International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 4 July-Aug 2024, pp: 738-747 www.ijprajournal.com ISSN: 2456-4494

The Uniqueness of Albumin as a Carrier in Nano Drug Delivery

Subhashish Mahakur[1], Dr.Himani Tiwari[2], Dr.Kaushalkiashore Chandrule[3]
1 Student Of M.Pharma (2nd Year), 2 H.O.D Of Pharmacy, 3 Dean Of Pharmacy
Department Of Pharmacy Mewar University Chittorgarh (Rj), India

Date of Submission: 20-07-2024 Date of Acceptance: 30-07-2024

ABSTRACT
Human serum albumin (HSA)-basedodrug delivery systems (HBNDSs) have attracted a lot of attention in nanomedicine. There are reasons behind this! Many clinical trials have shown great success, plus nanotechnology is advancing quickly. However, we're still missing in-depth reviews that look at the broader uses of HBNDSs outside just cancer treatment. Albumin, with its unique qualities, makes an excellent carrier in nanomedicine—it's great at compatibility, breaks down nicely, doesn't cause immune reactions, & is very safe. Being the most plentiful protein in our blood makes it perfect for treating illnesses.
Also, the chemical structure and shape of albumin mean it can work well with many medications. This can help protect them from being broken down in the body & boost their effectiveness. Plus, albumin can connect with receptors that are more common in sick tissues. This means we can target disease locations without needing extra ligands in the nano carrier! That's pretty nifty, right?
Albumin's serum half-life is about 19 days. This helps prolong the effects of drugs and makes sure they are delivered just where needed. Nanodrug delivery works to change how we treat illnesses by giving powerful medications exactly where they're needed while reducing side effects & improving results. This fits perfectly into precision medicine, too! It requires careful control over how drugs are given for tailored treatments. Albumin steps in as a vital player here, bringing a bunch of benefits that make it a fantastic option for creating nanocarriers.
Keywords: albumin, clinical trial, human serum albumin, nano drug delivery

I. INTRODUCTION

The world of medicines is really excited about nanotechnology. It shows a lot of promise, especially when it comes to delivering drugs effectively. With the help of tiny materials, scientists can create special platforms. These platforms can help with how we deliver, protect, and move hard-to-handle medicines. This includes things like proteins, gene therapies, & medicines that don't dissolve well in our bodies. They aim for specific cell targets too! What's cool is that nanoparticles can break through barriers that older methods couldn't. These nanoparticles, which are made from fats, polymers, or even metals, have repeatedly shown they can control where the medicine goes in our bodies and how it's released. So they might help us get the medicine exactly where it's needed, especially in sick areas. But, there's a catch! Depending on how they are made, some of these tiny carriers have faced challenges. Sometimes they struggle to get into cells where the drugs need to be. Other issues include triggering the immune system in ways that we don't want or ending up in places we didn't aim for. Also, there can be trouble with controlling how the drugs are released once inside our bodies. On the flip side, traditional ways of delivering drugs—like taking pills or getting injections—are not perfect either. Pills can be tricky since they might not work well after passing through the stomach & liver. Sometimes they don't get absorbed as we'd hope! Meanwhile, injections can do their job quickly but may also spread around our bodies and cause some unexpected side effects.

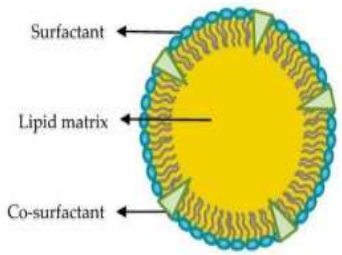

Fig No. 1: Overview of Nanoparticles

Nanodrug Delivery Advantage:-
1. Poorly soluble drugs can really benefit from being wrapped up in nanoparticles. This makes them more bioavailable & effective!
2. When we add ligands or other special targeting bits to nanoparticles, they can stick to specific receptors on sick cells. This clever approach keeps

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 4 July-Aug 2024, pp: 738-747 www.ijprajournal.com ISSN: 2456-4494

more of the medicine away from healthy tissues, which means fewer side effects!
3. Isn't it neat? We can design nanoparticles so that they slowly release their medication over time. This leads to longer-lasting effects and means you don't have to take doses as often.
4. Also, nanoparticles act like tiny shields! They help protect medications from enzymes & chemicals that might break them down, boosting their stability and effectiveness.
Albumin: -Albumin makes up about 55% of the in human blood plasma. Wow, that's a lot! It's the most common protein found there. This molecule does so many important things. It bind & detoxify harmful stuff, carries hormones, delivers minerals, and keeps our bodily fluids balanced.

STRUCTURE AND PROPERTIES OF ALBUMIN

Now, albumin is a globular protein made from around 585 amino acids. You can think of its shape like a heart—it's kind of cool! There are three main parts, or domains, each with its own special pocket for binding. Because of these pockets, albumin can attach to lots of different molecules, which is super useful!

