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Nanodispersion of flavonoids in aqueous DMSO-BSA catalysed by cationic surfactants of variable alkyl chain at $T = 298.15$ to 308.15 K

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ABSTRACT

Density ρ, sound velocity u, surface tension γ, viscosity η and conductance for (0.01 to 0.10 mol·kg^{-1}) alkyltrimethyl ammonium bromide (C_nTAB, DTAB n = 12, TDTAB n = 14 and HDTAB n = 16) with (0.999 millimol·kg^{-1}) quercetin, apigenin and naringenin flavonoids and (2 g·kg^{-1}) bovine serum albumin (BSA) in aqueous 10% DMSO (w/w) at $T = 298.15$, 303.15, 308.15 K and $p = 0.1$ MPa are reported. The ρ, u, γ and η data have calculated apparent molar volume V_ϕ, isentropic compressibility k_s, apparent molar isentropic compressibility $k_{s,\phi}$, intrinsic viscosity [η] and activation energy E^*, to determine the contribution of methylene (—CH_2) groups of C_nTAB. The γ, surface excess concentration Γ_{max}, molecular surface area A_{min}, hydrodynamic radius R_h, hydrodynamic volume V_h, friccohesity σ and k on increasing C_nTAB alkyl chain length infer higher dispersion. Hydrophobicity of BSA in aq-DMSO with flavonoids is as quercetin < apigenin < naringenin, on the weakening of cohesive forces and increasing intermolecular forces with a decrease in surface tension and increase in viscosity for homogenization. The C_nTAB develops stronger electrostatic and hydrophobic interactions with BSA and flavonoids denature native BSA structure. Increasing alkyl chain length has catalysed BSA with flavonoids on mutual interactions strengthening their interacting activities, proven with higher η and lower γ values.

1. Introduction

Water-soluble globular proteins as a special class of biomolecules form colloids in aqueous and perform several vital roles in biological systems such as a biocatalyst in the form of enzymes, messengers to regulate the biological processes, maintenance of blood osmotic pressure, transportation of ions and biomolecules [1]. Thus the transport properties like viscosity and conductance become most desired sciences to define interacting activities of biomolecules in dynamics liquid mixtures which intricately ensemble with surface energy, activation energy and sound velocity. Molecular mixtures in general become a more viable medium for optimizing their structural abilities for accommodating and activating the additives for initiating and advance molecular model of the sciences. The BSA as one of the major constituents of blood circulatory plasma proteins acts as a transport protein by non-specifically binding several hydrophobic biomolecules like steroid hormones, porphyrins, bilirubin, fatty acids and others [2,3]. BSA as a crystalline structure and water-soluble nature is used as a model protein system for interaction study with flavonoid, dye, surfactant, and other hydrophobic biomolecules [4]. Such liquid mixtures could generate the state functions with specific physicochemical properties (PCPs). In this regards, the protein study with flavonoids depicts a more significant view of activities as compared to their individual properties. Since the proteins and flavonoids are biologically functional molecules and perform several biochemical activities such as biocatalyst and antioxidant respectively. Thereby friccohesity which define interacting molecular activities in a medium of lower activation energy, to substantiate the chemical factor to monodisperse chemical constituents. The concept was further exposed to their state of liquid mixture an increasing thermal to kinetic energy, as per thermal energy relationship with molecular structure and equation. The increased thermal energy induces oscillation in atom along the chemical bond for generating favorable molecular motions for better dispersion and interaction. Since the hormones, enzyme and biocatalyst basically are proteins and there remains a vibrant possibility with free radical to encounter, these said chemical substances stabilizing chemical linkages. Such science basically further depends on the mobility and 1:1 distribution in the medium. Such medium explores the possibility to have stay period of free radicals. Thereby flavonoid could get an opportunity to interact with them; however, such hypothesis has never been reported yet by any other researcher working in the area of biophysics. Our model is aimed to extract out interacting coordinates and their interacting mechanism for a better understanding of free radical-protein antioxidant linkages. However, restrictions of their mutual solubilization have hindered and their studies together have not been reported yet despite being valuable interfaces. Flavonoids as polyphenolic compounds are poorly water-soluble having a benzo-γ-pyrone structure with 15 carbon atoms and

