Bioavailability of Iron in Goat Milk Compared with Cow Milk Fed to Anemic Rats[1,2]

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ABSTRACT

Bioavailabilities of iron from dehydrated whole and skim goat milk were investigated using iron-deficient rats. Hemoglobin regeneration efficiencies were determined as the percent conversion of dietary iron into hemoglobin. The respective hemoglobin regeneration efficiencies for groups fed whole goat milk, whole cow milk, skim goat milk, and skim cow milk were 50.6, 13.1, 26.0, and 13.0%, indicating that iron bioavailability of goat milk was greater than cow milk. However, rats fed each milk had negative net increases in hemoglobin concentrations, implying that the iron contents of each milk were not adequate. For animals consuming whole goat milk supplemented with ferrous sulfate, the slope relating hemoglobin iron gained versus iron intake was .95. Respective bioavailabilities relative to ferrous sulfate were 54, 14, 28, and 14% for the four sources of milk. Iron bioavailability of goat milk is superior to cow milk when fed to anemic rats.

INTRODUCTION

Iron is deficient in milk of most species including human and goat. Very little research has been done on the iron bioavailability of goat milk, whereas almost all of the previous reports involved cow milk-based diets. "Goat milk anemia" in rats fed goat milk was reported during the 1920's and 1930's (2, 5, 15). Also, exclusive feeding of cow milk to 4- and 8-week-old rats led to hypochromic anemia characteristic of iron deficiency, which was cured by the administration of iron (15). Similarly, 8-week-old animals fed goat milk developed anemia (15). However, a hyperchromic anemia, which was not cured by supplemental iron, was observed on feeding goat milk to 4-week-old rats (15). Gyorgy (5) also observed a hyperchromic anemia in infants consuming goat milk.

Human milk will not produce the characteristic anemia found in young rats fed either goat or cow milk (2, 17), and it was suggested that lactose in human milk was the protective agent against the nutritional anemia (17).

Very little information has been published on the nutritional value of goat milk; however, it continues to be used for infant feeding in many parts of the world. Infants fed human milk have a much lower incidence of iron deficiency than those fed cow milk even though the iron contents of the two milks are similar. The purposes of this study were to examine the iron bioavailabilities of goat milk with and without ferrous sulfate supplementation and to compare the iron bioavailabilities of goat milk with those of cow milk fed to anemic rats.

MATERIALS AND METHODS

Preparation of Dehydrated Goat Milk

Milk used was a composite fluid milk from a milking herd of 65 dairy goats of Alpine and Nubian breeds at the International Dairy Goat Research Center, Prairie View A&M University TX. Goats were fed a complete diet of 69.3% oats, 1.35% soybean meal, 26.0% alfalfa meal, 2.05% corn, .93% cottonseed hulls, and .31% dicalcium phosphate with free access to baled mature coastal bermudagrass hay. The fluid

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goat milk was dehydrated by a vertical Anhydro-flat-bottom vacuum sweeping atomizing spray dryer (Type III- A No. 2, Copenhagen, Denmark) at a drying rate of 37.8 L fluid milk/h and inlet drying temperature at 193 to 210°C. The skim goat milk was produced by separating cream from the whole milk using an West-falia cream separator (Type SA 7-06, Oelde, West Germany) set at 8400 rpm rotating speed at a feeding rate of 4.16 L/min. The fluid skim milk was dehydrated as described for whole milk. Respective crude protein percentages of the dried whole and skim goat milk were 27.8 and 36.5%.