- Fatty acids
- Bile acids
- Hormones
- Drugs
- Metals
- Toxins

Function of Albumin:
1. Keeping fluid balance: Imagine albumin in your blood like a tiny sponge. It attracts water molecules due to its size & negative charge. This creates a **colloid osmotic pressure** that pulls fluid from the space between cells into the blood vessels. This stops fluid from piling up in tissues & helps keep blood volume just right. Think of it like a dam that holds back water, making sure the right amount stays in the bloodstream without leaking out.
2. Transporting molecules: Albumin is like a delivery truck zooming around the body, moving important things. It has little pockets that grab onto various types of cargo, such as:

* Hormones like insulin & thyroid hormones that need to get to their target cells.
* Fatty acids, which are energy-packed, travel from the intestines or fat stores to muscles and other parts for energy.
* Bile acids help with digestion; they ride with albumin to get to the intestines and help break down fats.
* Vitamins, especially fat-soluble ones like A, D, E, & K, depend on albumin for a smooth trip through the bloodstream.
* Metals like copper, zinc, & calcium tag along with albumin to reach where they're needed.

3. Buffing pH: Our body needs a perfect pH balance—slightly alkaline—to work well. Albumin acts like a chemical buffer by soaking up extra hydrogen ions when the pH is too low and releasing them if it gets too high. This helps keep the pH in a happy range that's key for enzymes and cells to do their jobs properly.
4. Binding & detoxifying toxins: Albumin is kind of like a bouncer in your bloodstream. It grabs and neutralizes nasty substances such as:

* Drugs—it can hold onto drugs longer, slowing their release so they don't hit toxic levels in our tissues.
* Metals—heavy metals like mercury & lead can be really bad for us, but albumin binds them up & keeps us safe from damage.
* Toxins—from those made by bacteria to waste products our bodies produce—albumin helps neutralize & get rid of them safely.

CHARACTERISTICS OF ALBUMIN FROM DIFFERENT SPECIES

Approximately 60% of the protein in the b lood consists of albumin, the most abundant protein in the blood. It is a small globular protein with a m olecular weight of 67 kDa and a halflife of 19 days. It is very soluble in water. It can be heated to 60°C for 10 hours and stable at pH 4 to 9. It can be colle cted from various sources such as albumen (ovalbu min, OVA), rat serum (rat serum albumin, RSA), h uman serum (human serum). serum albumin, HSA) (Figure 1) and bovine serum (bovine serum albumi n, BSA). However, the two most commonly used d rugs are HSA10 and BSA.

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 4 July-Aug 2024, pp: 738-747 www.ijprajournal.com ISSN: 2456-4494

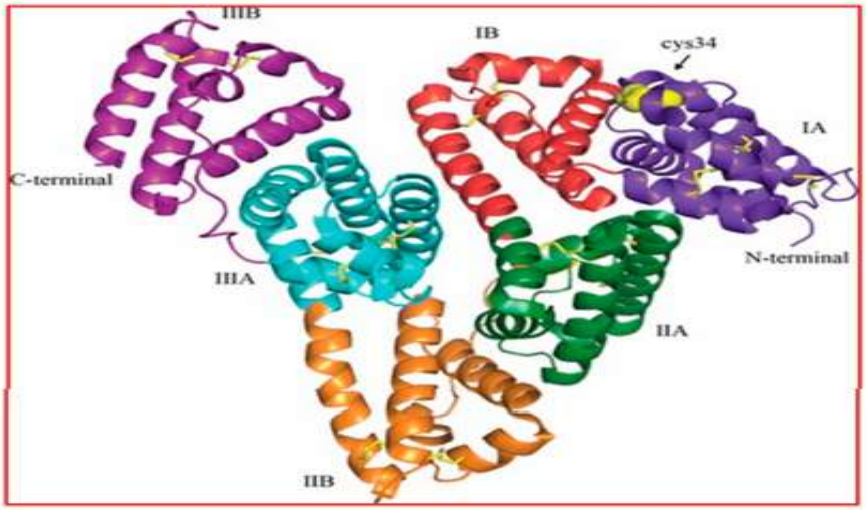

Figure 1. Structure of human serum albumin, a single polypeptide containing 585 amino acids. The three homologous domains [(I) residues 1—197, (II) residues 189—385, (III) residues 381—585] assemble to form a heart-shaped protein. Each of the domains is composed of two subdomains (A, B) with common structural motifs. The domains of albumin are shown in purple (IA), red (IB), green (IIA), orange (IIB), blue (IIIA), and violet (IIIB). The yellow sticks indicate the disulfide bridges, and the yellow spheres represent the free cysteine residue at position 34 (cys34) in domain IA. From ref 6 with permission.

This protein is ideal for drug administratio n because its main functions include the regulation of blood pressure and is important for hydrophobic substances such as hormones and fatty acids. lipoph ilicity. Therefore, it is important to find a safe, gene ric and good carrier to improve antibiotic and trans port. Three names (I, II, III) have been used to desc ribe albumin, as shown in Figure 1. The most impo rtant part of human serum albumin binding sites for hydrophobic drugs (especially drugs with negativel y and neutrally charged hydrophobic substances) ar e called Sudlow domains I and II. . A long hydroph obic pocket containing arginine and lysine residues, respectively. There are 13 specifically because dru gs like warfarin, phenylbutazone, and azaperidone bind to site I, sometimes called the warfarin site. Si te II is sometimes called the benzodiazepine site be cause it binds drugs such as tryptophan, ibuprofen, and diazepam. This allows different medications, s uch as docetaxel and paclitaxel, to be effective and delivered to the tumor site.

