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FULL PAPER

Study and analysis of L-methionine and L-cysteine complexes

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Most investigations of speciation are carried out in aquatic environments, simulating circumstances seen in physiological systems. These are used as examples of the kinds of systems found in biofluids and water cycle. However, metabolic processes occur in highly compartmentalized environments and biological systems are linked to low dielectric mediums of varying strengths. To simulate these circumstances, some research has been conducted in aqua-organic mixtures, but little effort has been made to account for the compartmentalization. Accordingly, the distribution of species in surfactant media, where microporation is known to cause compartmentalization, was studied. In this regard, the protonation equilibria of L-methionine and L-cysteine, as well as their binary complexes with Ca(II), Mg(II), and Zn(II) in micellar fluids of various compositions, were investigated. In addition, computer-enhanced modeling was employed to reach the most appropriate chemical models and to assess the validity of these models.

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Introduction

Cysteine, with the chemical formula $C_3H_7NO_2S$, is an amino acid crucial for various biological processes. Derived from the Greek word ''kustis'', meaning bladder, cystine, its oxidized form, plays a structural role in proteins due to the formation of disulfide bonds. While the human body can synthesize cysteine, it is often classified as semi-essential, as its availability may be insufficient in certain populations, such as infants, the elderly, or individuals with specific metabolic conditions [1]. Cysteine's thiol (-SH) side chain acts as a nucleophile, participating in enzymatic reactions and redox processes. Its ability to undergo redox reactions contributes to its antioxidant properties, essential for cellular defense against oxidative stress. Notably, cysteine is a precursor to glutathione, a tripeptide antioxidant composed of cysteine, glycine, and glutamate. Glutathione plays a vital role in protecting cells from damage caused by free radicals [1]. While oral supplementation of glutathione is common, its systemic availability is limited, necessitating intracellular synthesis. Understanding the role of cysteine in glutathione synthesis and its significance in cellular function provides insights into potential therapeutic interventions targeting oxidative stress-related conditions.

Cysteine, a semi-essential amino acid, serves as the rate-limiting substrate for glutathione production, primarily due to the abundance of glutamate and glycine in typical North American diets. Glutathione, often referred to as the "master antioxidant," exerts its biological action through the sulfhydryl (thiol) group (-SH) of cysteine, acting as a proton donor. This antioxidant plays a crucial role in controlling the activities of other antioxidants, such as vitamins C and E, and is considered as a predictor of lifespan [2].

The toxicity and instability of cysteine supplements are unfortunately constraints. Procystine, also known as L-2-oxothiazolidine-4-carboxylate, is a product of cysteine that does not stimulate glutathione production unless it is converted intracellularly to cysteine. Two assays were conducted to examine the potential toxicity of cysteine and procystine after a single intravenous infusion in neonatal rats (10 per group; 3 at 1 day of age). One research compared survival rates after very high doses of L-cysteine or procysteine. Mortality rates after 7 days following a single intravenous administration of L-cysteine at 1.52 or 1.14 g/kg or procysteine at 1.80 or 1.35 g/kg were 80, 50, 10, and 0%, respectively. In the second experiment, the effects of a moderate dose of procysteine or an equal or lower dose of L-cysteine on clinical pathological indices and body and organ weight were studied. Administration of L-cysteine (369, 185, or 37 mg/kg) or procysteine (450 mg/kg) once intravenously resulted in no changes in clinical pathology parameters or body or organ weight after 14 days Happened. Moreover, the shelf life of procysteine solutions was measured in months, whereas that of l-cysteine solutions was measured in hours [3].

L-methionine has the chemical formula $C_5H_{11}N_2S$ and is an essential amino acid that contains sulfur. It's also known by the names 2-amino-4-(methylthio) butyric acid, -ethylthio -amino butyric acid, and -amino-methyl mercapto butyric acid. Although Mueller discovered methionine in 1921, its structure was not determined until 1928 because to the Strecker3 reaction and the work of Barger and Coyne. It needs around 2 gram of food every day [4]. There are two distinct pathways for methionine synthesis in plants and certain bacterial species [5]. It is produced from cobalamine-enzyme by mammalian tissues and by many bacteria, and from homo-cysteine by all plants and certain bacteria. Active transport of methionine from the small intestinal lumen into the enterocytes is responsible for its absorption. Enterocytes are involved in methionine metabolism to some extent. Methionine, along with other amino acids, is involved in protein synthesis in the liver. D-glucose and glycogen may be created by its metabolism [4].

