



Viscometric measurements of dipeptides of alanine in aqueous solutions of antibacterial drug ampicillin at different temperatures



Harsh Kumar*, Meenu Singla, Rajeev Jindal

Department of Chemistry, Dr B R Ambedkar National Institute of Technology, Jalandhar 144 011, Punjab, India

ARTICLE INFO

Article history:

Received 7 October 2013

Received in revised form 6 December 2013

Accepted 9 December 2013

Available online 22 December 2013

Keywords:

L-Alanyl-L-alanine

L-Alanyl-L-valine

L-Alanyl-L-leucine

Ampicillin

Viscosity B-coefficient

ABSTRACT

The viscosities, of L-alanyl-L-alanine (Ala-Ala), L-alanyl-L-valine (Ala-Val), L-alanyl-L-leucine (Ala-Leu) with drug ampicillin (AMP) have been measured as a function of temperature at $T = (305.15, 310.15 \text{ and } 315.15) \text{ K}$. The change in viscosity of dipeptides with increase in AMP concentration and temperature is attributed to dipeptide-AMP interactions. The viscosity B-coefficients and viscosity interaction parameters obtained from Jones-Dole equation and transition state theory respectively have been discussed to interpret interactions between ions of dipeptides and ampicillin.

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1. Introduction

Physicochemical and thermodynamic investigations attract the inquisitive minds of researchers owing to the important role that drugs play to understand the nature and the extent of the patterns of molecular aggregation that exist in binary or ternary liquid mixtures [1,2] and their sensitivities to variations in composition and the molecular structure of the pure components [3]. Various concepts regarding molecular processes in solutions, electrostriction [4], hydrophobic hydration [5], micellization [6], and cosphere overlap during solute-solute interactions [7] to a large extent have been derived and interpreted from the partial molar volume data of many compounds. In biophysical chemistry, drug-macromolecular interaction is an important phenomenon involving a complex mechanism [8]. Drug macromolecular interactions involved in drug transport, protein binding and anesthesia are important phenomena in physiological media [9]. The mechanisms of these molecular processes are not yet clearly understood. Attempts are being made to understand these interactions through the properties like partial molar volume, partial molar compressibility and viscosity studies [10,11]. As regard biomolecules, studies on amino acids have been made by Millero [12] and only these measurements have been adopted for a few drug molecules [13]. Despite years of investigations, many important drug actions [14] and their mechanisms are not fully understood. Among drugs broad spectrum penicillins like ampicillin and amoxicillin constitutes a major budget of hospitals. Several experimental investigations have been carried out to understand the action of

drugs in aqueous solution [15,16] as they exert their activity by interaction with biological membrane. Viscosity studies of solution provide valuable information regarding the solute-solvent interactions. Structure making and breaking effects of an electrolyte on solvent can be determined by various parameters resolved from viscosity studies. Recent literature on the physical and thermodynamics studies of drugs and other materials of biological importance shows increasing interest by a number of workers in this area of study [17–21]. A number of researchers have determined viscosity B-coefficients of amino acids and peptides in aqueous media [22–27] and in aqueous drug solutions [28]. As part of the long-term objective to investigate the thermodynamics studies and various aspects of drug-macromolecular interactions [29–32], we report the results of determination of viscosity of the drug ampicillin with dipeptides of alanine viz. L-alanyl-L-alanine, L-alanyl-L-valine, and L-alanyl-L-leucine in situ conditions. The temperature chosen for the present study is our body temperature that is 37°C and 5°C higher and lower of our body temperature. To the best of our knowledge no data on thermodynamic studies of ampicillin with dipeptides have been reported so far except for few studies [33–35] on volumetric properties of aqueous alanine dipeptides solutions at 298.15 K .