- **Human Serum Albumin: -**

Human serum albumin consists of 585 ami no acids that form a single chain. Its secondary stru cture is highly conserved, with 67% α-helices and 17 6-turn disulfide bridges connecting the three homolog ous domains. The protein is one of the most abunda nt and important proteins in plasma, and plasma alb umin levels range from 3.5 to 5 g/dL 15. It is produ ced by hepatocytes in the liver at a rate of 912 g/da y. Although albumin is the most abundant plasma p rotein, most of it does not circulate in the blood. Th e intermediate region contains up to 60% albumin. Its biological half-life is 19 days, but it only lasts 16-18 hours in circulation. The body needs to control it s properties. In particular, hypoalbuminemia or con ditions such as insulin, thyroxine and cortisol incre ase their production, while potassium and hepatocy tes exposed to high osmotic pressure inhibit their pr oduction. In addition, albumin production depends on adequate nutrition. In fact, the liver's ability to p rocess protein decreases due to inadequate nutrient absorption. Maintaining blood osmotic pressure, su pporting tissues, and transporting hormones, vitami ns, drugs, and divalent cations (such as zinc and cal cium) throughout the body are carried out by album in. Processes such as coagulation It also has antioxi dant properties and causes antithrombin III activity, similar to heparin. In fact, coagulopathy can be cau sed by hypoalbuminemia. There are two types of dr ugs that bind to albumin: endogenous and exogeno us. All elements already present in the body, such a s hormones, fatty acids, cations, free radicals, vitam

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 4 July-Aug 2024, pp: 738-747 www.ijprajournal.com ISSN: 2456-4494

ins and bilirubin, fall into the first category. Drugs t hat enter the body from outside, such as antibiotics, antibiotics, anti-inflammatory drugs, anti inflammatory drugs, heart and kidney drugs, central nervous system drugs, and hypoglycemic drugs, fa ll into the second category. In , the albumin molecu le has many amino acid residues with a value of -17 mV. Thus, albumin actively attracts sodium ions and other cations. Chronic liver disease and kidney disease are two conditions that can alter albumin c oncentrations. One of the kidney's main functions is to retain plasma proteins (such as albumin) and pre vent them from being excreted in the urine along w ith waste products. When the kidneys are damaged, such as in diabetes, high blood pressure, or nephrot ic syndrome, their ability to control albumin and pl asma protein levels is reduced.

- **Serum Albumin from Other Species:-**

Bovine serum is a source of albumin that h as many similarities with HSA. Its isoelectric point (pI) in water (25°C) is 4.7; This means that at neutr al pH it is negatively charged and at acidic pH it is positively charged. Its molecular weight is 69.323 k Da. When present in BSA, the combination of posit ive and negative amino acids can bind both positive ly and negatively charged particles. Its availability, low cost, and ease of cleaning and maintenance ma ke it one of the best choices as a drug delivery vehi cle in the literature. It is also a flexible material due to its high carrying capacity, water solubility, and ability to bind both hydrophobic and hydrophilic su bstances. Immunity in mice and humans may be jus t as bad. BSA has 80% contact with human serum a lbumin, its weight difference is less than 1%, and it s isoelectric point is the same. An important differe nce is the number of tryptophan (Trp) residues. BS A contains two tryptophans, while human serum al bumin contains only one. Spectrophotometry can b e used to distinguish between human and bovine se rum albumin because tryptophan is responsible for the fluorescence of the protein. This protein was us ed as a protein model to study the immune response to the protein, and the antibody response to BSA w as investigated in animal models. Humans are expo sed to bovine serum albumin early in life through t he consumption of milk and meat, as well as throug h injections and medications. A quantitative radioas say was developed in 2005 to measure anti-BSA IgG in cancer patients and healthy individuals . Anti-BSA antibodies have been detected by Western blo t analysis after human exposure to BSA, but neither cancer patients nor healthy individuals showed any symptom syndrome associated with high levels of anti-BSA. In another study, three species of rabbits wer e given BSA. The findings suggest that the immuno genicity of BSA varies among different rabbit strai ns, with some rabbits not responding at all to stimul ation. This lack of response may be genetic or may be due to the antigen itself. Studies have also show n that the molecular state of BSA is related to its an ti-inflammatory properties. BSA is partly in monomer ic form and partly in aggregated form and may act as an antibody. The lack of immunogenicity of BS A in some rabbits may be attributed to its similarity to rabbit serum albumin, which shares some simila rities with BSA. Storage proteins are the most exte nsively described, although their exact role is uncle ar. It is a globular acidic glycoprotein, consisting of a single polypeptide chain of 386 amino acids, wit h a molecular weight of 42-47 kDa, and is a member of the serine protease inhi bitor family. Its isoelectric point with BSA and HS A is 4.8. However, due to its immunogenicity, OV A is often chosen as one of the most widely used an tigens. All serum albumins are expected to have si milar binding sites to those of HSA because albumi ns from different animals are compared by amino a cid sequence. However, many theories have been p ut forward over time. Panjehshahnin et al. compare d 6 animal serum albumins and examined different compounds (phenylbutazone, diazepam, and fatty a cids) using warfarin and dansyl cosine as fluoresce nt markers for sites I and II, respectively. Six mam malian serum albumins were compared and evaluat ed in the presence of different translocating agents (fenbutazone, diazepam, and fatty acids) using warf arin and dansyl cosine as fluorescent markers for re gions I and II, respectively. Findings show that all s erum albumins, except RSA, have similar affinity t o HSA. In particular, rat serum albumin has been s hown to reduce the conversion of warfarin by phen ylbutazone compared with other types of albumin; t his indicates differences in the warfarin binding site properties of this particular albumin type. In contra st, binding site II showed only slight changes. In an other study, Schmidt and Janchen showed differenc es in the ligand binding sites of other acidic compo unds of RSA compared to HSA. In a comparison of HSA, RSA, and rabbit serum albumin, Massolini e t al. examined these changes and found that stereos elective binding of subprofen and ketoprofen was o bserved in HSA and rabbit serum albumin, but not i n RSA. In addition, Aubry et al. noted significant di fferences in the binding properties of RSA and rabb it serum albumin to HSA. Two warfarin binding sit es have been identified in rabbit serum albumin; on

