ELSEVIER

Inorganica Chimica Acta 223 (1994) 9–11

Inorganica Chimica Acta

Preliminary Communication

Mössbauer spectroscopy of iron dextran: comparison of solid and frozen solution

Emma M. Coe[a], Lawrence H. Bowen[a], Robert D. Bereman[a], William T. Monte[b]

[a]*Department of Chemistry, Box 8204, North Carolina State University, Raleigh, NC 27695-8204, USA*

[b]*Department of Chemical Research and Development, Chemical and Agricultural Products Division, Abbott Laboratories, North Chicago, IL 60064-4000, USA*

Received by Editor 19 January 1994; received by Publisher 20 April 1994

Abstract

An injectable iron dextran complex used as a hematinic has been studied using Mössbauer spectroscopy (18–295 K), both as a frozen aqueous solution and in the solid state. The iron in the complex was found to be all high-spin Fe^{3+}. The spectra were fitted to a distribution of doublets at room temperature and to a distribution of sextets at low temperatures. There is also a range of temperatures over which both sextet and doublet co-exist. The relatively large distribution of particle sizes gives rise to a broad and asymmetric sextet distribution. The results show that the iron core in the frozen solution and in the solid state is essentially the same species.

Keywords: Mössbauer spectroscopy; Iron complexes; Dextran complexes

1. Introduction

Great interest has been shown in the soluble, stable complexes of iron which have been used in the treatment of anemia, the illness which can be caused by iron deficiency [1]. Iron dextran complexes have been used both as an oral iron supplement (as a solid) [2], and as an injectable source of iron (as a solution) in severe cases [3]. These complexes are capable of maintaining relatively high concentrations of iron in a soluble, non-toxic form at physiological pH, and are effective sources of iron in the human biological system [4].

The efficacy of iron dextrans might be explained by the fact that the iron core has some physical properties in common with the iron storage protein, ferritin. EXAFS [5,6] and Mössbauer spectroscopic [6,7] studies have shown a similarity between the iron core of Imferon, an iron dextran pharmaceutical [8], and horse spleen ferritin. The electron diffraction pattern of Imferon, however, was found to be more similar to β-FeOOH, (akaganéite) [9], than to the proposed ferrihydrite structure of ferritin.

Relatively few studies of the chemical and physical properties of the iron dextran complexes have been carried out to date. The present study is concerned primarily with the Mössbauer spectroscopic comparison of an iron dextran pharmaceutical in the solid state with the same complex as a frozen aqueous solution.

2. Experimental

The iron dextran samples were supplied by Abbott Laboratories and used without modification. The complex was prepared by adding a solution of dextran to a base-neutralized $FeCl_3$ solution, followed by heating up to 100 °C and then sterilizing by autoclaving. The solution was a 5% Fe by weight aqueous solution made from the powdered complex and in the form used as a pharmaceutical.

Mössbauer spectra were obtained at various temperatures using a ~ 25 mCi ^{57}Co(Rh) source. The spectra collected below room temperature were obtained with the absorber in a closed-cycle helium cryostat (maintained to within ≈ 0.1 K). In all cases the source was at room temperature. The velocity was calibrated by laser interferometry [10].

The solid absorber was made from a mixture of the iron dextran sample (approximately 40 mg) and powdered sucrose pressed flat into a uniform thickness. The sample was mounted in a brass ring having an inside area of 1.75 cm^2. A benzene/styrofoam mixture

SSDI 0020-1693(94)04001-C

was used to seal the sample within the ring and aluminum foil was used as the backing. The 5% iron dextran solution was used as supplied, and contained by a brass holder within mylar windows compressed by an o-ring.

The spectra were fitted, after subtraction of the Fe in the spectrometer windows and in the aluminum foil used, to a distribution of doublets at room temperature, mixtures of doublets and sextets at intermediate temperature and a distribution of sextets (and doublets if needed) at lower temperature [11]. All lines were assumed to be of Lorentzian shape, with the full width at the half maximum fixed at 0.35 mm/s. The fitting program allowed the isomer shift, quadrupole splitting and peak area ratios to vary.

3. Results and discussion

The 295 K Mössbauer spectrum for the solid sample of iron dextran is compared to those of ferritin, Imferon and akaganéite [6,9] in Table 1. Like Imferon, iron dextran has a marked asymmetry in the maximum and mean quadrupole splittings. However, the values for the iron dextran complex are significantly higher. Ferritin does not exhibit such asymmetry, and has lower values of QS(mean) than both Imferon and iron dextran. The quadrupole splittings for iron dextran are quite distinct from the values for akaganéite, which is best fit to two doublets at r.t.

It can be seen that the solid and frozen solution Mössbauer spectra of the iron dextran give essentially the same temperature variation of percent doublet (Fig. 1). The low temperature hyperfine fields, both H_{max} and H_{av}, are in agreement within about 10 kOe between the solution and the solid (Fig. 2). Recognizing that the probability distribution of fields is broad (a typical standard deviation for H is for example, 90 kOe at 50 K), the curves for H_{av} are essentially superimposed, with an extrapolated intercept at 0 K of about 465 kOe. The intercept for H_{max} is about 490 kOe, for the solid, but appears to be closer to 500 kOe for the solution. Oshtrakh et al. [12] mention that Mössbauer spectra of the iron dextran frozen solutions were similar to those of the solid at 87 K, but the present results are the first to compare frozen solution to solid in a detailed way over a range of low temperatures.