Table 1
Specification of chemical samples.

| Chemical name | Provenance | Mass fraction purity |
|--------------------|----------------------|----------------------|
| Ampicillin | M P Biomedicals, USA | >0.99 |
| L-Alanyl-L-alanine | M P Biomedicals, USA | >0.99 |
| L-Alanyl-L-valine | M P Biomedicals, USA | >0.99 |
| L-Alanyl-L-leucine | M P Biomedicals, USA | >0.99 |

* Corresponding author.

E-mail addresses: h.786.man@gmail.com, manchandah@nitj.ac.in (H. Kumar).

Table 2
Viscosities (η) of dipeptides of alanine in aqueous solutions of AMP at different temperatures.

| $\frac{m}{(\text{mol}\cdot\text{kg}^{-1})}$ | $\frac{\eta}{(\text{mPa}\cdot\text{s})}$ | | |
|---|--|--------------|--------------|
| | T = 305.15 K | T = 310.15 K | T = 315.15 K |
| <i>Ala-Ala + water</i> | | | |
| 0.00000 | 0.7651 | 0.6965 | 0.6406 |
| 0.00215 | 0.7669 | 0.7029 | 0.6416 |
| 0.00421 | 0.7674 | 0.7032 | 0.6452 |
| 0.00596 | 0.7681 | 0.7033 | 0.6473 |
| 0.00831 | 0.7688 | 0.7061 | 0.6487 |
| 0.00955 | 0.7719 | 0.7067 | 0.6499 |
| 0.01169 | 0.7741 | 0.7084 | 0.6499 |
| 0.01422 | 0.7782 | 0.7089 | 0.6519 |
| 0.01594 | 0.7795 | 0.7115 | 0.6548 |
| 0.01778 | 0.7798 | 0.7139 | 0.6573 |
| 0.01983 | 0.7828 | 0.7167 | 0.6608 |
| <i>Ala-Ala + 0.0005 mol · kg⁻¹ AMP</i> | | | |
| 0.00000 | 0.7656 | 0.7019 | 0.6419 |
| 0.00194 | 0.7685 | 0.7031 | 0.6428 |
| 0.00392 | 0.7706 | 0.7042 | 0.6458 |
| 0.00604 | 0.7738 | 0.7054 | 0.6483 |
| 0.00794 | 0.7774 | 0.7063 | 0.6497 |
| 0.00996 | 0.7785 | 0.7064 | 0.6509 |
| 0.01207 | 0.7837 | 0.7081 | 0.6532 |
| 0.01405 | 0.7839 | 0.7089 | 0.6549 |
| 0.01607 | 0.7841 | 0.7111 | 0.6556 |
| 0.01842 | 0.7860 | 0.7148 | 0.6589 |
| 0.02002 | 0.7912 | 0.7192 | 0.6618 |
| <i>Ala-Ala + 0.002 mol · kg⁻¹ AMP</i> | | | |