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 4 July-Aug 2024, pp: 738-747 www.ijprajournal.com ISSN: 2456-4494

e of these is similar to the warfarin site in HSA (sit e I). A few years later, Kosa and colleagues suggest ed that preliminary studies should be conducted to clarify drug compounds, including their locations a nd drug products, to be able to compare drug intera ctions between animal and human albumin. Throug h a rigorous competitive search, they attempted to f ind different types of albumin using the drug-binding sites of site I-binding drugs (warfarin and phenylbutazone) and tr aditional site II-binding drugs (ibuprofen and diazepam). Their stud y showed that the binding affinities of domain I to BSA, RSA, and rabbit serum albumin were close to those of HSA. However, canine albumin has been shown to be lower than human albumin. In contrast , the binding properties of diazepam to BSA, RSA, and rabbit serum albumin appear to differ from thos e of HSA. They suggest that these differences may result from changes in the binding site microenviro nment through changes in the size and/or hydropho bicity of the binding envelope rather than changes i n amino acid residues. In particular, the defect in ca nine albumin may be present in the position corresp onding to zone I. The structural change in the large cavity weakens the hydrophobic interaction of DZ and BSA, rabbit serum albumin, and RSA, but not t he loss of hydrophobic residues.

HSA-Based Multifunctional Nanocarrier: Excellent biocompatibility, non-toxicity, nonimmunogenicity, and extended circulation duration are just a few of the positive qualities that have drawn attention to HBNDSs for a variety of biological applications. They have become essential vehicles for delivering a wide range of therapeutic medications, such as inorganic materials, bioactive components, and small-molecule pharmaceuticals, improving imaging capabilities and treatment effectiveness for a variety of illnesses. We will methodically review the most significant developments in HSA-based multifunctional nanocarriers during the last five years in this part.

Human serum albumin: Human serum albumin, composed of 585 amino acids, exhibits a highly flexible secondary structure. This structure comprises 17 disulfide bridges, 6 turns, and a 67% alpha-helix content, which facilitate cross-linking between its three homologous domains. As the most abundant protein in blood plasma, human serum albumin is synthesized by hepatocytes in the liver at a rate of 9-12 grams per day. Despite its prevalence, a significant proportion of albumin (up to 60%) is stored in the interstitial space, rather than circulating in the blood. Its biological half-life is approximately 19 days, although its circulating half-life is shorter, ranging from 16-18 hours. The transcapillary migration of albumin is reversible, allowing it to re-enter the plasma via the lymphatics to maintain steady protein concentrations. The production of albumin is regulated by the body's needs, with factors such as insulin, thyroxin, and cortisol promoting its synthesis, while potassium and high osmotic pressure inhibit it. Additionally, adequate nutrient availability is essential for albumin production, and impaired nutritional absorption can diminish the liver's protein synthesis capacity. Albumin degradation occurs primarily in the liver and kidneys, and its effective plasma concentration is determined by the balance between production, degradation, and transport between intravascular and interstitial spaces.

PREPARATION METHODS OF ALBUMIN NANOPARTICLES

Albumin-based nanoparticles can be fabricated using various techniques, categorized into chemical and physical methods. Chemical methods involve adding substances like ethanol, cottonseed oil, or β-mercaptoethanol to create nanoparticles. Physical methods utilize heat, pressure, or other physical elements. Common chemical techniques include self-assembly, emulsification, and desolvation, while physical techniques include thermal gelation, NAB-technology, and nanospray drying. These methods will be explored in greater detail later. Consistency and reproducibility are crucial, and manufacturing processes should aim to produce nanoparticles with predictable and repeatable characteristics.

1. **Desolvation (Coacervation):-** One of the most popular methods for creating albumin nanoparticles is desolvation. It entails gradually adding a desolvating chemical, like ethanol or acetone, drop wise to an albumin aqueous solution while agitating the mixture until the solution reaches turbidity. Thedesolvating chemicals cause phase separation and protein aggregation by progressively altering the albumin's tertiary structure. Actually, the homogeneous solution splits into two phases: albumin, the solute that forms submicronic aggregates, and solvent, which makes up the majority of the second phase.In most cases, the resulting formulation is not sufficiently stable, and a cross linker—such as glutaraldehyde—is employed to further

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 4 July-Aug 2024, pp: 738-747 www.ijprajournal.com ISSN: 2456-4494

maintain and stabilize the resulting nanoparticles' shape. The process parameters, including pH, protein content, cross-linker concentration, desolvating agent level, ionic strength, and stirring speed, all affect the final formulation's characteristics. The preparation process is shown in figure A

