESSION OF A VIRAL FUSION PROTEIN IN CELL MEMBRANE

In this study, the surface of mRNA-loaded nanoparticle cores was coated with a cell membrane modified to produce a viral fusion protein. This allowed the resulting HA-mRNA-NP formulation to replicate the ability of some viruses to achieve endosomal escape [285]. Influenza On the surface of mouse cells, a virus of the HA subtype H7 attached to 2, 3-linked sialic acid, causing endocytic absorption. The reduced pH in the late endosomes caused the HA to induce membrane fusion, allowing the contents of the nanoparticles to be released into the cytosol [287, 289].

We examined the modified cell membrane-coated nanoparticles' capacity to exit the endosomal compartment and stimulate the expression of two representative reporter genes in vitro in order to demonstrate our theory [291]. The HA-expressing nanoparticles greatly outperformed a control formulation created using the membrane of wild-type cells devoid of the viral transgene in both instances. In vivo tests revealed that CLuc-mRNA-loaded HA-mRNA-NP could considerably increase levels of the encoded protein in both local and systemic injection settings [293 – 298].

XIX. MRNA-BASED VACCINATIONS

It would be ideal to have efficient means of delivering mRNA, especially considering the recent interest in mRNA vaccines brought on by the COVID-19 pandemic [302]. One of the main challenges in mRNA Nano delivery is endosomal escape since the payload needs to be in the cytosol to perform its biological function [308, 310]. Using naturally occurring viral fusion proteins, such as influenza virus HA, could offer a sophisticated answer to this problem, as we have shown here [303,305]. We were able to put HA in its natural context on the surface of nanoparticles using cell membrane coating technology in conjunction with genetic engineering, a feat that would otherwise be challenging using traditional functionalization techniques [307]. Future research will be needed to confirm the effectiveness of this method in particular mRNA applications, like vaccination and gene therapy. In the end, this kind of research may produce brand-new methods for regulating the subcellular localization of therapeutic payloads, hence enhancing the applicability of biomimetic nanomedicine [310].

XX. ORGANIC COATED NANOPARTICLES

Using an eco-friendly Ag+ in situ reduction technique, a soy protein isolate Nano-silver hydrosol was created. The soy protein was then ultrasonically combined with polyacrylic resin to create a polyacrylate-nano silver antibacterial wood coating. The structural, antibacterial, and mechanical properties of the film were examined, as well as the structure of the soy protein isolate Nano-silver hydrosol [312 – 315]. The outcomes demonstrated that the silver nanoparticles (AgNPs) were equally dispersed throughout the emulsion and had good crystallinity. Escherichia coli, gram-negative bacteria, and Staphylococcus aureus, gram-positive bacteria were used as models for the composite film's antibacterial performance. The diameter of the inhibitory zone grew from 0 to 30 mm and from 18 to 50 mm for the two bacteria, respectively, with increased Nano-silver content. Additionally, as the AgNPs content changed from 0.1 to 1%, the film's elastic modulus increased from 8.173 to 97.912 MPa and its elongation at break fell from 240.601 to 41.038%. Thus, a new technique for creating aqueous polyacrylate coatings with outstanding antibacterial properties [316 – 322].

XXI. ANTIBACTERIAL COATINGS

Based on the types of antibacterial agents applied, antibacterial coatings can be categorized as natural antibacterial coatings, organic antibacterial coatings, inorganic antibacterial coatings, and composite antibacterial coatings [324]. Natural antibacterial compounds, like chitosan, have strong antibacterial capabilities and good biocompatibility but cannot be mass-produced because they start to carbonize and degrade above 160–180°C [326]. Organic antibacterial agents use small, poisonous compounds but have good performance, strong color persistence, and short-term antibacterial effects [326, 327]. Because they have the potential to be developed, researchers are looking into inorganic antibacterial agents more and more. Among them, AgNPs demonstrate low toxicity, great anti-fouling and broad-spectrum antibacterial efficacy, and strong adsorption capacities [329]. They combine the benefits of inorganic antibacterial materials and Nano antibacterial materials. As a result, these substances show promise as super antibacterial substances. Ag+ ions released over time are what give AgNPs their biocidal action, and the photocatalytic qualities of their surfaces can cause oxidative damage to nearby cells [330 – 334].

XXII. SILVER NANOPARTICLE COATING

The current techniques for making Nano-silver can be categorized based on their physical or chemical preparation [337]. Laser ablation, microwave reduction, quenching, and mechanical grinding are examples of physical preparation techniques [339, 340]. Physical methods offer excellent purity and a straightforward process, but they also require more equipment and have significant manufacturing costs [342]. A reducing agent, such as sodium borohydride or sodium zirconate, must be added to a silver precursor using chemical reduction procedures in order to convert the precursor into elemental silver, which then develops into silver particles. Because silver particles tend to clump together readily, stabilizers or dispersants like polyethylene glycol, mercaptan derivatives, aniline, long-chain amines, and surfactants are frequently used to prevent this from happening [343 – 346]. The reagents employed in traditional chemical procedures are toxic to both people and the environment, and some stabilizers and dispersants are even carcinogenic, yet they are low cost and high yield. The need for non-toxic preparation substances is therefore increasing [346, 348]. Researchers have focused a lot of attention on soy protein since it is safe, affordable, biodegradable, and environmentally friendly. Two significant soy protein constituents that predominate are soy glycinin (11S globulin) and glycinin (7S globulin) [350]. Additionally, specific amino acids from soy protein isolate (SPI), like tyrosine and cysteine, can be employed as reducing agents for metal ion precursors. Additionally, the SPI surface's amino and carboxyl groups have a great affinity for silver particles and can be employed to stabilize the silver particles [351, 353].