| 0.00000 | 0.7729 | 0.6993 | 0.6442 |
| 0.00193 | 0.7732 | 0.7034 | 0.6456 |
| 0.00402 | 0.7739 | 0.7046 | 0.6481 |
| 0.00585 | 0.7746 | 0.7058 | 0.6487 |
| 0.00802 | 0.7751 | 0.7068 | 0.6511 |
| 0.00983 | 0.7756 | 0.7086 | 0.6519 |
| 0.01190 | 0.7791 | 0.7101 | 0.6535 |
| 0.01411 | 0.7843 | 0.7105 | 0.6552 |
| 0.01589 | 0.7873 | 0.7113 | 0.6562 |
| 0.01783 | 0.7907 | 0.7173 | 0.6595 |
| 0.02019 | 0.7952 | 0.7211 | 0.6628 |
| <i>Ala-Ala + 0.004 mol · kg⁻¹ AMP</i> | | | |
| 0.00000 | 0.7701 | 0.7032 | 0.6399 |
| 0.00199 | 0.7734 | 0.7042 | 0.6467 |
| 0.00399 | 0.7742 | 0.7052 | 0.6486 |
| 0.00612 | 0.7748 | 0.7063 | 0.6501 |
| 0.00809 | 0.7755 | 0.7089 | 0.6518 |
| 0.01014 | 0.7763 | 0.7105 | 0.6525 |
| 0.01233 | 0.7798 | 0.7116 | 0.6539 |
| 0.01403 | 0.7849 | 0.7134 | 0.6559 |
| 0.01612 | 0.7878 | 0.7167 | 0.6589 |
| 0.01828 | 0.7912 | 0.7198 | 0.6601 |
| 0.02026 | 0.7964 | 0.7219 | 0.6615 |
| <i>Ala-Val + water</i> | | | |
| 0.00000 | 0.7651 | 0.6965 | 0.6406 |
| 0.00201 | 0.7756 | 0.7078 | 0.6470 |
| 0.00414 | 0.7779 | 0.7083 | 0.6501 |
| 0.00605 | 0.7783 | 0.7121 | 0.6523 |
| 0.00791 | 0.7805 | 0.7125 | 0.6554 |
| 0.01019 | 0.7822 | 0.7162 | 0.6591 |
| 0.01179 | 0.7866 | 0.7192 | 0.6601 |
| 0.01396 | 0.7955 | 0.7239 | 0.6623 |
| 0.01551 | 0.8038 | 0.7284 | 0.6675 |
| 0.01805 | 0.8095 | 0.7327 | 0.6689 |
| 0.01971 | 0.8143 | 0.7351 | 0.6701 |
| <i>Ala-Val + 0.0005 mol · kg⁻¹ AMP</i> | | | |
| 0.00000 | 0.7656 | 0.7019 | 0.6419 |
| 0.00199 | 0.7758 | 0.7053 | 0.6491 |
| 0.00409 | 0.7782 | 0.7112 | 0.6505 |
| 0.00599 | 0.7805 | 0.7156 | 0.6529 |
| 0.00794 | 0.7856 | 0.7201 | 0.6561 |
| 0.01032 | 0.7901 | 0.7225 | 0.6601 |
| 0.01226 | 0.7954 | 0.7256 | 0.6618 |
| 0.01438 | 0.8012 | 0.7289 | 0.6647 |