2. **Emulsification:** A nonaqueous solution (oil phase) is added to a water phase (albumin solution) during the emulsification process (Figure B), agitating the mixture to create a crude emulsion. With the use of a high-pressure homogenizer, the emulsion can be made homogenous. Following that, the nanoparticles can be stabilized by either chemical treatment using a cross-linker, like glutaraldehyde, or thermal heating (temp >120 °C).
3. **Self-Assembly Method:** Self-assembly depends on the production of albumin nanoparticles as a result of the protein becoming more hydrophobic by breaking down disulfide bonds brought about by the use of β-mercaptoethanol or by having a lipophilic compound reduce the amount of primary amine groups on the protein's surface. As a result, albumin begins to self-assembly and forms nanoparticles in an aqueous medium. Figure C illustrates the process of self-assembly.
4. **Thermal Gelation:** Figure D illustrates how heat causes protein structural change and unfolding, which is followed by protein-protein interactions including hydrogen bond formation, electrostatic interactions, hydrophobic interactions, and disulfide-sulfhydryl exchange processes. The process parameters, including pH, protein, concentration, and ionic strength, determine the characteristics of the resulting formulation.
5. **Nanospray Drying:** A typical method for turning a liquid phase into a dry powder is nanospray drying (Figure E). The fact that this approach produces particles in a single, continuous stage is one of its key advantages. The spray creation of droplets from a liquid solution is what distinguishes it. A number of phases are involved in the process, including atomizing the feed into a spray, contacting the spray with air, drying the spray, and separating the dried product from the drying air. When a drying gas and a liquid feedstock are in contact, the liquid atomizes into a spray of droplets at a temperature high enough to cause moisture to evaporate.The interaction occurs in a drying chamber containing an aqueous albumin solution. An electrostatic particle collector is used to produce and collect the solid dried particles as the moisture evaporates. By adjusting the nanospray drying conditions, one may control the characteristics of the nanoparticles and tailor them for certain uses.

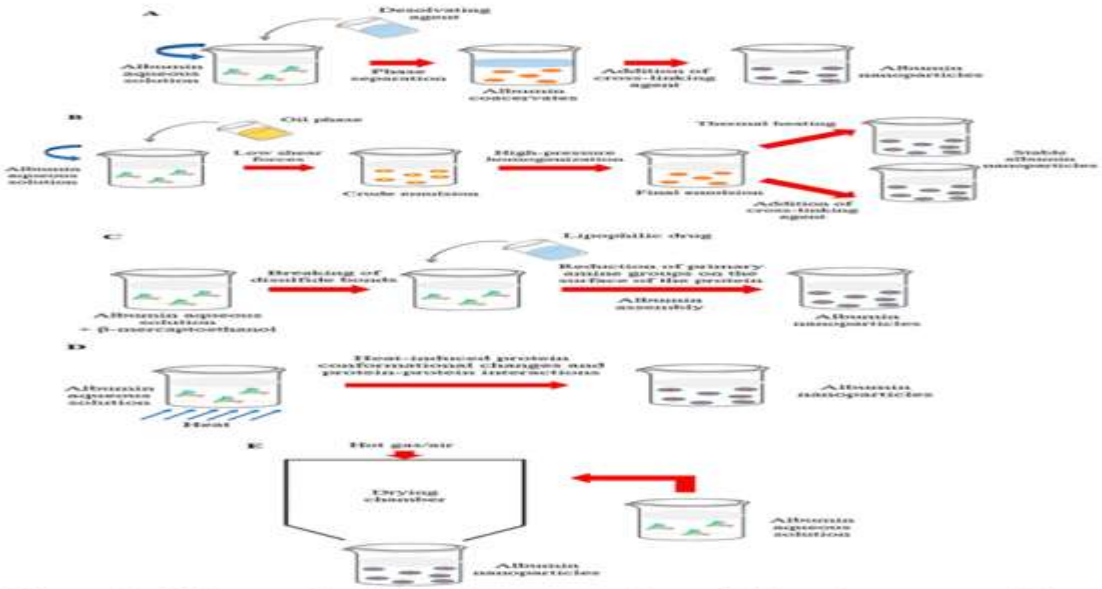

Figure 3. Main methods for the preparation of albumin nanoparticles: (A) desolvation, (B) emulsification, (C) self-assembly, (D) thermal gelation, (E) nanospray drying.

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 4 July-Aug 2024, pp: 738-747 www.ijprajournal.com ISSN: 2456-4494

Microfluidic Mixing: Microfluidic technology is another method, though less studied, for creating albumin nanoparticles. It offers a viable substitute for the synthesis of polymeric, lipid, and serum albumin nanoparticles. This method produces particles with a limited size distribution and customizable size through a controlled preparation process. It also offers a special chance for automated large-scale pharmaceutical manufacture. Few investigations on the synthesis of albumin nanoparticles underflow circumstances have been published in the literature. In a recent study conducted in 2020, successful outcomes were achieved regarding the synthesis of drug-loaded albumin-based nanoparticles in the core-shell type. The first syringe pump's channel 1 (v1) was filled with the stabilizing poly(allylamine hydrochloride) (PAH), and the second syringe pump's channel 2 (v2) was filled with the drug and carrier solution (BSA/KYNA).Following their passage through the syringe pumps, the two solutions were combined in the 250 μL μ-mixer cell together with a pressure controlling device. The sample was then gathered at certain intervals of time. Figure 4 shows a schematic representation of how this microfluidic system prepares the core-shell NPs.

