Impact of Vroman's Effect on Pharmacodynamics and Pharmacokinetics on Nanoparticulate Drug Delivery Systems

Chinthaginjala Haranath1,*, Krishnam Sai Vamsi1, Yousef AM Qarmout1, Hindustan Abdul Ahad2, Samuluru Chandana3
1Department of Pharmaceutics, Raghavendra Institute of Pharmaceutical Education and Research (RIPER)- Autonomous, Ananthapuramu, Andhra Pradesh, INDIA.
2Department of Quality Assurance, Raghavendra Institute of Pharmaceutical Education and Research (RIPER)- Autonomous, Ananthapuramu, Andhra Pradesh, INDIA.
3Department of Industrial Pharmacy, Raghavendra Institute of Pharmaceutical Education and Research (RIPER)- Autonomous, Ananthapuramu, Andhra Pradesh, INDIA.

ABSTRACT
Nanoparticle drug delivery can produce a unique pharmacokinetic and pharmacodynamic effect and unveiled better safety in vivo and in vitro toxicity profiles when compared with conventional drugs. In 1960, Vroman revealed that competitive protein exchange is a general phenomenon that occurs when a protein mixture adsorbs to a surface is called ‘Vorman’s effect’ which is responsible for the fate of the nanoparticles. The development and formation of protein corona on nanoparticles is due to the adsorption of proteins on the surface. It is vital in specific targeting and alter the size and composition of the nanoparticle. The entropy-driven binding manages this adsorption of protein on the surface. Binding of polyethylene glycol to the nanoparticles decreases the non-specific binding and increases the targeting of tissue via enhanced permeability and retention effect. An individual disease state and components in biofluids can modify the structure and shape of protein corona on nanoparticles. By label-free transducers, we can detect targets using Vroman’s effect. The biological identification of nanoparticles can lead to deleterious consequences, such as immunotoxicity, due to the formation of the protein corona.

Keywords: Vroman's effect, Nanoparticles, Protein corona, Disease state, Biofluids.

Correspondence
Dr. Chinthaginjala Haranath,
Associate Professor and Head, Department of Pharmaceutics, Raghavendra Institute of Pharmaceutical Education and Research (RIPER), KR Palli Cross, Chiyyedu Post, Anantapur-515721, Andhra Pradesh, INDIA.
Email id: haranathriper@gmail.com
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INTRODUCTION
Nano-drug delivery shows long-term effectiveness in the blood and produces therapeutic action up to a specific period. Nano-drug delivery can deliver the drug to the mutated cells by carrying the diversified cargos, including the hydrophobic and amphiphilic drugs and genes. Nano-particle drug delivery can produce a unique pharmacokinetic and pharmacodynamic effect. After entering the nanoparticles (NP) into the body, they interact with proteins present in the blood. By giving drugs in low doses, it minimizes the chances of drug toxicity. Nano-drug delivery systems decrease dosage frequency, improve patient compliance, safety and biocompatibility, minimize toxic effect and maintain therapeutic effect (Figure 1). Physicists have studied the Vroman effect, in which proteins bound on a surface are displaced by later entering proteins. Competitive protein exchange is a general phenomenon that occurs when a protein mixture adsorbs to a surface.

Hard and soft coronas
The hard, soft, and interfacial protein coronas make up the protein corona on the Nanoparticle surface. The Corona consists of a strongly bonded monolayer, whereas the soft part is bounded and present on the top, and rapid exchange of proteins occurs. The Vroman effect involves the exchange of proteins competitively on the surface of a protein mixture. Small molecular proteins were initially coated and adsorbed onto the surface, followed by larger molecular weight proteins. This protein interchange was depending on the molecular weight of the proteins - ranging from low to high.

Development of the protein corona - molecular aspects
The fate of nanoparticles is determined by the coat of protein corona that surrounds their surface. The type of corona formation on the nanoparticles could depend upon the binding strength, dissociation rate, surface area and charge. Blood contains different types of proteins like a soft and hard corona.

Impact of the np-biomolecule corona on the biological system
Polyethylene glycol-modified the surface of the nanoparticles decreases the degradation of immune-mediated Nanoparticle or folic acid, over expresses folate receptors, and enhances the intended site drug delivery. The uneven development of blood vessels in the tumor setting has resulted in leaky vasculature. The ideal parameters of the surface ligand of the nanoparticles are modified for effective targeting. Other variables, such as tumour kind, level, height, and systolic blood pressure, among others, have a significant impact. In this domain, PEGylation has become the global standard. According to several studies, binding of
Factors Influencing Corona Formation

The nanoparticle nature of the protein corona is modified by the environment. For instance, protein glycation improves the anaerobic metabolism of low-density lipoproteins (LDLs) in diabetic patients, allowing soluble albumin to decrease. Liver diseases can also alter the detected amount of albumin in the blood. Therefore, as therapeutic biomarkers, some plasma proteins, including albumin, help to diagnose medical conditions. Smoking contributes to increases in nitrotyrosine plasma protein alterations, decreasing fibrinogen (coagulation factor) and surfactant protein (SP)-A. The cancer secretome refers to the huge amount of proteins released into physiological secretions by cancer cells and organs. Hundreds of tumor-derived proteins, such as autoantibodies, have been discovered. Plasma proteins from disease states such as cancer can contribute to the production of coronas on nanoparticles. Muller et al. Research focused on how polymeric NPs infuse lipids into the PC, Physicochemical properties of two oppositely charged lipid nanoparticles treated with plasma from patients with pancreatic cancer or stable have been studied. The zeta potential of simple, ionised lipid nanoparticles treated with plasma from patients with pancreatic cancer or stable have been studied. The zeta potential of simple, ionised lipid nanoparticles treated with plasma from patients with pancreatic cancer or stable have been studied.

