

International Journal of Innovative Research in Science, Engineering and Technology

(A High Impact Factor, Monthly, Peer Reviewed Journal)

Visit: www.ijirset.com

Vol. 8, Issue 2, February 2019

A Basic Concepts of Hyaluronic Acid and Albumin

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ABSTRACT: Because of its versatility, albumin is frequently employed in the production of nanocarriers. The natural glycosaminoglycan hyaluronic acid (HA) has been shown to bind to particular receptors, including cluster of differentiation-44. Consequently, HA is frequently employed as ligands for the surface modification of adaptable nanocarriers. Albumin and HA used together as nanocarriers have numerous advantages, such as specific targeting, small particle size, pH and/or hyaluronidase sensitive drug release, drug combination capacity, biocompatibility, non-immunogenicity, biodegradability, and high stability. To the best of our knowledge, however, a systematic review of HA and albumin-based nanoparticles for drug delivery has not yet been conducted. Brief descriptions of the procedures used to create HA and albumin based nanocarriers are provided, as well as an introduction to the relevant background material. Additionally, the potential and promise in combination therapy and theragnostic of HA and albumin-based nanoparticles as drug delivery carriers in cancers, joints, vitreum, and skin tissue is carefully examined.

KEYWORDS: Hyaluronic Acid, Albumin, HAS , HA , Serum, non - immunogenic, non - adhesive

I. INTRODUCTION

Hyaluronic acid is a naturally occurring, non-immunogenic, non-adhesive glycosaminoglycan that has been shown to play an important part in a variety of wound-healing processes and to be angiogenic when broken down into smaller fragments. Initiating wound healing requires inflammation, which is facilitated by hyaluronic acid. Later, hyaluronic acid moderates the process, allowing matrix stabilisation and reducing long-term inflammation. Although hyaluronic acid can be found in almost every type of mammalian cell and tissue, it is most abundant in the synovial fluid, vitreous humour of the eye, and loose connective tissue (including rooster combs, umbilical cords, the dermis, and the artery wall). [1] Additionally, it is present in the capsular part of bacteria like Streptococcus and Staphylococcus. These have been biotechnologically developed to become a primary source of Hyaluronic acid for the pharmaceutical, medicinal, and cosmetic industries. [2]

Because it is not immunogenic, hyaluronic acid has important biological and medicinal applications. In pathological situations, a highly viscous solution of hyaluronic acid can function as a lubricant, a fluid substitute, and an excellent moisture retainer. Hyaluronic acid is widely employed as a sustaining medium in ophthalmic procedures such cataract, glaucoma, corneal transplant, retinal, and vitreous surgery. [3] The concept of viscosurgery was born from the use of high-molecular-weight @ hyaluronic acid (1%). As a result of its hydrophilic properties, it is a great addition to cosmetic moisturising lotions.

The most prevalent protein in plasma (35-50 g/L human serum) is albumin, which is stable in the pH range of 4-9, soluble in 40% ethanol, and can withstand heating at 60°C for 10 hours without degrading. Albumin has many desirable properties for drug delivery, including stability, commercial availability, biodegradability, nontoxicity, and low immunogenicity. 4-6 Specifically, a Phase III trial is investigating the efficacy of nanoparticles (NPs) of human serum albumin-bound paclitaxel (Abraxane®; Celgene Corporation, Summit, NJ, USA) in the treatment of a wide range of cancers, including breast and non-small-cell lung cancer, for which they have received FDA approval. [4]

Hyaluronic acid (HA) is a linear polysaccharide that has been widely employed in medication administration and tissue engineering because it is biodegradable, biocompatible, and non-immunogenic. 9-12 It's a big part of synovial fluid and it's important for the cartilage's growth and development. In addition, HA is a naturally occurring polysaccharide

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that has been found in the joints and is known to interact with the cells via their CD44 receptors (such as chondrocytes). Since CD44-expressing chondrocytes are a potential target or biodistribution site, we hypothesise that decorating NPs with HA will increase their affinity for these cells. [5]

Effect of pH on the interaction of serum albumin with hyaluronic acid

Hyaluronic acid and bovine serum albumin soluble complex formation was examined in four buffer solutions at three distinct hydrogen-ion concentrations, using Tiselius electrophoresis. A third barrier (Pi complex) with mobility between that of albumin and hyaluronic acid was detected at pH 8.6 in barbital (Veronal) buffer, pH 8.5 in borate buffer, and pH 7.4 in phosphate buffer. In acetate buffer, neither the pH 7.1 nor the pH 5.3 conditions were conducive to the development of the pi-complex. Formation of a complex was also suggested by the mobilities of the boundaries observed when each component was examined individually and compared with patterns obtained on solutions containing both components in acetate buffer[6]. The data suggest that complex-formation at high pH, resulting in the appearance of a third electrophoretic boundary, may represent a different type of binding than that which occurs at lower pH, which is probably a hydrogen bond.