Methionine is an essential amino acid since the patient body cannot produce it on its own. Daily needs for an adult person average about 20 mg/kg. Threonine is produced in plants and bacteria by the synthesis of -aspartyl-semialdehyde and homoserine from aspartic acid. Homoserine is *o*-phosphorylated, and the phosphate ester that results is hydrolyzed and the OH group is transferred to a new site. Two pathways exist for the metabolism of methionine [1]. The enzyme threonine dehydrogenase converts it to pyruvate in many organisms. Thiolysis of a route intermediate with CoA results in the formation of acetyl-CoA and glycine. The human threonine dehydrogenase gene is a pseudogene, therefore the amino acid is metabolized to the ketone body beta-ketobutyrate instead. Mechanism of the initial step is similar to that done by serine dehydratase, suggesting that the same enzyme catalyzes both the serine and threonine dehydratase processes [5]. Section 2 of this study covers literature review, section 3 materials and methods, section 4 results analysis and discussion, and section 5 includes conclusion and further study.

Cysteine and methionine are essential amino acids with significant roles in various biological processes. While much is known about their biochemical properties, there remains a need to further understand their behaviour in complex environments, particularly in surfactant media. This study aims to investigate the protonation equilibria of L-methionine and L-cysteine, as well as their binary complexes with select metal ions, in surfactant media. By studying these systems, we seek to gain insights into the distribution of species and the influence of micellar environments on their speciation behaviour. In addition, computer-enhanced modelling will be employed to refine chemical models and validate their accuracy. The objective of this study is to advance our understanding of amino acid speciation in complex environments, with implications for various fields including biochemistry, pharmaceuticals, and environmental science. This study builds upon our previous work in [6], the overall purpose of which is to determine accurate thermodynamic data throughout the saturation curve for a set of proteinogenic amino acids.

Literature Review on the L-Methionine and L Cysteine Complexes Study and Analysis

L-cysteine, L-serine, L-threonine, L-lysine, and L-methionine are white crystalline compounds at ambient temperature that break down at or before melting at 523-573 K [7,8].

Formulations to increase the solubility and oral bioavailability of poorly water-soluble drugs use amino acids as excipients to stabilize their amorphous state.

L-lysine is commonly used as sulfide or hydrochloride due to its low stability and severe hygroscopicity [9].

Many aspects of the title and other amino acids are examined in reviews [10].

In [11], thermal-relaxation calorimetry (2-300 K) was used to quantify L-lysine and L-threonine, which had doubtful adiabatic values.

Nanozymes are inorganic nanomaterials that catalyse like enzymes [12].

Several metal, metal-oxide, metal sulfide, and carbon-based nanozymes exhibit enzyme-like catalytic activity [13]. From analyte detection to bacterial growth regulation to prodrug treatment to photodynamic therapy, this feature is useful.

According to a recent evaluation [14], over 200 laboratories worldwide are developing new nanozymes and expanding their application.

Catalytic activity of nanozymes was boosted by ATP and inhibited by cysteine [15].

In [16], nanozyme activity is inhibited like natural enzyme activity, where an inhibitor molecule binds to the enzyme's active site or away from it, reducing catalytic activity or efficiency.

However, irreversible inhibitors covalently attach to the enzyme, inactivating it indefinitely [17].

Only reversible inhibition has been found in nanozymes [18].

This information has helped develop new inorganic nanozyme inhibitor chemicals. However, no irreversible inhibitors have been found [19].

A nanozyme sensor is produced by L-cysteine, which inhibits the peroxidase-mimic's catalytic activity [20].