Formulation of Experimental Diets

Seven isocaloric and isonitrogenous experimental diets were prepared from whole or skim powdered goat and cow milk. Vitamin (20 g/kg diet) and mineral (11.6 g/kg diet) mixtures were also added to all seven diets (Table 1). Diets 1 to 4 were whole goat milk (WGM) groups; composition of these four diets was identical except for iron concentration, which was varied with ferrous sulfate to create a standard curve for use in determining relative iron bioavailabilities. Diets 5, 6, and 7 were prepared with whole cow milk (WCM, obtained from United States Biochemical Corp., Cleveland OH), skim goat milk (SGM), and skim cow milk (SCM, obtained from a retail store), respectively. For diets 2, 3, and 4, ferrous sulfate was ground to an appearance of talc by mortar and pestle and added proportionally to the control diet 1. The final iron concentration of each diet was determined by chemical analysis. Although goat milk contains less folic acid and vitamin B_{12} than cow milk, the vitamin and mineral mixtures in the diet would ensure that iron was the only limiting nutrient in this experiment.

Animals and Feeding Experiment

Sixty-three weanling, male, Sprague-Dawley rats (Simonsen Laboratories, Gilroy, CA) were individually housed in stainless steel cages having wire mesh bottoms and fronts. Animals were made anemic by feeding the low iron (12.7 ppm Fe) skim cow milk diet and bleeding approximately .7 ml of blood from the rectro-ocular capillary bed twice, 3 days apart, during the 7-d pretest period. Then the rats were assigned randomly to seven groups of 9 animals each so that the average hemoglobin concentration and body weights were similar. Seven to 10 g of test diet were weighed and fed daily to each rat for 10 d. Spilled food and orts were weighed and recorded to determine the net consumption of the diet. Demineralized water was offered ad libitum. Blood samples were taken from the rectro-ocular capillary bed at 0 and 10 d of the experiment for hemoglobin determination. On the 10th d of the experiment, all animals were weighed and blood samples were taken before animals were killed. Livers were taken for iron analysis.

Analytical Procedures

Concentrations of protein in the goat milks were determined by micro-Kjeldahl procedure (1) before diet formulation.

Diet samples (approximately 2 g) and whole livers were first charred in porcelain crucibles before ashing in a muffle furnace at 550 to 600°C for 24 and 48, respectively. Livers required longer ashing time than the diets. Ashed samples were solubilized with 10 ml 6 N HCl and diluted to volume in 25-ml volumetric flasks with double deionized water for iron analysis by an atomic absorption spectrophotometer. Hemoglobin concentrations were determined in duplicate by the cyanmethemoglobin method (4).

Statistical Analysis

Hemoglobin regeneration efficiency (HRE) was calculated by the method of Mahoney et al. (10, 11). It represents the percent of iron consumed that is gained as hemoglobin. The data were analyzed statistically for analysis of variance, correlation coefficients, and multiple mean comparisons (3, 18). When the F value was significant at the 5% probability, least significant differences (LSD) were determined for evaluating differences among treatment means. Least squares was used for the dose-response curve for ferrous sulfate added to the WGM diet; this made it possible to make comparisons relative to ferrous sulfate while adjusting for any variations in Fe intake from the test diets.

TABLE 1. Composition of the experimental diets.

Diet	1	2	3	4	5	6	7[1]
Whole goat milk, g[2]	918.4	918.4	918.4	918.4	...	...	...
Whole cow milk, g[3]	...	...	...	...	918.4	...	...
Skim goat milk, g[2]	...	...	...	...	...	625	...
Skim cow milk, g[3]	...	...	...	...	...	...	625
$FeSO_4 \cdot 7H_2O$, mg	0	50	100	200	...	...	...
α-Cellulose, g	50	50	50	50	50	50	50
Vitamin mix, g[4]	20	20	20	20	20	20	20
Mineral mix, g[5]	11.6	11.6	11.6	11.6	11.6	11.6	11.6
Corn oil, g	...	...	...	...	...	293.4	293.4
Iron, μg/g[6]	8.36	12.4	16.6	24.8	19.1	10.8	12.7

[1] Used as basal diet during iron depletion.

[2] The whole and skim goat milk were composite milks from Alpine and Nubian breeds. The milks were spray-dried in the Food Protein Research and Development Center at Texas A&M University, College Station. Crude protein contents of the whole and skim goat milk were 27.8 and 36.5%, respectively.