In a microfluidic platform, paclitaxel-loaded disulfide-cross-linked HSA nanoparticles were created as a biocompatible substitute for glutaraldehyde cross-linking. There are four steps in all to the procedure, as Figure 5 illustrates. To convert the 17 disulfide bonds into free sulfhydryl groups, HSA was incubated in deionized water with GSH in the first step, known as the pretreatment stage.The HSA/water solution was combined with paclitaxel/tertiary butyl alcohol (TBA), an organic solvent that is used as an antisolvent to water, in a microchannel reactor during the second step of mixing and coprecipitation. As a result, three liquid inlets and one air inlet were created, creating a segmented gas-liquid flow. Both albumin and paclitaxel saw a significant drop in solubility in the mixing solution; as a result, they precipitated out together to create PTX-HSA nanoparticles.In order to create disulfide bonds, the suspension was incubated at 37 °C for the third stage, which was the reaction step. To eliminate TBA, the suspension was dialyzed against deionized water at 4 °C in the last step, dialysis.Selecting a suitable antisolvent for the precipitation step and adjusting the reaction time for the reaction step are two essential components of the microfluidic technology that allow for the production of stable nanoparticles.

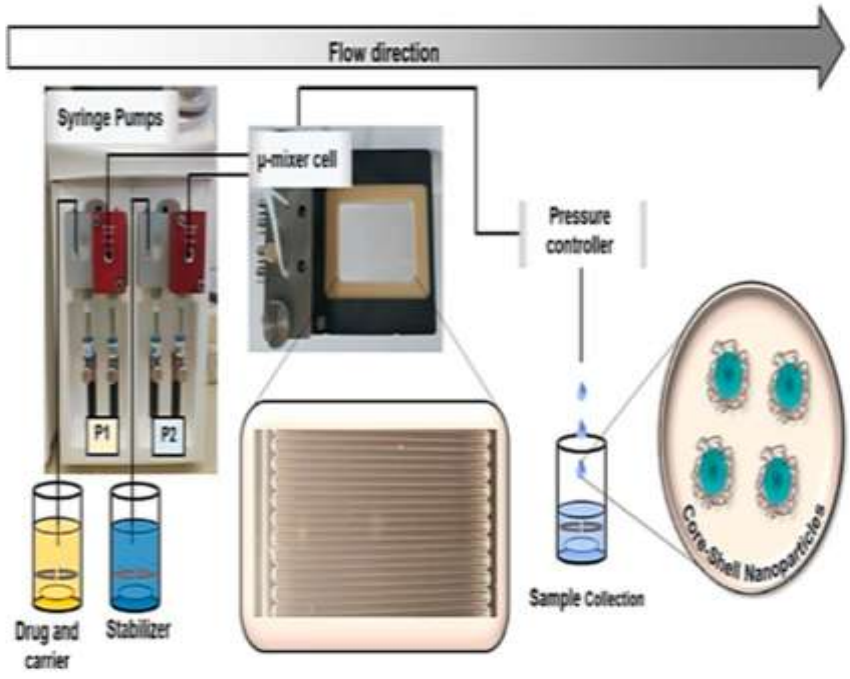

Figure 4. Flow system used to prepare BSA core−shell nanoparticles with the pumps and the μ-mixer cell. Adapted from ref 75 with permission.

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 4 July-Aug 2024, pp: 738-747 www.ijprajournal.com ISSN: 2456-4494

II. FUTURE PERSPECTIVES

To date, numerous preclinical and clinical investigations have provided ample evidence of albumin's enormous potential. Further research is needed to determine the role of gp30 and gp18 and how they interact with albumin nano vectors, even though gp60 and SPARC are known to be in charge of the active internalization of albumin in tumors and inflammatory tissues. It's also critical to understand how ligand-albumin binding impacts the activity of the ligands. Studying albumin preparation and loading methods in further detail is necessary.Additional research should be done on albumin preparation techniques and loading procedures. In light of this, additional research should be done on the creation of safe cross-linkers to stabilize albumin NPs. Tumors are known to be able to capture plasma proteins and use the byproducts of their breakdown to grow and proliferate.It is thought that the albumin nanoparticles infiltrate and accumulate in solid tumors and inflammatory joints by taking advantage of both the EPR effect and active targeting. Since albumin is a necessary protein for the survival and growth of malignancies, the increased accumulation of albumin nanoparticles in solid tumors cannot be entirely attributed to leaky vasculature and poor lymphatic drainage.Further patient data is required to support the involvement of this mechanism. Similar to cancer patients, rheumatoid arthritis patients frequently experience hypoalbuminemia, which is brought on by increased albumin consumption at the sites of inflammation. Cachexia is a multifactorial phenomenon characterized by significant weight loss and muscular wasting. It is associated to all clinical diseases, including cancer, infections, and autoimmune disorders, that promote albumin accumulation in the affected tissue... These factors make it worthwhile to look into whether the buildup of injectable albumin-based formulations, independent of the medications they contain, may help or hinder the growth of tumors. Additionally, research on mice with syngeneic ovarian and mammary carcinomas revealed that nab-paclitaxel functions as a radiosensitizer, enhancing the effectiveness of radiotherapy when combined with radiation (especially when given before to radiation).The radio-response of healthy tissue was completely unaffected, in stark contrast to the significant amplification of the tumor radio-response. Consequently, when used as a single drug, nab-paclitaxel demonstrated anticancer effects and improved the supra-additive antitumor efficacy of radiation therapy.Its effectiveness in raising the therapeutic benefit of radiation therapy is a fascinating aspect that merits more research in the future. Future advancements in the field of albumin-assisted drug delivery could concentrate on combination therapy and chemical albumin changes to accommodate a wider range of therapeutic entities and imaging agents. Lian et al. created multifunctional nanoparticles in this context by combining docetaxel with IR780, a near-infrared dye, in human serum albumin nanoparticles.Castration-resistant prostate cancer may be treated with this formulation because of its strong targeting and theranostic potential. Li et al. created stimuli-responsive albumin nanoplatforms in 2019 for use in cancer multimode therapy and combined theranostic treatment.