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are naturally synthesized by plants in response to fighting the microbial infection. Because of their high hydrophobicity flavonoids are not soluble in water, and their better dispersion in aqueous medium remains a challenging task. We have resolved this difficulty by preparing aqueous formulations by using DMSO, BSA, and surfactants (C_nTAB, n = 12, 14 and 16). We had dissolved flavonoids in DMSO for dispersion by decreasing cohesive forces (CF). Flavonoid-DMSO solution was added in aqueous BSA (2 $g \cdot kg^{-1}$) BSA to formulate flavonoids in a hydrophobic medium. Separately varying C_nTAB concentrations were mixed with the aqueous flavonoid-DMSO-BSA formulation and in WBD formulations. Both the mixtures of BSA and flavonoid with unique PCPs reflect their chemical structural activities in processes, but no such studies are reported in the literature. The purpose of our studies has been to widen data base along for exploring their working mechanism. Therefore stoichiometric combinations for the compatible formulation of flavonoids, BSA and surfactants have been the new dimension of physicochemical properties derived from most adequate molecular mixing and interacting stoichiometric balance. Such operational approach has given new strengths and hopes about our studies vis-a-vis major challenge is to enhance the solubility of flavonoid in aqueous media for wider physicochemical studies as a valuable database for academic and industrial applications as a stable medium, as nanoparticle capping formulations and others. Truly such studies based on physicochemical properties could be proven very substantial on tagging a role of temperature, which is noted as a fundamental overtone in the science of thermodynamics for pH interlinked interfacing of cationic surfactant antioxidants.

Our intensified literature review has revealed a lack of formulation of such systems and their physicochemical studies derived experimental observations which are noted as basic parameters and authentic indicators in the area of molecule interactions. We have extended our explanations of such data in a most interdisciplinary manner by choosing cationic surfactant with alkyl chain of C = 12, 14 and 16, with flavonoids and BSA. Our study is aimed to bring the research on flavonoids at centrestage for high industrial as well as of academic new database. Originally the flavonoids being secondary plant metabolites and are responsible for the coloring of vegetables and fruits. Flavonoids are divided into six major subgroups: chalcone, flavone, flavonol, flavanone, anthocyanins and isoflavonoids, based on their position of —OH groups, and double bond [5,6], which control the interaction. Despite their wider uses no systematic studies are reported investigating an exact role of their phenolic —OH groups and a double bond so our studies become useful. Free- radicals such as hydroxyl radical (OH•), superoxide anion radical ($O•^-$), hydrogen peroxide (H_2O_2), oxygen singlet, hypochlorite ($HClO•_4$), nitric oxide radical (N•═O) and peroxynitrite radical (O═N—O—O^-) are unstable, reactive, which damage biomolecules such as DNA, proteins, carbohydrates, and lipids [7] on developing binding forces (BF). Flavonoids are antioxidant to scavenge free-radicals, but have poor dispersibility in aqueous medium, so medium 0.01–0.1 mol $\cdot kg^{-1}$ C_nTAB have increased their disparity in aqueous medium. The C_nTAB dispersed flavonoid formulations express a high surface area as compared to flavonoids poorly dispersed in pure water. In C_nTAB-formulation, higher surface areas of quercetin with homogeneous dispersibility express better free-radical scavenging activity. Thus to prepare a stable solution of flavonoid, it is necessary to find a role played by solute-solute and solute-solvent interactions which reflect the kinetic and thermodynamic stability of their formulations. Since friccohesity is a multiplication of cohesive force (CF) into frictional force (FF) of solvents, a decrease in CF is compensated for developing FF causing solute-solvent interactions. Strengthening flavonoid solute-solute interactions have increased their dispersibility in formulation studies which effectively scavenge free-radicals. So our studies are important for finding their scavenging activities with protein and C_nTAB. The metal ions like iron, chromium, vanadium, copper, cadmium, lead, mercury and nickel could undergo a redox process by flavonoid free-radicals, which could enhance a production of reactive oxygen species (ROS) [8]. So a combination of flavonoid with protein could rapidly prevent ROS, but such interaction could form a complex to detect BSA and flavonoids. Non-hazardous free-radical protection mechanism is needed where —OH groups in flavonoids can scavenge free-radicals, where chelating metal ions are avoided [9,10]. Potential health benefits arising out of antioxidant activities of flavonoids could be obtained by understanding their physicochemical profile with their natural combination of BSA on increasing C_nTAB hydrophobicity. Since the increments in AC of C_nTAB have decreased the size of nanoemulsion with better kinetic energy that has made medium vibrant. Thus, it is a fundamental query that the H^+ releasing activities of quercetin, apigenin and naringenin from their phenolic —OH groups, whether increases or decreases with increasing AC, such basic and most relevant studies have never been reported yet. Our studies have proven that vibrant of medium in presence of hydrophobic C_nTAB (HDTAB) has facilitated the proton H^+ mechanism for lowering the pH (Fig. S1). This explored a possibility between an inductive effect of AC of C = 14 and H^+ releasing capacity of flavonoid. Probably the +I effect at terminal CH_3 of C = 14 could have catalysed the flavonoid to release the H^+ due to moderate +I effect. Such new observations have never been reported yet thereby the BSA interaction with flavonoids in an aqueous medium is of immense importance to extend flavonoid activities. Our study could enhance flavonoid understanding in interacting mechanism vis-a-vis diseases like cardiovascular diseases and cancer, including antioxidant, anti-tumor, and anti-inflammatory effects. Hydrophobically and hydrophillically driven liquid mixtures weaken CFs with the adequate strength of intermolecular forces where micelle with Vander Waal forces could induce binding forces with a definite friccohesity. A homogenisation of flavonoids undergoes nanoemulsion formation that enhances their bioavailability for bionanotechnological and biochemical applications.