[3] Obtained from commercial sources.

[4] Vitamin mixture contained (g/kg): vitamin A concentrate (200,000 IU retinyl acetate/g), 45; vitamin D concentrate (400,000 IU calciferol/g), .25; α-tocopherol, 5; ascorbic acid, 45; myo-inositol, 5; choline-HCl, 75; menadione, 2.25; p-aminobenzoic acid, 5; niacin, 4.5; riboflavin, 1; pyridoxine-HCl, 1; thiamine-HCl, 1; Ca panthothenate, 3; biotin, .02; folic acid, .909; vitamin B_{12}, .0013, and glucose to make 1 kg.

[5] Mineral mixture contained (g/kg): KCl, 196.7; $MgCO_3$, 121; $MnSO_4$, 12.7; $CoCl_2 \cdot 6H_2O$, .7; $ZnSO_4 \cdot 7H_2O$, 38; $CuSO_4 \cdot 5H_2O$, 1.6; KI, .8, $NaMoO_4 \cdot 2H_2O$, .12 and glucose, 528.4.

[6] By analysis.

RESULTS AND DISCUSSIONS

Cows milk used in this study contained more iron than goat milk in both whole milk (19.1 vs. 8.36 ppm) and skim milk (12.7 vs. 10.8 ppm) (Table 1). The greater difference in iron content between whole and skim cow milks compared with goat milks was probably caused by the different commercial sources of the dried products. The iron concentrations of the ferrous sulfate-supplemented diets were not exactly mathematically additive (Table 1). However, the correlation between iron intake determined using these values and iron gained as hemoglobin was r = .963 (Figure 1), indicating the importance of analyzing diets for iron. This is similar to our experience in previous studied (13, 14).

Although the goat milk diets contained less iron than the cow milk diets, the bioavailability of goat milk iron was higher than cow milk iron (Table 2, Figure 1). The differences in HRE between WGM and WCM or SCM were significant ($P<.01$) while those among WCM, SGM,

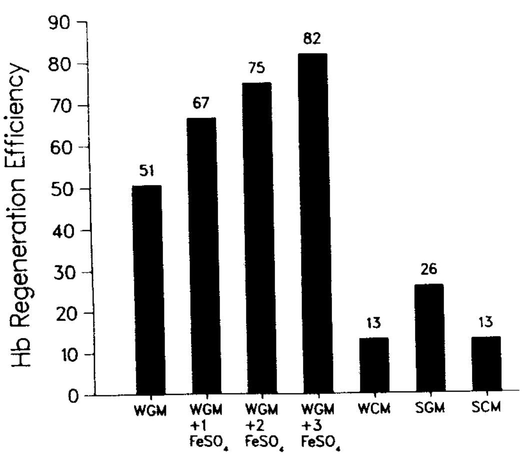

Figure 1. Hemoglobin (Hb) regeneration efficiencies of whole goat milk diet (WGM) whole goat milk diet supplemented with 50, 100, or 200 ppm ferrous sulfate, whole cow milk diet (WCM) skim goat milk diet (SGM), or skim cow milk diet (SCM) fed to anemic growing rats for 10 days. Hemoglobin regeneration efficiencies for WGM is greater than that for WCM ($P<.01$), and SGM is greater than the SCM group ($P<.05$).

TABLE 2. Bioavailability responses of iron from goat and cow milk fed to anemic rats.