The majority of these studies proved in [21] that L-cysteine prevents light from reaching the nanozyme's surface, limiting its colorimetric substrate catalysis.

In [22], it was initially revealed that L-cysteine competes with the nanozyme substrate and briefly inhibits $Gd(OH)_3$ nanozyme catalysis.

In [23], nanozymes' surface atoms behave as enzyme active sites, unlike regular enzymes where one inhibitor molecule inactivates one enzyme molecule by attaching to the active site.

According to [24], the nanoparticle surface atoms represent enzyme active sites, allowing a single inhibitor molecule to inactivate an enzyme molecule by interacting with it.

In [25], glutathione, a popular antioxidant, relies on cysteine as its rate-limiting amino acid.

Cysteine's role in cell signalling pathways and its capacity to stabilize both endogenous and foreign proteins were both uncovered in [26].

In [27,28] Rodney Levine *et al.* conducted a comprehensive assessment that defined several of methionine's unusual properties, opening the door to additional investigation into the amino acid's significance beyond protein synthesis.

Similar antioxidant capabilities to cysteine have been shown in [29], demonstrating crucial protein protective roles.

As we have a better idea of the many ways in which methionine contributes to protein and cellular function, we can turn our attention to determining whether or not these roles are necessary [30]. Cysteine, as new studies have shown, is just as hydrophobic as methionine.

Materials and methods

GR grade (E-Merck, India) sodium hydroxide pellets dissolved in 3x distilled water produced a 4.0 mol dm^{-3} stock solution. Adding water changed solution concentration. Titrating against a standard solution of oxalic acid and potassium hydrogen phthalate determined alkalinity and sodium hydroxide determined hydrochloric acid normality. ANOVA employing COST4 (concentration of solution by titration) was used to assess concentration measurement error. The Gran plot technique was used to quantify the alkalinity of a solution. Analysis of variance (ANOVA) was performed on the deviations in ligand, metal ion, and alkali concentrations. Calibration of glass electrode by buffer solution is still in use. Establishing the glass electrode response throughout a broad pH range is necessary for electrometric experiments. However, there was not a single titrand that could be used to cover all of the bases. Titrations with sodium hydroxide were performed on hydrochloric acid, acetic acid, and protonated 2-aminoethanol in triplicate. Bates and Dinching's published value for the ionization constant of 2-aminoethanol was utilized to get the concentration of free hydrogen ions. The functions for analysing these acid-base titrations were computed using the formulas presented in the article.

Method

All solutions were made in triple-distilled water that had been purged with nitrogen gas for approximately 30 minutes to remove any trace amounts of oxygen or carbon dioxide. All experiments were conducted using "A" quality (Borosil) glassware, and all solutions were standardized in accordance with protocol. To prevent metal ion hydrolysis, the stock solutions were made somewhat acidic. Complexometric titration against an EDTA standard solution using Eriochrome Black T as an indicator and NH_3/NH_4Cl as a buffer to keep the pH constant at 10.0 allowed for the determination of metal ion concentrations. Gran plots were used to quantify how many free hydrogen ions were present in each metal ion solution.

Proposed model

One benefit that has received a lot of attention in contemporary computer systems is that they will converge not just on the real values, but also on wild constants that are quite distant from them. This has been proven to be true for basic systems. However, Sylva and Davidson36 noted that somewhat accurate predictions of the stability constants are required at the outset. Otherwise, the true species may be overlooked, and an unfit matrix may result. They suggested that it was

not a MINIQUAD75 constraint but rather a general difficulty with numerical analysis of mathematically intricate systems. As can be seen in Figure 1, the MINIQUAD75 main line may be split into three distinct sections. The program begins by reading the input parameters and calling the subroutines MQ and FACT, which in turn call the subroutine DINP, which calculates the free concentrations of components at each site using the supplied constants. Adjustments are made to MINIQUAD75's main line and DINP to facilitate streamlined data input for SCPHD and MINIQUAD75. Table 1 indicates data from MINIQUAD75's L-methionine and L-cysteine complexes (Figure 1).