XXIII. COATINGS MADE OF MAGNETIC NANOPARTICLES

Magnetic nanoparticles (MNPs) offer a lot of potential in biochemistry and medical research. Due to their strong magnetic characteristics, substantial surface area, durability, and ease of functionalization, iron oxide nanoparticles in particular have shown a potential effect in a variety of biomedical applications [355 – 357]. For their use in vivo, MNPs' colloidal stability, biocompatibility, and potential toxicity in physiological settings are essential considerations [359]. Numerous research articles in this regard concentrated on potential methods for coating MNPs to enhance their physical-chemical and biological features [362]. The review focuses on a practical method for producing biocompatible iron oxide nanoparticles that uses human serum albumin (HSA). HSA has numerous roles in numerous essential processes; however it is primarily a transport protein [363, 365]. None of the drugs in the blood pass without it because it is one among the most prevalent plasma proteins. It binds to the surface or forms a protein corona to affect the stability, pharmacokinetics, and bio distribution of several drug-delivery methods [367, 368].

XXIV. MAGNETIC NANOPARTICLES COATED WITH ALBUMIN BASED DRUG CARRIER

The creation of albumin-based drug carriers is becoming more and more significant in the targeted administration of cancer therapy, which is why magnetic nanoparticles with albumin coating are used [370]. In light of this, HSA is a highly promising candidate for the theranostics and nanoparticle coating fields and can offer biocompatibility, longer blood circulation, and perhaps even a solution to the drug-resistant cancer problem [374, 376].

Magnetic nanoparticles (MNPs) have a wide range of uses, including as contrast agents in MRI, in material science, for magnetic transport, for magnetic fluid hyperthermia, for structural biology, for delivering drugs and genes, and for theranostics. Due to their great stability, cost effectiveness, and ideal MRI and hyperthermia characteristics, iron oxide MNPs are promising tags [382 – 388].

The separation of MNPs from any liquids and the intended site is made simple by manipulation with an external magnetic field [391, 393]. Theranostics (treatment + diagnostics) and targeted drug delivery are two areas where combining ways of induction local heating in the tumor location, anticancer medicines, and good monitoring by MRI has a tremendous promise [395, 396]. Magnetite, Fe3O4, is one of the most prominent ferromagnetic MNPs. However, Fe3O4 aggregates because of its high surface energy and instability under oxidation. Surface functionalization is therefore necessary for such MNPs [398]. The development of highly reactive oxygen species (ROS) in cell lines and animal models as a result of the incorrect coating causes instability in the bloodstream and immediate or delayed toxicity [399 – 402].

XXV. DISCUSSION & CONCLUSION

Protein coating often has reduced cytotoxicity of MNPs and is biocompatible, biodegradable, and less immunogenic. Human serum albumin (HSA) has recently been used in biotechnological applications, such as coating nanoparticles and creating materials that are inspired by living things [405]. Instead, the aforementioned protein coating contains albumin, one of the main proteins found in human plasma, which decreases unintentional blood component adsorption and improves tissue and cell targeting [408, 411].

Gp60, Gp30, Gp18, and FcRn receptor binding enables albumin-constructions transcytosis in the cells. Additionally, binding to the SPARC receptor and the increased permeability and retention effect (EPR) promote accumulation in a tumor [413 – 417]. Many pharmacological or naturally occurring ligand binding sites can be found in the albumin structure, which can be utilized for therapeutic loading. Here, the human serum albumin is coupled with coating characteristics for magnetic nanoparticles [420, 422]. This evaluation presents an overview of the available options for the first time and offers suggestions for potential future technological developments. Studies have been done on the structure of albumin, drug

binding sites, and its passive and targeted distribution, which show how versatile and biocompatible albumin [425, 428].

It is also mentioned that albumin modification with reporter groups, medicines, and imaging residues may be employed to further coat MNPs. Such approaches are appropriate for the creation of theranostics or multimodal imaging smart platforms based on MNPs core [430]. MNPs' coating by albumin as a water solution, Biosystems stability, low toxicity, tailored distribution in vivo, and some physical property enhancements are their benefits. Researching MNP stability and coating techniques paves the path for bioinspired and multifunctional materials, probes, and devices [432 – 436].

The advantages of enzyme-assisted hydrolysis include minimal side effects, mild hydrolysis responses, and minimal amino acid degradation. Therefore, the soybean protein isolate's peptide bonds were broken while leaving the amino acid structure and configuration intact by using bromelain hydrolysis [440 – 445]. Tyrosine was used to decrease silver ions and stabilize elemental silver during the in-situ preparation of AgNPs, which were subsequently ultrasonically blended with a polyacrylic resin emulsion [452]. After that, the matching antibacterial coating was created by UV curing, and its antibacterial effectiveness was assessed [458]. This environmentally friendly formulation of Nano-silver hydrosolized soybean protein isolate for antibacterial wood coatings has promise and numerous development opportunities [460 – 463].

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