Diet number	WGM[1] 1	WGM[2] + $FeSO_4$ 2	WGM[2] + $FeSO_4$ 3	WGM[2] + $FeSO_4$ 4	WCM[3] 5	SGM[4] 6	SCM[5] 7	SE[6]	LSD[7] .05/.01
Food intake, g/d	5.59	6.26	6.46	6.55	6.01	5.91	5.78	.49	.20/.27
Total Fe intake, mg	.468	.776	1.072	1.625	1.164	.638	.734	.046	.023/.031
Body weight,									
Initial	70.6	70.7	73.4	71.4	71.4	72.0	74.0	1.01	NS
Gain	23.0	30.1	28.7	30.2	18.8	31.2	26.3	.78	4.5/6.0
Hemoglobin, g/dl									
Initial	5.78	5.42	5.82	5.75	5.71	5.74	5.79	.11	NS
Gain	−.35	.69	1.92	4.10	−.44	−.99	−1.02	.24	.67/.90
Liver weight g (wet)	3.52	3.65	3.75	3.76	2.93	3.51	3.23	.05	.24/.32
Liver Fe, ppm (wet)	18.8	18.1	17.3	25.9	19.1	18.2	21.3	.72	5.00/8.22
Hemoglobin Fe gain, mg	.237	.518	.805	1.333	.153	.166	.098	.055	.108/.144

[1] Whole goat milk.

[2] Whole goat milk supplemented with $FeSO_4$.

[3] Whole cow milk.

[4] Skim goat milk.

[5] Skim cow milk.

[6] Standard error.

[7] Least significant difference. Mean differences must equal or exceed the LSD value to be statistically significant at $P<.05$ or $P<.01$.

and SCM were not different. This finding is in contrast to a study by Beard and Boggess (2) in which the drop in erythrocytes and hemoglobin in the cases of cow milk anemia was somewhat slower than in the cases of goat milk anemia. In this study, all four diet groups of WGM, WCM, SGM, and SCM have negative hemoglobin gain, which clearly showed that goat and cow milks are deficient in iron; however, the degree of loss in hemoglobin was slightly greater in WCM than WGM, even though the WCM diet contained more iron. The situation was similar for the respective skim milks.

There were significant ($P<.05$) differences in food and iron intake among diet groups (Table 2). The group fed WGM (diet 1: without Fe supplementation) had the lowest food and iron intakes. The WCM, SGM, and SCM groups also consumed less diet than the iron-supplemented groups, indicating that iron deficiency probably was causing depressed appetite or anorexia (19) in these groups. Rats fed WGM (diet 1) consumed the least amount of diet among all unsupplemented groups, and they gained very little weight.

There was the same tendency in the response of body weight gain as was observed in hemoglobin iron gain. Rats fed goat milk grew better than those on cow milk diets, except that growth of WGM group without Fe supplementation was not statistically different from that of WCM group (Table 2). This result contrasts with observations of Beard and Bogess (2) that the feeding of cow milk caused slightly better growth than goat milk. Rats fed the WCM group had the highest iron intake but lowest body weight gain. Mack (8) reported that children fed cow and goat milk had excellent growth during the experiment, but the group fed goat milk surpassed the group fed cow milk in skeletal mineralization, vitamin A in blood plasma, and calcium in blood serum. He also observed that children consuming goat milk had a slightly greater concentration of hemoglobin and larger structural measurements. Our finding that the iron bioavailability of goat milk was greater than cow milk agrees with some results of Mack (8) such as growth and hemoglobin concentration.

There were significant differences in liver weight between WGM and WCM ($P<.01$) or SGM and SCM ($P<.05$) groups. Response of liver weight appeared parallel with that of whole body weight gain, which was forementioned. We have not found any information on iron availability from skim goat milk in the literature. The WGM group with highest iron supplementation (diet 4) had the highest iron bioavailability for all measured parameters (Table 2). However, some measurements for the rats fed diet 4, such as food intake, weight gain, and liver weight, were not statistically different from those of the other diet groups. The weight and color of the livers from iron-supplemented groups were normal, whereas those from unsupplemented groups were smaller with faint or pale red color, which was observed in our previous studies (13, 14).

