Thermochimica Acta, 205 (1992) 5–9
Elsevier Science Publishers B.V., Amsterdam

Heat of solution of Desferal at 298.15 K

Gabriele D'Andrea and Felice Fantauzzi

Dipartimento di Scienze e Tecnologie Biomediche e di Biometria, Università dell'Aquila, 67100 L'Aquila (Italy)

(Received 8 November 1991)

Abstract

The heat of solubilization of Desferal in three different aqueous solutions was measured at 298.15 K. Both at pH 7.402 and in milli-Q water an endothermic reaction was observed; in contrast, at pH 9.410 the reaction was exothermic.

INTRODUCTION

Desferal (deferoxamine methanesulfonate, deferoxamine mesylate) is a chelating agent which complexes mainly trivalent ions such as Fe and Al. Notably, it has a high affinity and specificity for the ferric ion (affinity constant 10^{31}) and chelates it in a 1:1 molar ratio. Owing to these properties, Desferal is widely used for therapeutic purposes where iron or aluminum poisoning occurs, because the ferrioxamine and aluminoxamine complexes are completely excreted in the urine or feces, reducing pathological accumulations of these two ions. Moreover, the Desferal test is used for diagnosis when an accumulation of iron or aluminum is suspected. In biochemical studies, Desferal is used to produce the corresponding N-terminal monoferric form of human transferrin starting from the fully iron saturated molecule. Because an accurate knowledge of the thermodynamic properties of Desferal is desirable, in this paper we report the heats of solubilization of this compound at 298.15 K in two different buffer solutions and in milli-Q water.

EXPERIMENTAL

Lyophilized Desferal (Ciba-Geigy; used without purification) was weighed and handled in a nitrogen-filled dry box. Two stock bicarbonate buffer solutions were prepared using milli-Q water (10 M$\Omega \times$ cm) to contain 0.05

Correspondence to: Dr. G. D'Andrea, Dipartimento di S.T.B.B., Università Collemaggio, 67100 L'Aquila, Italy.

M Tris and 5 mM $NaHCO_3$; pH values of 7.402 and 9.410 were obtained using 1 M HCl. Weighed amounts of buffer solution or milli-Q water were loaded in the reaction vessel of a Tronac 450-458 isoperibol calorimeter; then pre-determined amounts of lyophilized Desferal were added by means of glass bulbs. Thermal equilibrium was usually obtained within 20 min after charging the apparatus, and about 10 min was allowed for the reaction to reach completion after mixing the reagents. The temperature changes in the vessel were measured using a thermistor and a Fluka model 8810A digital multimeter, and were recorded by means of an Olivetti M24 personal computer. Calculation methods and computer programs (in BASIC) for the determination of solubilization heats and reaction in isothermal and quasi-adiabatic calorimeters were used [1–3].

RESULTS AND DISCUSSION

Lyophilized Desferal was dissolved in three different aqueous solutions and the heats of solubilization were calculated by processing the thermograms with a specific computer program. In view of the fact that Desferal at pH 7.4 removes iron preferentially from the C-terminal site of human serum transferrin (producing the corresponding N-terminal form) [4], and because it is known that around pH 9.4, starting from the apo-form of human serum transferrin, the N site is preferentially loaded using the Fe–nitrilotriacetic acid complex as metal donor [5], we have chosen these pH values for our measurements. However, it should be kept in mind that this drug is administered mainly intravenously, where the pH is around 7.4.

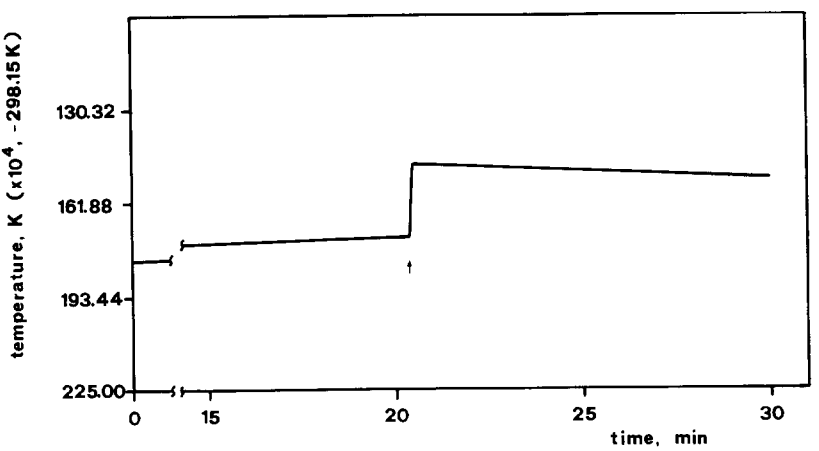

Fig. 1. Thermogram obtained in Tris buffer, pH 7.402. Arrow shows the point of addition of Desferal.