TABLE 1 The information in the L-methionine and L-cysteine complexes of MINIQUAD75

Parameters	MINIQUAD 75					L-methionine	L-cysteine
	INP2	INPH	MQ	FUNCT	CALC		
INP1	224	968	539	10469	10445	22645	1280
DINP	53	48	39	50	52	242	576
MAMIN	–	3098	3120	3123	3103	12444	240
DOUT3	301	795	1066	8891	3461	14514	575

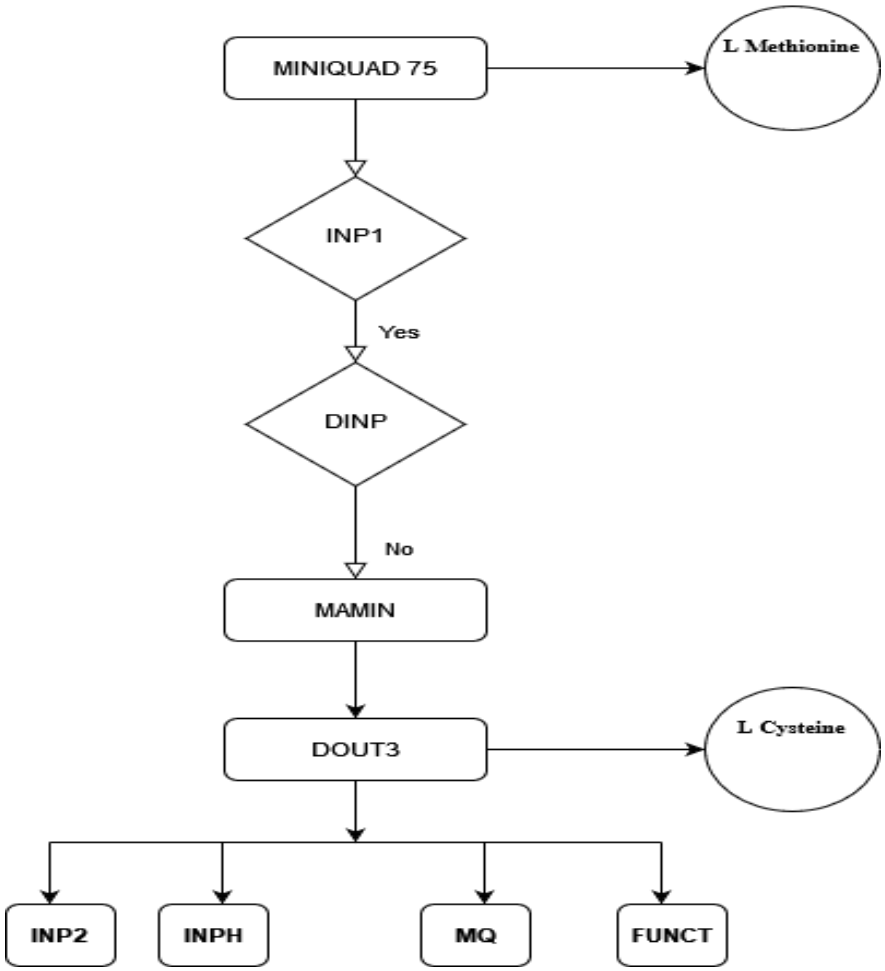

FIGURE 1 Architecture of proposed system

Simulation results

To lower dropout rates caused by subpar biopharmaceutical qualities, it is essential to conduct physicochemical evaluations of novel chemical entities at an early stage of medication development. Ionization constants (pKa) are one such property that is required for predicting ADME (absorption, distribution, metabolism, and excretion) behaviour to comprehend permeation processes and solubility features that are pH-related. Understanding solution dissociation and solvation is necessary for studying amino acids and other physiologically active chemicals. Amino acid protonation constants were calculated using acid-base titration data and also techniques were assessed. Large datasets describe amino acids and simple peptides' protonation and stability constants in water and organic solvents. Since micellar media are amphiphilic, their amino acid and carboxylic acid protonation constants vary from those in water. Experiments have shown that a single solvent is not a suitable model for *in vivo* processes, but little is known about amino acid chemistry in mixed solvents, particularly protonation constants. Cystein and methionine alkalimetric titration curves in aqueous and SLS, water combinations are depicted in 2,3,4 (Figures 2-4). The titration curves show that acid-base equilibrium work between pH 2.0 and 11. The computer software SCPHD15 was used to reduce noise in numerous studies' data, and the program's logs are used to refine the data.