The C_nTAB could catalyse to enhance interacting flavonoids activities with proteins by inducing hydrophobic and hydrophilic interactions. Stable BSA-Flavonoid-C_nTAB colloids could develop diversified homogeneous protein-drug-surfactant formulations with aprotic polar solvents with van der Waals forces and hydrogen bonding (HB) for better solubility. DMSO as a universal aprotic solvent dissolves several nonpolar and polar molecules due to its amphipathic nature. And in pharmaceuticals it is used as an anti-inflammatory, antioxidant for in-vivo and in-vitro experiments, as a drug vehicle, aqueous 10% DMSO in BSA solution is used as a cryoprotectant for freezing and long-term storage of stem cells without damaging structure from T = 298.15, 303.15 and 308.15 K temperature. Papadopoulou et al. [11]. have reported their work on flavonoid-BSA interaction in aqueous 10% DMSO as latter does not affect flavonoid and BSA without changing its conformation. Flavonoids dispersion capacity with surfactant is from 25 μM to 0.001 M as compared to studies on flavonoid-protein interaction [12–15]. Y.J. Hu et al. have reported naringenin interaction with BSA in Tris-HCl buffer solution using fluorescence spectroscopy while, X. N. Zhao et al. reported BSA-flavonoid with a surfactant in Tris–HCl buffer using fluorescence spectroscopy. Similarly Chakraborty; et al. has reported BSA-surfactant physicochemical and conformatory interaction in an aqueous medium. Apart from spectroscopic inputs, our study provides a deeper insight of flavonoids interacting behaviour with BSA facilitated by a series of C_nTAB. The PCPs (Fig. 1) have been overlooked so our pioneer findings provide an enhanced solubility of poorly water-soluble flavonoids for better scavenging activities. Our findings could be extended further to the fields of the solution and biochemical processes for drug delivery and bioavailability of poorly water-soluble flavonoids. Further experiments are being pursued in our laboratory on flavonoid-BSA aqueous formulations by minimizing the DMSO concentration using various non-ionic and anionic surfactants.

2. Experimental section

2.1. Materials

Specifications of chemicals used without further purification are given in Table 1. Prior to use, surfactants were stored in P_2O_5 filled