*Pakistan Journal of Pharmaceutical Sciences*
*Vol.17, No.1, January 2004, pp.83-87*

## SHORT COMMUNICATION

# THERMODYNAMIC DISSOCIATION CONSTANT STUDIES OF CAFFEINE AT DIFFERENT TEMPERATURES AND IN ORGANIC WATER SOLVENT MIXTURE

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**ABSTRACT:**
Thermodynamic dissociation studies have been carried out potentiometrically at various temperatures from 25 to 50°C and in 10, 20, 30 and 40% v/v dioxane-water solvent mixture at 25°C. The influence of temperature and nature of solvent on dissociation equilibria of caffeine is being investigated A computer program in GW-BASIC has been used to calculate the pK values.

## INTRODUCTION

Caffeine, theophlline and theobromine are three closely related alkaloids, that occur in plants widely distributed geographically. Caffeine is 1,3,7-trimethylxanthine relax various muscles, notable bronchial muscle, stimulate cardiac muscle and act on the kidney to produce diuresis. Persons ingesting caffeine or caffeine containing beverages usually experience less drowsiness, less fatigue and a more rapid and clear flow of thoughts (Goodman & Gilman, 1990).

The dissociation constant (pK) of weak acids and bases is widely used in pharmaceutical industries, in biological sciences, in preparative chemistry and in structure elucidation of newly isolated species (Albert & Serjeant, 1984). There are different methods (Albert & Serjeant, 1984; Asuero *et al.,* 1986; Papanastiou & Ziogas, 1989; Barbosa *et al.*, 199l; Song Li & Purdy, 1991 and Saeeduddin & Khanzada, 1995; 1996; 1997 & 2002) which are being used for determination of dissociation constant of weak acids and bases. These methods have certain limitations. Such as solubility, range of pK, time requirement etc. The quick method for this purpose is potentiometry while spectorphotometric method is very accurate but it is time consuming.

There is still possibility to work on determination of dissociation constants of biologically important substance, where data on various temperature and in different solvents mixture is not available frequently.

The potentiometric titration has been improved by elimination of carbon dioxide using dried and purified nitrogen gas (Albert and Serjeant, 1984) standardized glass e1ectrode, precision pH-meter, temperature control accurate to ± 0.1°C and availability of computer program for calculation of accurate pKb values from experimental data.

## EXPERIMENTAL

All chemicals were of analytical grade and were used without further purification. Doubly degassed distilled water was used in preparation of all solutions. Fresh and distilled dioxane was

also used. Stock solution of 0.01M caffeine in water and 0.1M HCl containing 10, 20, 30 and 40% dioxane, were also prepared. The potentiometric titrations were performed into thermostated double walled glass cell containing 50ml of sample solution with HCl. The pH was determined with PHILIPS PW 9420 digital pH meter which was coupled with ingold combined glass and reference electrode dipped in sample solution whose temperature was controlled by circulating water through the jacket measuring cell, JULABO HC thermostated bath accurate +0.1$^{o}$C was used for controlling the temperature.

Prior to experiment the glass electrode was calibrated with 0.05 M potassium hydrogen phthalate (pH at 25$^{o}$C=4.005) and potassium dihydrogen phosphate and disodium hydrogen phosphate, each 0.035 M (pH at 25$^{o}$C= 6.863) in aqueous and in respective organic-water solvent mixture (Albert, 1984 and Galster, 1991). Sample solution was kept mixed by stirring with magnetic stirrer and inert by bubbling nitrogen gas which was dried and purified by passing through Fieser's solution (Albert and Serjeant, 1984). For dispensing titrant, Mettler burette DV-10 accurate to 0.01 ml was used.

The potentiometric measurement was performed on sample solution at different temperature and in 10, 20, 30 and 40% of dioxane-water solvent mixture.

The potentiometric data was analysed by a computer program written in GWBASIC for calculation of dissociation constants of monoacidic basis (Khanzada, unpublished computer program).

## RESULTS AND DISCUSSION

A change in temperature causes a shift in equilibrium point which is of both practical and theoretical interest. Mostly reported pKs values are determined at 25$^{o}$C or 18$^{o}$C so efforts have been made to see the effect of temperature variation on pK values. We extended temperature range from 25 to 50$^{o}$C with 5$^{o}$C interval. Results obtained at 25$^{o}$C agree with the reported results (Robert, 1987).

Results presented in Table-1 help to view the effect of temperature on $pK_b$ values and thermodynamic constants of caffeine. Variation in $pK_b$ with temperature is considerable between 25 to 40$^{o}$C while there is no sharp decrease in $pK_b$ values between 40 to 50$^{o}$C (Fig. 1).

Table-1 and Fig. 2 are showing the effect of temperature on thermodynamic constant ($\Delta G$). Change in thermodynamic function can be calculated by using equation (1) (King, 1965).

$$\Delta G = — RT \ln K \qquad (1)$$
$$G = 2.303\ RT\ pKa$$

Mixture of water with organic solvents particularly dioxane is popular media for studying acid-base behaviour. In the present case we used dioxane solvent. Organic compounds that are not soluble in water are often brought into solution by addition of organic solvents. Organic solvents may be used as mixture with each other or with water. For this reason it is interesting to compare their behaviour with that of water. One of the most important property of a solvent is its dielectric constant, which defines to a considerable degree of solvating ability of the medium (Budevsky, 1979).