Least squares data analysis presupposes a Gaussian or normal residual distribution. When data are correctly fitted into models, residuals should be zero. Acceptable models have no statistically significant discordance between residuals and model errors. In addition, trendless residuals indicate a good model. Under the assumption that errors are random, residuals are normalized. Such measurements include skewness, kurtosis, and R-factor". The best-fit models capture methionine and cystein' acido-basic equilibrium states in SLS-water mixtures, according to these statistical measures. We supply the most realistic chemical models for CTAB and TX100 in water in 5 (Figure 5).

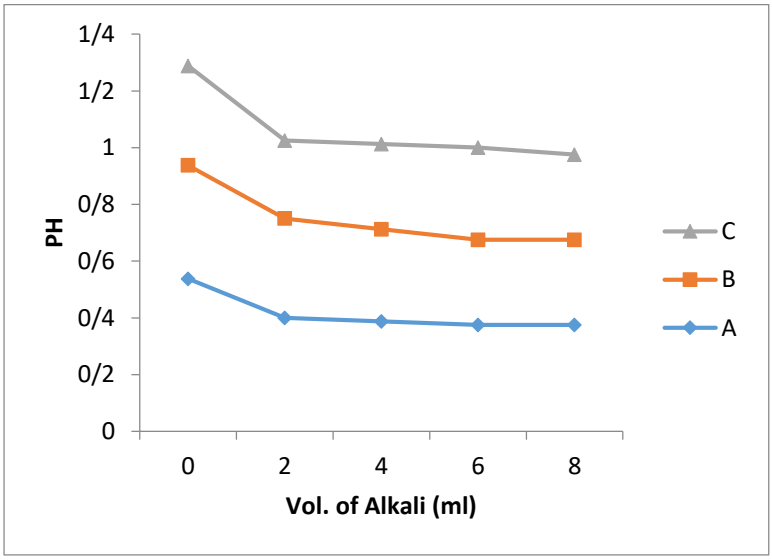

FIGURE 2 Alkalimetric titration curves L-methionine and L-cysteine complexes aqueous medium

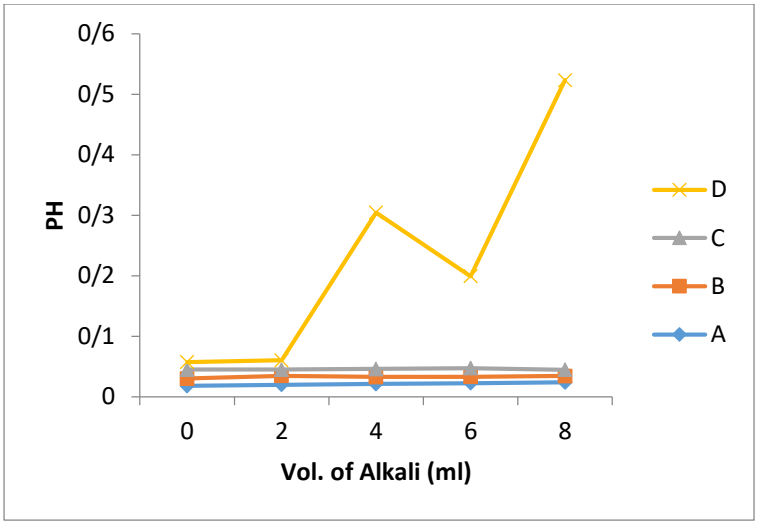

FIGURE 3 Alkalimetric titration curves L-methionine and L-cysteine complexes w/v SLS-water medium

