Powder diffraction data for ferrous gluconate

Joel W. Reid[a)]
Canadian Light Source, 44 Innovation Boulevard, Saskatoon, SK, S7N 2V3, Canada

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Synchrotron powder diffraction data have been obtained and indexed for ferrous gluconate, a common supplement used for the treatment and prevention of iron-deficiency anemia. Ferrous gluconate ($Fe(C_6H_{11}O_7)_2 \cdot x\,H_2O$, $Z = 4$) crystallizes in a monoclinic cell (space group $I2$, #5) with lattice parameters $a = 19.953\,16(9)$ Å, $b = 5.513\,92(3)$ Å, $c = 18.470\,58(9)$ Å, and $\beta = 111.3826(3)°$. The pattern shows no evidence of impurity reflections. © *2016 International Centre for Diffraction Data.*
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Key words: ferrous gluconate, iron (II) gluconate, synchrotron, powder diffraction

I. INTRODUCTION

Iron-deficiency is the most prevalent cause of anemia, and has been estimated to affect over two billion people, owing to a variety of causes including malnutrition, chronic blood loss and disease (Crohn's disease, chronic kidney disease, inflammatory bowel disease, etc.) among others (Camaschella, 2015). Oral iron supplementation is the typical therapy, and ferrous gluconate, $Fe(C_6H_{11}O_7)_2 \cdot xH_2O$, is a common iron supplement with a long history of usage (Reznikoff and Goebel, 1937). Ferrous gluconate has seen recent consideration for iron-deficiency prevention via fortification of food (Pizarro *et al.*, 2013) and milk for infants (Villalpando *et al.*, 2006). Ferrous gluconate used in conjunction with ascorbic acid has also been studied for replenishing iron stores for regular blood donors (Radtke *et al.*, 2005).

Despite longstanding and widespread usage, and a number of Mössbauer spectroscopic studies (Kulgawczuk *et al.*, 1989; Coe *et al.*, 1995), the only pattern for iron gluconate currently in the powder diffraction file (ICDD, 2015) is an old, un-indexed pattern with visually estimated intensities (PDF entry 00-005-0257). This work provides a high quality, indexed pattern for phase identification.

II. EXPERIMENTAL

A ferrous gluconate tablet manufactured by Apotex Inc. (product number 00545031, lot MP3827) was cut in half, and powder was scraped from the tablet centre to avoid the surface coating. The powder was loaded, with minimal grinding, into a 0.3 mm ID Kapton capillary that was sealed at both ends with a Loctite adhesive.

Powder X-ray diffraction (PXRD) patterns were collected using a Canadian Macromolecular Crystallography Facility beamline (CMCF-BM or 08B1-1, Fodje *et al.*, 2014) at the Canadian Light Source (CLS). 08B1-1 is a bending magnet beamline with a Si (111) double crystal monochromator. Two-dimensional (2D) data were obtained using a Rayonix MX300HE detector with an active area of 300×300 mm^2. The patterns were collected at an energy of 18 keV ($\lambda = 0.688\,80$ Å) and capillary-detector distance of 250 mm.

The 2D PXRD patterns were calibrated and integrated using the GSASII software package (Toby and Von Dreele, 2013). The sample-detector distance, detector centering and tilt were calibrated using a lanthanum hexaboride (LaB_6) standard reference material (NIST SRM 660a LaB_6) and the calibration parameters were applied to all patterns. After calibration, the 2D patterns were integrated to obtain standard 1D powder diffraction patterns. A pattern collected from an empty Kapton capillary (using the same conditions) was subtracted from the sample data during integration.

Ab initio indexing was performed using the programs DICVOL (Boultif and Louer, 2004) and McMaille (Le Bail, 2004), while EXPO2014 (Altomare *et al.*, 2013) was used to examine possible space groups.

Potential solutions were examined with Le Bail refinement (Le Bail *et al.*, 1988) using the FullProf program (Rodriguez-Carvajal, 2001).

III. RESULTS AND DISCUSSION

Initial indexing attempts on the first 20 reflections in the PXRD pattern performed using DICVOL, for monoclinic and higher symmetries, suggested three to five possible cells. The highest figures of merit ($M_{20} = 22.1$, $F_{20} = 133.2$) were obtained for a monoclinic cell ($a = 19.9518$ Å, $b = 5.5127$ Å, $c = 18.4689$ Å, $\beta = 111.386°$, $V = 1891.5$ Å^3). Subsequent indexing with McMaille yielded a larger number of monoclinic cells, but the same cell was identified with a McMaille figure of merit ($Mc_{20} = 195.98$) that was four times larger than the next closest candidate cell.

Assuming 17 Å^3 per non-hydrogen atom would yield 111 atoms in the unit cell, while four formula units of $Fe(C_6H_{11}O_7)_2$ yields 108 non-hydrogen atoms, suggesting the cell is consistent with $Z = 4$. While the hydration level is not definitively known, the label suggests that each tablet yields 35 mg of elemental iron contained in 300 mg of ferrous gluconate. Based on mass balance considerations, this would suggest the compound is a dihydrate, $Fe(C_6H_{11}O_7)_2 \cdot 2\,H_2O$ (expected yield of 34.7 mg of elemental iron). The anhydrous

a)Author to whom correspondence should be addressed. Electronic mail: joel.reid@lightsource.ca

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TABLE I. The crystal data and data collection parameters obtained for ferrous gluconate.