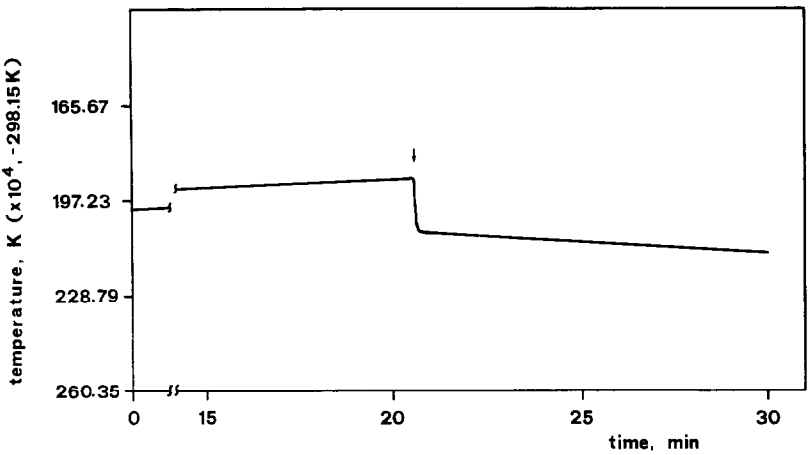

Fig. 2. Thermogram obtained in Tris buffer, pH 9.410. Arrow shows the point of addition of Desferal.

To gain a deeper insight into the thermodynamic properties of Desferal, the heat of solubilization was measured also in milli-Q water. Figures 1–3 show typical thermograms obtained at around 298.15 K. In the case of milli-Q water and Tris buffer, pH 7.402, one can see that during the solubilization process an endothermic reaction occurs, and is slightly more pronounced in the case of milli-Q water. Conversely, when Desferal was dissolved in Tris buffer, pH 9.410, an exothermic reaction was recorded. Table 1 shows the enthalpies of solubilization obtained using the same amount of solution (2.5 g) and almost the same molar amount of Desferal (around 2.5×10^{-5} mol). Interestingly, at pH 9.410 the standard deviation

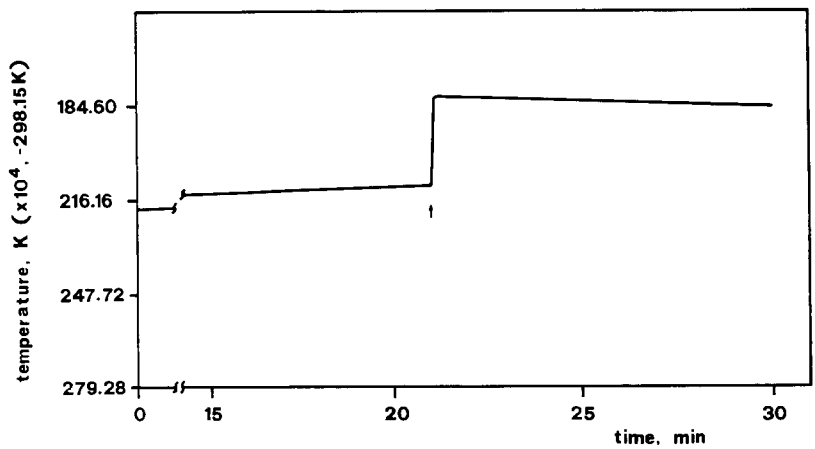

Fig. 3. Thermogram obtained in milli-Q water. Arrow shows the point of addition of Desferal.

TABLE 1

Change in enthalpy on solubilization of Desferal

Solvent (g)	Desferal (mol × 10^5)	ΔH (kJ mol^{-1})	Average	Standard deviation
Tris buffer, pH 7.402				
2.5	2.64612	+18.89		
2.5	2.61567	+19.32	+19.77	0.95
2.5	2.54450	+21.09		
Tris buffer, pH 9.410				
2.5	2.52736	−17.63		
2.5	2.37816	−17.67	−17.66	0.02
2.5	2.43145	−17.68		
Milli-Q water				
2.5	2.42536	+25.81		
2.5	2.56086	+24.93	+25.17	0.45
2.5	2.61415	+24.78		

was almost negligible, whereas around pH 7.402 a very high value of standard deviation was obtained (Table 1). This behavior could be explained by considering that the isoelectric point (pI) of Desferal is around 9.6 and thus at pH 9.410 a much more stable molecule could be postulated. The standard deviation obtained in milli-Q water was near to the average value between the two different buffers. It should be emphasized here that chelation programs for both acute iron intoxication and iron-overload anemias involve mainly the intravenous route in acute cases and nightly subcutaneous infusions combined with monthly intravenous infusions in chronic illness. It is reported that hypotension is the most alarming short term toxic effect of Desferal [6]; among other physico-chemical factors, a possible localized heat development could be suggested as contributing to venous dilation.

ACKNOWLEDGMENT

This work was supported by funds from M.U.R.S.T. (Ministero dell'Università e della Ricerca Scientifica e Tecnologica, Rome, Italy).

REFERENCES

1 F. Rodante and A. Onofri, Thermochim. Acta, 94 (1985) 239.
2 F. Rodante and R. Rosati, Thermochim. Acta, 117 (1987) 167.
3 F. Rodante, A. Onofri and P. Perticaroli, Thermochim. Acta, 124 (1988) 185.

4 D.C. Harris and P. Aisen, in T.M. Loehr (Ed.), Iron Carriers and Iron Proteins, VCH Publishers, New York, 1989, p. 277.
5 H.G. van Eijk, W.L. van Noort, M.J. Kroog and C. van der Heul, J. Clin. Chem. Clin. Biochem., 18 (1980) 563.
6 C.F. Whitten, G.W. Gibson, M.H. Good, G.J. Goodwin and A.J. Brough, Pediatrics, 36 (1965) 322.