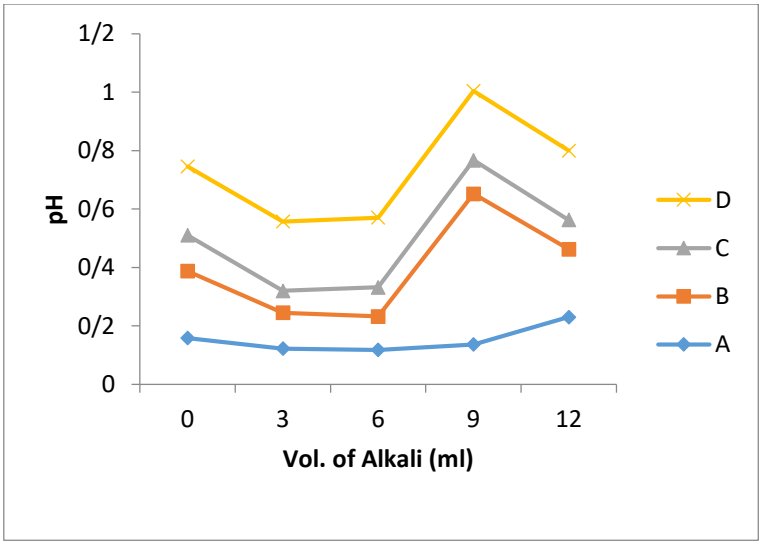

FIGURE 4 Alkalimetric titration curves of methionine in SLS-water medium

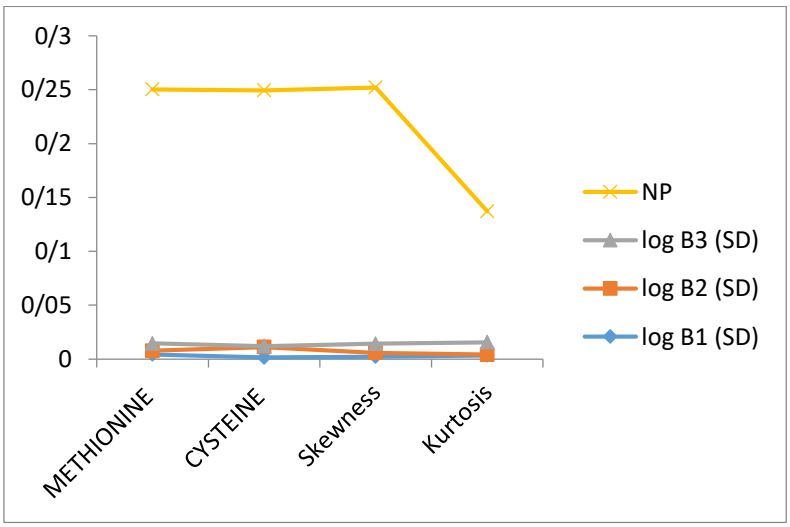

FIGURE 5 The best fit chemical models of protonation equilibrium of metionine and cystein in SLS-water mixtures Temp

Conclusion and further study

L-methionine and L-cysteine complexes both include one proton that is capable of dissociating and one amino group that is able to form an association with a proton. When the pH is lower, it exists as LH^{2+}, but when the pH is higher, it deprotonates, forming LH and L- in the appropriate proportions. L-Methionine and L-cysteine complexes have one amino group that is able to interact with a proton and two protons that are able to dissociate from one another. At lower pH levels, it is present as LH^{3+}; however, when the pH level rises, it deprotonates and generates LH^{2+}, LH, and L^-, respectively. Log k values change non-linearly for L-methionine and L-cysteine complexes. Electrostatic forces dominate protonation-deprotonation equilibria, causing linear variation. The non-linear variation of L-cysteine suggests non-electrostatic solute-solvent interactions. Systematic errors in key data show that alkali and mineral acid concentrations impact protonation constants more than ligands. This is because alkali and mineral acid concentration mistakes are more likely.

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Authors' Contributions

The main author is the one who conduct all the research.

Conflict of Interest

The authors report there are no competing interests to declare.

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