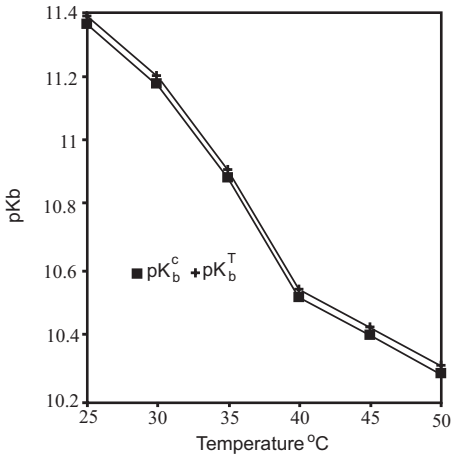


Fig. 1: Effect of temperature on pKb values of caffeine.

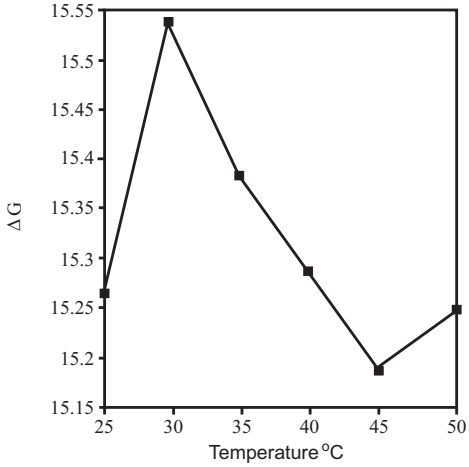


Fig. 2: Effect of temperature on ΔG values of caffeine.

**Table 1**
Effect of temperature on pK values and ΔG values of caffeine

| Temperature °C | pK values Evaluated | | pK values Reported* pK | ΔG values K cal/mol |
|---|---|---|---|---|
| | $pK_b^c$ | $pK_b^T$ | | |
| 25 | 11.357 ± 0.006 | 11.381 ± 0.009 | 11.2 | 15.265 |
| 30 | 11.178 ± 0.009 | 11.203 ± 0.006 | | 20.354 |
| 35 | 10.885 ± 0.01 | 10.911 ± 0.008 | | 20.278 |
| 40 | 10.521 ± 0.007 | 10.547 ± 0.01 | | 20.077 |
| 45 | 10.404 ± 0.006 | 10.430 ± 0.01 | | 15.187 |
| 50 | 10.287 ± 0.005 | 10.314 ± 0.003 | | 15.248 |

*Robert & Weast (1987).

Selection of the solvent based on the fact that water and dioxane are the solvent having dielectric constant values 78.5 and 2.21 respectively and water has the ability to form hydrogen bonds while dioxane having dielectric constant value 2.21, but has no ability to form hydrogen bonds.

Fig.3 shows that as composition of organic solvent (dioxane) increase in mixture then $pK_b$ values of caffeine increases. When composition of dioxane-water increase from 10 to 20% v/v

then minimum increase in $pK_b$ value has been marked, while when composition further increases from 20 to 30 and 30 to 40% then there is sizable increase in $pK_b$ values.

We marked in Fig.3 that as composition of organic solvent increases then $pK_b$ values also increases. The dielectric constant of a solvent is measure of a solvent efficiency to separate oppositely charged ions. According to Columb's Law the attraction of forces (F in Newton) between two ions of charged $q^-$ and $q^+$ (in coulombs) separated by distance r (in meter) is:

$$F = \frac{8.988x10^9 q}{\varepsilon_{R^2}}$$

Where "ε" is the dielectric constant of the solvent. The attractive force is inversely proportional to the dielectric constant. The larger the value of the dielectric constant, the smaller the attraction forces between the two ions ($H^+$ and $B^-$ for dissociation reaction of base).

$$BH^+ ===== H + B \text{ (for base)}$$

and thus the larger the acidity constant or pKb values decreases. The dielectric constant of water and dioxane are 78.5 and 2.21 respectively, with an increase of dioxane concentration, the dielectric constant value of solvent will decrease resulting in a decrease of acidity constant or increase in pKa values (Song Li *et al.*, 1991).

Fig. 4 show the effect of dioxane-water solvent mixture (v/v %) on ΔG values of caffeine. As composition of solvent (dioxane) increase in mixture then ΔG value increases. Actually thermodynamic property (ΔG) offered interesting insight into acid base behaviour particularly with regard to solvation effect.

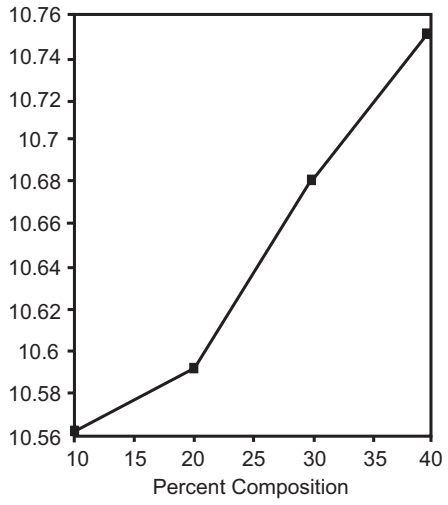


Fig. 3: Effect of organic-water solvent mixture on pKb values of caffeine.

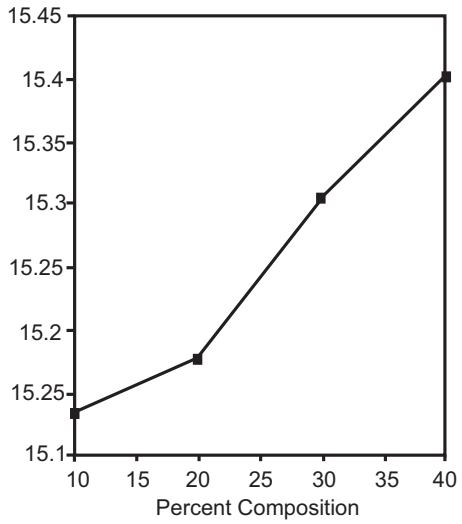


Fig. 4: Effect of organic-water solvent mixture on ΔG values of caffeine.

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