Self-diffusion in a hyaluronic acid–albumin–water system

Self-diffusion in solutions containing HA, bovine serum albumin (BSA), and water was studied using 1H pulsed field gradient nuclear magnetic resonance (PFG NMR), with particular attention paid to the HABSAD2O systems at a range of BSA and HA concentrations. It was demonstrated that the self-diffusion coefficient (SDC) of BSA decreases in the presence of even a trace amount of HA. Three hypotheses were put forth and evaluated in an effort to account for this observation. The first one considered how the presence of HA slowed the motion of water. The second theory postulated that BSA and HA molecules collide mechanically, causing an effect. [7] A third theory proposed that BSA and HA molecules form a complex, decreasing the mobility of BSA molecules. The third mechanism has been proven to be the most probable. From an NMR perspective, the BSAHAD2O system is in a 'rapid exchange' condition, since the time that BSA molecules spend in the 'free' and 'bound' (with HA) states is substantially shorter than the diffusion period of the PFG NMR experiment (7 ms).

Objectives

- To study DLS curve of the aqueous dispersion containing HSA/HyA – IBU particles
- To study CD curves of the HSA in pure form
- To study limiting viscosity number and hydrodynamic size of hyaluronic acid with various molecular weights
- To study Compositions of hyaluronic acid (HA), bovine serum albumin (BSA) and HA + BSA solutions in D2O

II. RESEARCH METHODOLOGY

A research methodology is a universal way to addressing a study subject through data collection, data evaluation, and results based on the findings of the study. A research technique is a plan for carrying out a research study. The methodical gathering and analysis of facts and information for the advancement of knowledge in any area may be loosely defined as research. The goal of the study is to use systematic techniques to find solutions to intellectual and practical problems. The current study is descriptive in nature and is based on secondary data gathered from a variety of sources, including books, education, and development, journals, scholarly articles, government publications, and printed and online reference materials.

III. RESULT AND DISCUSSION

The use of molecular modeling allows us to evaluate the influences of various factors, such as the presence of ions and solvation on the properties of proteins, including their ability to bind ligands. The aim of this study is to evaluate the

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effect of Na⁺, Mg²⁺, Ca²⁺ cations on the affinity of hyaluronate (Fig 1) to human serum albumin using molecular dynamics methods.[8]

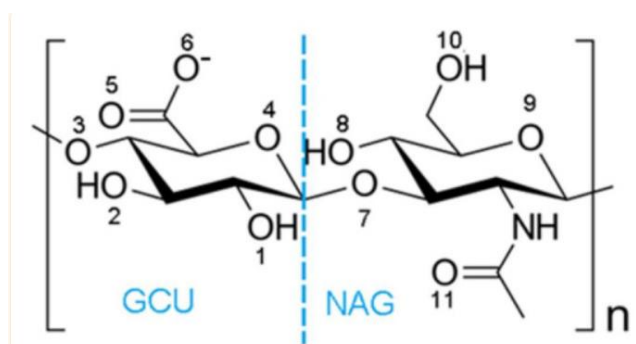


Fig. 1 Structure of the repeating disaccharide unit of hyaluronate, the deprotonated form of hyaluronic acid. GCU stands for D-glucuronic acid with pKa of about 3, and NAG means N-acetyl-D-glucosamine. The different oxygen atoms are numbered, and this numbering will be utilized when discussing the interaction with human serum albumin. [9-10]

Table 1. Limiting viscosity number and hydrodynamic size of hyaluronic acid with various molecular weights

M, kDa	L, nm	[η], cm ³ /g	V _s , cm ³ /g	$\langle r^2 \rangle^{1/2}$, nm	C for Coil Overlap, $\mu\text{g cm}^3$
100	250	290	120	52	8600
500	1250	1100	420	140	2400
1000	2500	1800	730	210	1400
3000	7500	4400	1800	400	570
6000	15000	7700	3100	600	320

The hydrodynamic size of the hyaluronic acid depends on the molecular weight (see Table 1). The hydrodynamic size as the final result effects the polymer concentration, as polymer coils start to interpenetrate each other. [11-12]

Table 2. Compositions of hyaluronic acid (HA), bovine serum albumin (BSA) and HA + BSA solutions in D2O (wt%)

Sample N	% BSA	% HA
1	4	-
2	2	-
3	1	-
4	-	2
5	-	4
6	-	8
7	4	0.25
8	4	0.75
9	2	0.25
10	2	0.75
11	1	0.25
12	1	0.75

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The compositions of the samples used are presented as percentages T1 of HA and BSA in Table 2. BSA solutions were prepared by mechanically mixing powdered BSA with deuterated water. The solutions were transparent at all concentrations studied. [13-14]