Crystal data	
Formula, Z	$Fe(C_6H_{11}O_7)_2 \cdot x\ H_2O$, $Z = 4$
Molecular mass (M_r)	482.169 g mol^{-1} ($x = 2$)
Symmetry, space group	Monoclinic, $I2$
Unit-cell parameters	$a = 19.953\ 16(9)$ Å, $b = 5.513\ 92(3)$ Å, $c = 18.470\ 58(9)$ Å, $\beta = 111.3826(3)°$
Volume	1892.3 Å^3
Density (ρ_{calc})	1.693 g cm^{-3} ($x = 2$)
Data collection	
Beamline	CLS 08B1-1
Monochromator	Si (111) double crystal monochromator
Detector	Rayonix MX300HE (300 × 300 mm^2)
Specimen mounting	0.3 mm Kapton capillary
Collection mode	Transmission
Wavelength	$\lambda = 0.688\ 80$ Å
Collection range, step size	1–39° (2θ), 0.005° step^{-1}

compound would yield 37.6 mg of elemental iron for 300 mg of ferrous gluconate.

Space group tests using EXPO2014 suggested space group $I2$ (#5) as the most likely candidate, with a general multiplicity (4) consistent with Z. Space group $P2_1$ (#4) was also examined closely, because every metal gluconate entry found in the Cambridge Structural Database (Groom *et al.*, 2016) belonged to either space group $P2_1$ or $P2_12_12_1$. But $P2_1$ yields numerous low angle Bragg reflection positions that are unobserved in the experimental pattern, and would require two formula units in the asymmetric cell ($Z' = 2$, based on a general multiplicity of 2). Therefore, $I2$ is believed to be the correct space group.

Table I lists the crystal data and data collection parameters, while Figure 1 illustrates the final Le Bail refinement obtained using space group $I2$, resulting in a reduced χ^2 of 1.01. Visually, the pattern is reasonably consistent with an unindexed pattern obtained by Coe *et al.* (1995), after accounting for the different wavelengths. The final reflection list extracted from the Le Bail refinement is plotted in Figure 2 with the raw data. The reflection list was prepared by summing reflections closer than 0.02°2θ as multiple reflections and assigning a weighted average reflection position, then

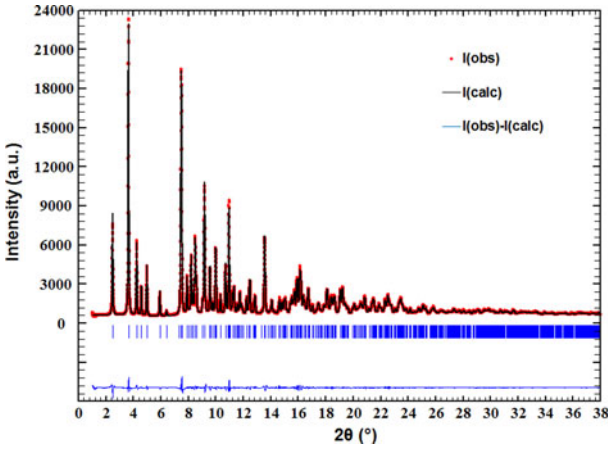


Figure 1. (Color online) The final Le Bail refinement obtained for ferrous gluconate using a monoclinic cell ($a = 19.953\ 16(9)$ Å, $b = 5.513\ 92(3)$ Å, $c = 18.47058(9)$ Å, $\beta = 111.3826(3)°$) with space group $I2$ (reduced $\chi^2 = 1.01$).

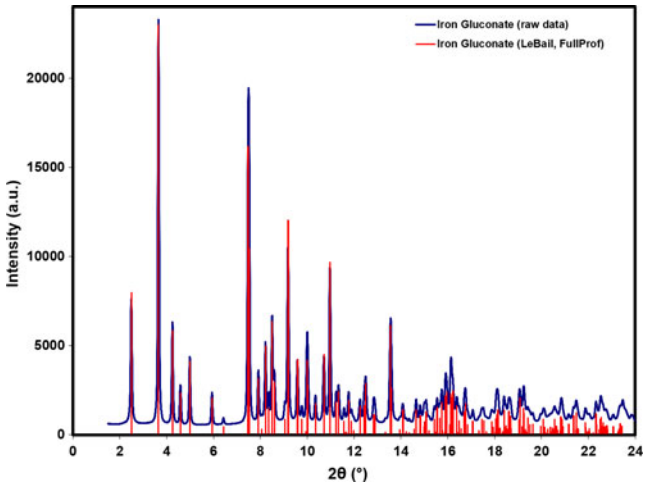


Figure 2. (Color online) The Bragg reflection list for ferrous gluconate obtained with Le Bail refinement. The reflection list is contained in a CIF file in the online supplementary material.

including all reflections with relative integrated intensities of 0.5% or greater up to 23°2θ. The full Bragg reflection list and raw data are contained in a crystallographic information file (CIF) in the online supplementary material.

SUPPLEMENTARY MATERIAL

The supplementary material for this article can be found at https://doi.org/10.1017/S0885715616000671

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