In order to accomplish both the diagnostic and the treatment, multimode therapy works with imaging technology and depends on chemotherapy, radiotherapy, hypothermia, and other treatments. Zhang et al. developed a dual-agent delivery method based on human serum albumin in 2020 for combination therapy aimed at inhibiting the growth of cancer cells and neovascularization within the tumor microenvironment.. Two acetylpyridines were the payloads.Copper(II) [Cu(Ap44 mT)]Cl with paclitaxel, for enhancing the therapeutic activity and targeting capability in vivo. 4,4-dimethyl-3-thiosemicarbazone.

III. CONCLUSIONS

The distribution of medications for the treatment of cancer, inflammatory illnesses, and other ailments is made more effective and clever by the field of nanomedicine, which is gaining popularity. Because of albumin's biocompatibility, biodegradability, nonimmunogenicity, and nontoxicity, it has garnered significant attention from researchers in recent years as a potential drug delivery vehicle... Because it is the most prevalent protein in the plasma, the immune system does not reject it and it is not a foreign substance, which only serves to increase its allure. Because of its strong affinity for hydrophobic medications, ability to modify its surface, and high loading capacity, it helps us get past significant obstacles caused by the nature of many chemicals that are currently on the market. It is a flexible drug carrier that can be applied to gene therapy and imaging applications in addition to therapeutic drug delivery.Furthermore, the target site can specifically recognize and actively target the albumin-based formulation due to its binding affinity for certain receptors on the

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 4 July-Aug 2024, pp: 738-747 www.ijprajournal.com ISSN: 2456-4494

surface of endothelial cells and other cells in sick organs. The most significant and distinctive characteristic of albumin that sets it apart from the other nanocarriers is this one.

Of course, optimization still presents obstacles. biocompatibility, target preference. Techniques and making sure it's economical. Scalability is a challenge that needs to be overcome. But the dream of a time when nanodelivery defeats illness and gives people the ability to take care of themselves is getting closer to reality with every technological advancement.

Thus, let's not just imagine how medication administration will develop in the future as we gaze toward the horizon. As nanotechnology presents a symphony where little Titans dance to the melody of human health, let us embrace the symphony of possibilities.By building on the themes introduced in the previous sections, this conclusion avoids plagiarism while providing a distinct and optimistic outlook on the direction of nano delivery. It highlights the possible influence on customized medication and ends with a metaphorical flourish that gives the reader a sense of excitement and expectation for what lies ahead.

REFERENCE

[1]. Emeje, M. O.; Obidike, I. C.; Akpabio, E. I.; et al. Nanotechnology in Drug Delivery. In Recent Advances in Novel Drug Carrier Systems; Sezer, A. D.; IntechOpen, 2012; pp 1−38.

[2]. Lombardo, D.; Kiselev, M. A.; Caccamo, M. T. Smart Nanoparticles for Drug Delivery Application: Development of Versatile Nanocarrier Platforms in Biotechnology and Nanomedicine. J. Nanomater. 2019, 2019, 1−26.

[3]. Mitchell, M. J.; Billingsley, M. M.; Haley, R. M.; et al. Engineering precision nanoparticles for drug delivery. Nat. Rev. Drug Discovery 2021, 20 (2), 101−124.

[4]. Wang, S.; Su, R.; Nie, S.; et al. Application of nanotechnology in improving bioavailability and bioactivity of diet-derived phytochemicals. J. Nutr. Biochem. 2014, 25 (4), 363−376.

[5]. Toy, R.; Roy, K. Engineering nanoparticles to overcome barriers to immunotherapy. Bioeng. Transl. Med. 2016, 1 (1), 47−62.

[6]. Karimi, M.; Bahrami, S.; Ravari, S. B.; et al. Albumin nanostructures as advanced drug delivery systems. Expert Opin. Drug Delivery 2016, 13 (11), 1609−1623.

[7]. Loureiro, A.; G. Azoia, N.; C. Gomes, A.; Cavaco-Paulo, A.; et al. Albumin-Based Nanodevices as Drug Carriers. Curr. Pharm. Des. 2016, 22 (10), 1371−1390.

[8]. An, F.-F.; Zhang, X.-H. Strategies for Preparing Albumin-based Nanoparticles for Multifunctional Bioimaging and Drug Delivery. Theranostics 2017, 7 (15), 3667−3689.