Factors that influence corona formation.

PEG to NPs reduces non-specific serum protein binding, improving the targeting of passive tumor tissue via the EPR effect.

Choosing the optimal surface density and PEG length for the NP delivery procedure is crucial. In certain situations, various preparations of PEG-liposome generated unique coronas on NPs, inhibiting cellular absorption. Increased PEG length lowered liposome protein adsorption, apolipoprotein affinities, and even the absolute amount of opsonins collected. On the other hand, Papi et al. PEGylation of Onivyde, a liposomal FDA-approved medicine, was revealed to be somewhat vital than particulate chemistry for stealth effects. Whereas prolonged circulation times are necessary for active targeting, effective absorption of NP cargo by target cells is essential for therapeutic efficacy.

DISEASE STATE ON CORONA FORMATION

The Vroman effect can be explained without using any bioreceptors. Surface plasmon resonance (SPR) may be a label-free technique. The adsorption of proteins is examined by angle shift SPR, i.e., high molecular proteins displace low relative molecular mass proteins. An individual’s disease state or lifestyle may alter plasma proteome and also the shape of a PC. For instance, protein glycation improves the anaerobic metabolism of low-density lipoproteins (LDLs) in diabetic patients, allowing soluble albumin to decrease. Liver diseases can also alter the detected amount of albumin in the blood. Therefore, as therapeutic biomarkers, some plasma proteins, including albumin, help to diagnose medical conditions. Smoking contributes to increases in nitrotyrosine plasma protein alterations, decreasing fibrinogen (coagulation factor) and surfactant protein (SP)-A. The cancer secretome refers to the huge amount of proteins released into physiological secretions by cancer cells and organs. Hundreds of tumor-derived proteins, such as autoantibodies, have been discovered. Plasma proteins from disease states such as cancer can contribute to the production of coronas on NPs. Muller et al. Research focused on how polymeric NPs infuse lipids into the PC, Physicochemical properties of two oppositely charged lipid nanoparticles treated with plasma from patients with pancreatic cancer or stable have been studied. The zeta potential of simple, ionised NPs incubated in plasma from pancreatic and healthy people differed only little, hinting that NPs with differing charges might attract distinct
proteins.\(^{42-44}\) NPs function as a nano-concentrator by generating a corona peculiar to the liquid sample and isolating rare plasma proteins with therapeutic value.\(^{44}\) A study of the properties of carbon nanotubes (CNTs) generated underlying flaws, which was not detected with stable mouse serum. Protein corona (PC) may be generated by an overabundance of cholesterol binding to NPs in other proteins. Lipids play a key role in PC proliferation.\(^{45-46}\)

Research by Shannahen et al.\(^{47}\) shows the capacity for the inflammatory response aortic endothelial cells of sera-treated iron oxide NPs from hyperlipidemic individuals show capacity for an inflammatory response.

Intermediates such as glucose or cholesterol impact the immunogenicity of fibrinogen-NP complexes. Modifying plasma components and influencing the development of NP coronas are also conceivable. NPs travel through the lining of the Respiratory tract fluid (RTLF) and influencing the development of NP coronas are also conceivable. NPs interact with the pulmonary surfactant substrate, they can form a PC that differs from that produced in the blood. The PCs produced on NPs comprised core proteins, like as SP-A, SP-B, and SP-D, and lipids, which appeared to be devoid of molecular properties.\(^{50-51}\)

**BIO-FLUIDS MODULATE THE STRUCTURE OF CORONA**

The structure of the corona is modulated by the biofluids present in the body. Corona protein's long-term development is influenced by the physical and chemical features of nanoparticles. The underlying biological environment is the most effective tool for encouraging the PC structure.\(^{52-55}\) Protein absorbent in the surrounding atmosphere was depending on protein content, according to an early investigation of NPs in plasma utilising silica and sulfonated polystyrene NPs. This was one of several studies to indicate that because of environment-influenced variations in the PC, the same NPs can behave differently.\(^{56}\)

Another study found that minor discrepancies in the PC generated on NPs can occur due to factors such as blood selection, whether whole using EDTA or RPMI and PBS media to counteract coagulation.\(^{55}\) The detection and behavior of NPs have vital implications for the design of nanomaterials as diagnosis and treatment plan, affected by changes in the physiological system. NPs were developed for human PCs containing immunoglobulins, supplements, and apolipoproteins, while different proteins, such as fibrinogen, were absorbed by the same NPs in the mouse serum.\(^{57}\)

**NANOTOXICITY AND THE BIOMOLECULE CORONA**

The formation of the Precursor polycyclic plate (PC) by macrophages can alter the identification of non-potentiated Phagocytic Phosphates (NP) in response to Bovin Serum Albumin. By potentiating NPs holding titanium dioxide (TiO\(_2\)) in the PC, enhanced release of inflammatory cytokines IL-18 and IL-6 from human macrophage was seen.\(^{37}\) PC was made with disulphide-stabilized poly(methacryl) acid nonporous polymeric NPs, which inhibited the NPs' ability to be internalised by human monocytes (THP-1) in a way similar to how BSA defined FBS-containing media for PC development.\(^{58}\)

**CONCLUSION**

Vroman has observed competitive exchange of proteins on the surface of nanoparticles. Nanoparticles interact with body fluids like blood and forms corona on the nanoparticles surface. Corona size and composition are altered by the generated corona, which varies depending on the protein present in the surrounding systems. The creation of hard corona around nanoparticles is primarily due to apolipoprotein A-1, whereas Human serum albumin is responsible for forming soft corona in the biological environment. Disease state can be detected by label free transducers by using Vromans effect.

**CONFLICT OF INTEREST**

The authors declare that there is no conflict of interest.

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