Table 1
Comparison of 295 K Mössbauer data (solid samples)

Compound	Isomer shift	QS(mean/max.)	Reference
Ferritin	0.36	0.64/0.62	[6]
Imferon	0.36	0.72/0.61	[6]
Akaganéite	0.38	0.55	[9]
	0.39	0.95	[9]
Iron dextran	0.36	0.77/0.72	this work

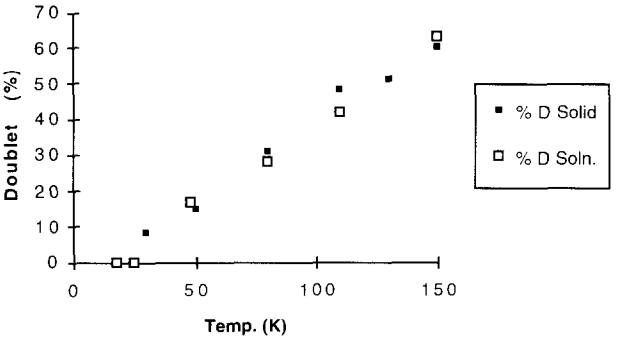

Fig. 1. Percent doublet vs. temperature.

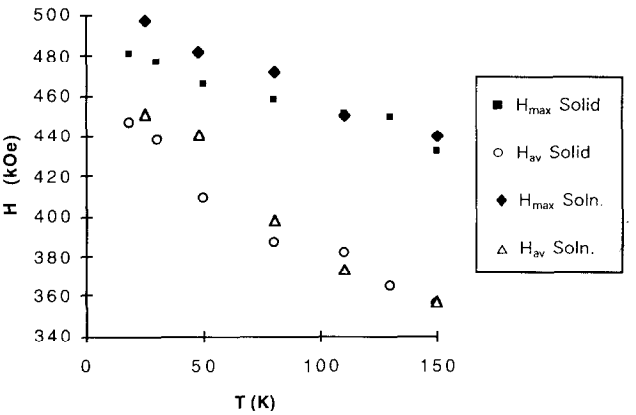

Fig. 2. Field of maximum probability and mean hyperfine field vs. temperature.

Comparing the present spectra to reported low temperature spectra of Imferon [6], it is clear that there are differences, due presumably to subtle differences in synthesis. However, there are also differences between Imferon samples. In contrast to earlier [6,7] work that reported the Imferon Mössbauer spectra to be entirely doublet, a recent paper mentions that at 87 K the Mössbauer spectrum of an Imferon sample was a mixture of doublet and sextet, although the relative areas are not reported [12]. The field value given for this Imferon at 87 K, 488 kOe [12], is distinctly higher than the value obtained for the present iron dextran samples at a comparable temperature. The field values reported earlier for Imferon [6] at 20 K are, in contrast, somewhat lower (H_{max}/H_{av} = 466/373 kOe) than the present sample (H_{max}/H_{av} = 481/447).

The present samples give lower percentage doublet at all low temperatures than the lyophilized Imferon of Yang et al. [6] and have higher fields at 20 K, both H_{max} and H_{av}. Thus there are significant differences in the iron cores of the iron dextran under study and Imferon. Our results indicate that the core properties are for the most part unaffected by particle–particle interactions in the solid or by solvent effects in the frozen solution. Thus the iron core in the frozen solution and the solid state is essentially the same species.

However, other samples should be studied both as solution and solid to observe if the slightly increased H_{max} observed for the solution in the present case is a significant general occurrence.

References

[1] S.A. Barker, P.J. Somers and J. Stevenson, *Carbohyd. Res., 36* (1974) 331.
[2] K.A. Berg, L.H. Bowen, S.W. Hedges, R.D. Bereman and C.T. Vance, *J. Inorg. Biochem., 22* (1984) 125.
[3] F. Fletcher and E. London, *Br. Med. J., 1* (1954) 984.
[4] E. London and G. Twigg, Imferon (tm), *British Patent No. 78 024* (23 Feb. 1954).
[5] M.A. Brown, D.E. Sayers and E.C. Theil, *J. Biol. Chem., 254* (1979) 8132.
[6] C.-Y. Yang, A.M. Bryan, E.C. Theil, D.E. Sayers and L.H. Bowen, *J. Inorg. Biochem., 28* (1986) 393.
[7] P.R. Marshall and D. Rutherford, *J. Colloid Interface Sci., 37* (1971) 390.
[8] K.M. Towe, *J. Biol. Chem., 256* (1981) 9377.
[9] E. Murad, *Clay Miner., 14* (1979) 273.
[10] E. DeGrave, L.H. Bowen and S.W. Hedges, *Nucl. Instrum. Methods, 200* (1982) 303.
[11] D.D. Amarasiriwardena, E. DeGrave, L.H. Bowen and S.B. Weed, *Clays Clay Miner., 34* (1986) 250.
[12] M.I. Oshtrakh, E.A. Kopelyan, V.A. Semionkin, A.B. Livshits, V.E. Krylova and A.A. Kozlov, *Mater. Sci. Forum, 105–110* (1992) 1679.