[9]. Elzoghby, A. O.; Samy, W. M.; Elgindy, N. A. Albumin-based nanoparticles as potential controlled release drug delivery systems. J. Controlled Release 2012, 157 (2), 168−182.

[10]. Larsen, M. T.; Kuhlmann, M.; Hvam, M. L.; Howard, K. A. Albumin-based drug delivery: harnessing nature to cure disease. Mol. Cell Ther. 2016, 4, 3.

[11]. Ge, P.; Yang, H.; Lu, J. M.; et al. Albumin Binding Function: The Potential Earliest Indicator for Liver Function Damage. Gastroenterol. Res. Pract. 2016, 2016, 1−7.

[12]. Phan, H. T. M.; Bartelt-Hunt, S.; Rodenhausen, K. B.; et al. Investigation of Bovine Serum Albumin (BSA) Attachment onto SelfAssembled Monolayers (SAMs) Using Combinatorial Quartz Crystal Microbalance with Dissipation (QCM-D) and Spectroscopic Ellipsometry (SE). PLoS One 2015, 10 (10), e0141282.

[13]. Elzoghby, A. O.; Samy, W. M.; Elgindy, N. A. Albumin-based nanoparticles as potential controlled release drug delivery systems. J. Controlled Release 2012, 157 (2), 168−182.

[14]. Hilton, J.; Dearman, R. J.; Sattar, N.; et al. Characteristics of antibody responses induced in mice by protein allergens. Food Chem. Toxicol. 1997, 35 (12), 1209−1218.

[15]. Mogues, T.; Li, J.; Coburn, J.; et al. IgG antibodies against bovine serum albumin in humans焗their prevalence and response to exposure to bovine serum albumin. J. Immunol. Methods 2005, 300 (1−2), 1−11.

[16]. Perrudet-Badoux, A.; Frei, P. C. Immunogenicity of Bovine Serum Albumin in Adult Rabbits of Various

Strains. Int. Arch. Allergy Immunol. 2004, 40 (6), 928−933.

[17]. Lv, L.; Chi, Y.; Chen, C.; Xu, W. Structural and Functional Properties of Ovalbumin Glycated by Dry-Heating in the Presence of Maltodextrin. Int. J. Food Prop. 2015, 18, 1326−1333. (18) Huntington, J. A.; Stein, P. E. Structure and properties of ovalbumin. J. Chromatogr., Biomed. Appl. 2001, 756 (1−2), 189−198.

[18]. Groschel, C.; Sasse, A.; Monecke, S.; Rohrborn, C.; Elsner, L.; Didie, M.; Reupke, V.; Bunt, G.; Lichtman, A. H.; Toischer, K.; Zimmermann, W.-H.; Hasenfuß, G.; Dressel, R.; et al. CD8+-T Cells With Specificity for a Model Antigen in Cardiomyocytes Can Become Activated After Transverse Aortic Constriction but Do Not Accelerate Progression to Heart Failure. Front. Immunol. 2018, 9, 2665.

[19]. Basto, A. P.; Badenes, M.; Almeida, S. C.P.; Martins, C.; Duarte, A.; Santos, D. M.; Leitao, A.; et al. Immune response profile elicited by the model antigen ovalbumin expressed in fusion with the bacterial OprI lipoprotein. Mol. Immunol. 2015, 64 (1), 36−45.

[20]. Fanali, G.; di Masi, A.; Trezza, V.; et al. Human serum albumin: From bench to bedside. Mol. Aspects Med. 2012, 33 (3), 209−290.

[21]. Sudlow, G.; Birkett, D. J.; Wade, D. N. The Characterization of Two Specific Drug Binding Sites on Human Serum Albumin. Mol. Pharmacol. 1975, 11 (6), 824−832.

[22]. Fu, Q.; Sun, J.; Zhang, W.; et al. Nanoparticle Albumin - Bound (NAB) Technology is a Promising Method for Anti-Cancer Drug Delivery. Recent Pat. Anti-Cancer Drug Discovery 2009, 4 (3), 262− 272.

[23]. Yang, H., He, J., He, X., Wang, M., Huang, Y., Sun, X., & Tang, F. (2013). Albumin-conjugated paclitaxel nanoparticles prepared by solvent evaporation method: physicochemical properties and in vitro/vivo evaluation. International Journal of Pharmaceutics, 441(1-2), 704- 714.

[24]. Zhang, Z., Sun, X., Shen, Y., Zhang, W., Zeng, Y., Zhu, X., ...& Li, X. (2011). Albumin-conjugated nanoparticles bearing paclitaxel for targeting drug delivery against glioma. Biomaterials, 32(30), 7705- 7714.

[25]. Chen, R., Zhang, X., He, J., Chen, M., Wu, X., Chen, G., ...& Yin, W. (2022). Development of HSAtargeted paclitaxel prodrug nanoparticles for synergistic inhibition of tumor angiogenesis and cancer growth. Actabiomaterialia, 149, 155-166.**

[26]. Li, M., Li, W., Song, W., Li, B., Wang, J., Sun, J., ...& Chen, X. (2021). Construction of Multifunctional Human Serum Albumin Nanoparticles for Co-delivery of Docetaxel and Bcl-2 siRNA for Enhanced Synergistic Chemo-Gene Therapy. Molecular Pharmaceutics, 18(7), 2205-2216