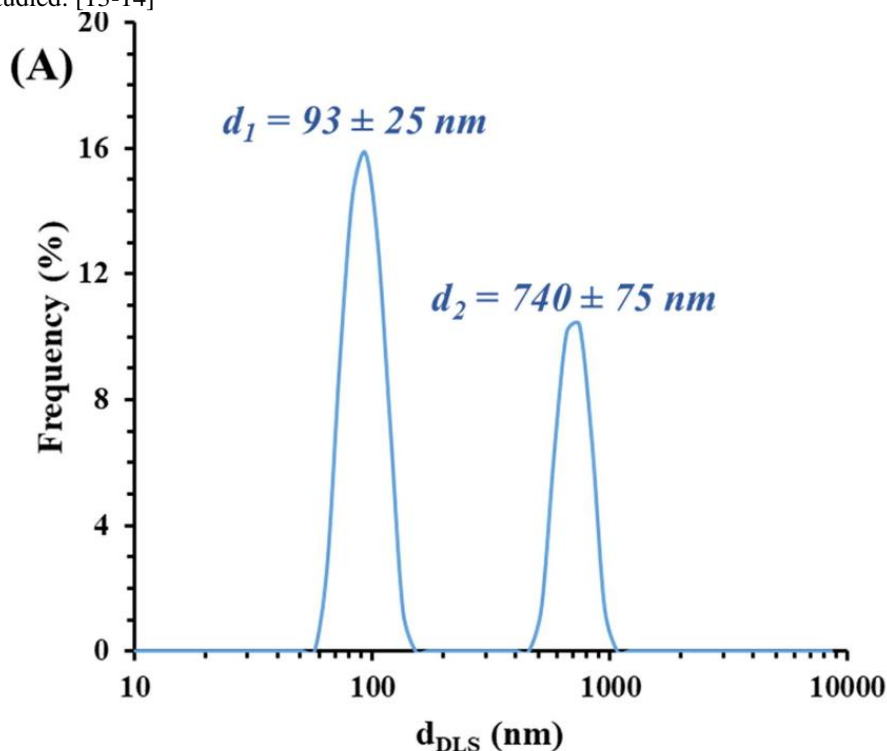


Fig. 2 (A) The CD curves of the HSA in pure form and pH = 4.5 and 6.5.

Both the macromolecules (albumins and HyA) and the IBU is fully deprotonated and have a negative charge at this pH. The prepared formulas were redispersed in PBS (pH = 6.5), and after 30 min the size of the particles was measured by DLS[15]

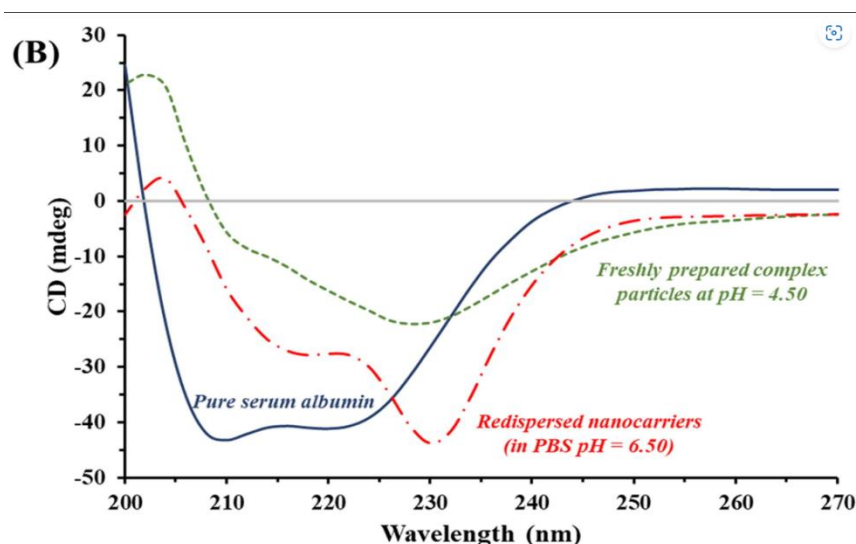


Fig. 3DLS curve of the aqueous dispersion containing HSA/HyA – IBU particles at pH = 6.5 (B) (cHSA = 0.0027 mg mL⁻¹).

IV. CONCLUSION

Hyaluronic acid, as a hydrophilic biopolymer with a unique set of structural, physical, physicochemical, and biodegradable properties, attracts a great deal of attention. This review focuses on the dependency of the key properties on molecular weight of hyaluronic acid. The application of intestine-solvent-gastroresistant capsules as carrier can be a suitable tool for protecting albumin/HyA formulations against acidic condition and enzymatic digestion of stomach. This approach can effectively support the targeted liberation of drug at the site of absorption.

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