Table 2 (continued)

| $\frac{m}{(\text{mol}\cdot\text{kg}^{-1})}$ | $\frac{\eta}{(\text{mPa}\cdot\text{s})}$ | | |
|---|--|--------------|--------------|
| | T = 305.15 K | T = 310.15 K | T = 315.15 K |
| 0.01643 | 0.8095 | 0.7301 | 0.6667 |
| 0.01851 | 0.8121 | 0.7332 | 0.6717 |
| <i>Ala-Val + 0.002 mol · kg⁻¹ AMP</i> | | | |
| 0.00000 | 0.7729 | 0.6993 | 0.6442 |
| 0.00204 | 0.7765 | 0.7065 | 0.6503 |
| 0.00409 | 0.7785 | 0.7159 | 0.6513 |
| 0.00598 | 0.7809 | 0.7204 | 0.6535 |
| 0.00799 | 0.7861 | 0.7229 | 0.6568 |
| 0.00984 | 0.7915 | 0.7235 | 0.6606 |
| 0.01198 | 0.8012 | 0.7269 | 0.6624 |
| 0.01432 | 0.8056 | 0.7297 | 0.6651 |
| 0.01607 | 0.8101 | 0.7303 | 0.6672 |
| 0.01724 | 0.8128 | 0.7335 | 0.6724 |
| 0.01961 | 0.8159 | 0.7359 | 0.6739 |
| <i>Ala-Val + 0.004 mol · kg⁻¹ AMP</i> | | | |
| 0.00000 | 0.7701 | 0.7032 | 0.6399 |
| 0.00203 | 0.7797 | 0.7123 | 0.6511 |
| 0.00409 | 0.7815 | 0.7162 | 0.6521 |
| 0.00579 | 0.7849 | 0.7208 | 0.6545 |
| 0.00777 | 0.7898 | 0.7235 | 0.6575 |
| 0.01015 | 0.7945 | 0.7278 | 0.6608 |
| 0.01212 | 0.8016 | 0.7301 | 0.6625 |
| 0.01399 | 0.8059 | 0.7315 | 0.6659 |
| 0.01536 | 0.8105 | 0.7324 | 0.6684 |
| 0.01788 | 0.8135 | 0.7339 | 0.6729 |
| 0.01905 | 0.8165 | 0.7368 | 0.6742 |
| <i>Ala-Leu + water</i> | | | |
| 0.00000 | 0.7651 | 0.6965 | 0.6406 |
| 0.00185 | 0.7759 | 0.7079 | 0.6492 |
| 0.00389 | 0.7781 | 0.7086 | 0.6505 |
| 0.00579 | 0.7785 | 0.7126 | 0.6525 |
| 0.00813 | 0.7806 | 0.7129 | 0.6559 |
| 0.00966 | 0.7826 | 0.7165 | 0.6596 |
| 0.01220 | 0.7869 | 0.7198 | 0.6605 |
| 0.01422 | 0.7960 | 0.7242 | 0.6629 |
| 0.01589 | 0.8042 | 0.7292 | 0.6678 |
| 0.01753 | 0.8098 | 0.7334 | 0.6692 |
| 0.02055 | 0.8149 | 0.7359 | 0.6709 |
| <i>Ala-Leu + 0.0005 mol · kg⁻¹ AMP</i> | | | |
| 0.00000 | 0.7656 | 0.7019 | 0.6419 |
| 0.00197 | 0.7901 | 0.7114 | 0.6507 |
| 0.00391 | 0.7945 | 0.7161 | 0.6532 |
| 0.00591 | 0.7976 | 0.7204 | 0.6567 |
| 0.00814 | 0.7999 | 0.7234 | 0.6602 |
| 0.01003 | 0.8042 | 0.7251 | 0.6634 |
| 0.01192 | 0.8056 | 0.7294 | 0.6649 |
| 0.01415 | 0.8099 | 0.7306 | 0.6652 |
| 0.01585 | 0.8112 | 0.7333 | 0.6698 |
| 0.01835 | 0.8135 | 0.7356 | 0.6718 |
| 0.01982 | 0.8159 | 0.7365 | 0.6736 |
| <i>Ala-Leu + 0.002 mol · kg⁻¹ AMP</i> | | | |
| 0.00000 | 0.7729 | 0.6993 | 0.6442 |
| 0.00191 | 0.7905 | 0.7116 | 0.6512 |
| 0.00393 | 0.7949 | 0.7162 | 0.6521 |
| 0.00602 | 0.7978 | 0.7215 | 0.6554 |
| 0.00799 | 0.8001 | 0.7236 | 0.6578 |
| 0.00993 | 0.8045 | 0.7255 | 0.6614 |
| 0.01227 | 0.8059 | 0.7299 | 0.6632 |
| 0.01451 | 0.8102 | 0.7312 | 0.6659 |
| 0.01635 | 0.8139 | 0.7335 | 0.6687 |
| 0.01824 | 0.8161 | 0.7359 | 0.6735 |
| 0.02026 | 0.8168 | 0.7368 | 0.6748 |
| <i>Ala-Leu + 0.004 mol · kg⁻¹ AMP</i> | | | |
| 0.00000 | 0.7701 | 0.7032 | 0.6399 |
| 0.00196 | 0.7906 | 0.7121 | 0.6516 |
| 0.00392 | 0.7952 | 0.7165 | 0.6526 |
| 0.00609 | 0.7989 | 0.7219 | 0.6559 |
| 0.00794 | 0.8005 | 0.7242 | 0.6579 |
| 0.00992 | 0.8049 | 0.7259 | 0.6619 |
| 0.01241 | 0.8062 | 0.7301 | 0.6636 |
| 0.01437 | 0.8104 | 0.7316 | 0.6662 |

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