"Goat milk anemia" was the designation given to a macrocytic-hyperchromic megaloblastic anemia, which was observed in infants fed a diet of goat milk in Europe during the 1920's and 1930's (5). Clinical trials by Gyorgy in 1934 (5) demonstrated that infants with goat milk anemia were not cured by iron, iron and copper, or vitamin B_2, but anemia was cured by giving the infants supplements of yeast, liver, or liver extracts. He suggested that the missing factor in goat milk may be the same as Castle's extrinsic factor. Later experience showed that infants with macrocytic hyperchromic megaloblastic anemia responded to therapy with folic acid and vitamin B_{12} with folic acid yielding the greatest responses (6, 7). Also, Mack (8) observed that children consuming goat milk tended to have higher hemoglobin concentrations compared with cow milk. However, the form of milks tested were raw fluid goat and cow milk, which were different from the dehydrated milks in this study.

Iron bioavailability, expressed as HRE, was greater ($P<.05$) for the unsupplemented goat milk diets than for the cow milk diets (Figure 1). Similarly, amount of hemoglobin iron and body weight gains were greater for rats fed the unsupplemented goat milk diets than was observed for the respective cow milk diets (Table 2). Also, the bioavailability of the ferrous sulfate iron was very high in the goat milk diet, indicating that goat milk did not depress the bioavailability of this important iron supplement. Saarinen et al. (16) observed that 49% of the iron in human milk is absorbed by human infants, which is similar to the 51% HRE found for whole goat milk in this study

TABLE 3. Correlation coefficients among different parameters of iron bioavailability for whole goat milk and ferrous sulfate-supplemented diets fed to anemic rats.[1]

	BW Gain	Initial Hb	Hb Gain	Food intake	Fe Intake	Liver weight	Liver Fe	Hb Fe Gain	HRE[2]
Initial BW[3]	−.382*	.023	.171	.228	.074	.513**	.040	.118	.250
BW Gain[4]		.014	.225	.520**	.381*	.210	.038	.383*	.376*
Initial Hb[5]			.226	.039	.049	.164	.025	−.104	−.246
Hb Gain				.720**	.921**	.249	.443**	.977**	.736**
Food intake					.778**	.443**	.186	.768**	.684**
Fe Intake						.366*	.481**	.963**	.536**
Liver weight							−.078	.316	.162
Liver Fe								.481**	.201
Hb Fe Gain									.730**

[1] Number of observation is 36. Pooled data for diets 1 to 4.

[2] Hemoglobin regeneration efficiency.

[3] Initial body weight.

[4] Body weight gain.

[5] Initial hemoglobin.

*$P<.05$.

**$P<.01$.

(Figure 1). They (16) also indicated that approximately 10% of the iron in cow milk is absorbed by human infants, which, too, is similar to the HRE for cow milk in this study (Figure 1).

On analyzing the data of the four WGM groups, HRE was significantly correlated with hemoglobin gain, food intake, iron intake, hemoglobin iron gain, and body weight gain (Table 3). Initial body weight was negatively and significantly correlated with body weight gain. Food intake, iron intake, hemoglobin gain, hemoglobin iron gain, body weight gain, and HRE are positively related with each other, so that there were definite cause-and-effect relationships, which were observed in previous studies (9, 11, 12, 13, 14). Some of the correlation coefficients listed in Table 3 are small (less than .5) but statistically significant, although cause-and-effect relations are not known.

There were high correlations among several parameters (Table 3). Amount of iron gained as hemoglobin was highly correlated ($r = .963$) with iron intake as ferrous sulfate. Iron bioavailability expressed as gain in hemoglobin iron relative to iron consumed was quite constant among experiments and laboratories, relatively insensitive to iron dose, and sensitive to food processing effects (9, 10, 11, 12, 13, 14). This relationship was linear for the entire range of iron intake (46.8 to 162.5 μg iron/d) and may be expressed as:

$$Y = .949\,X - .212; \quad r = .963$$

where Y is mg iron gained as hemoglobin, and X is mg iron consumed in 10 d. The slope may be considered as the HRE response for ferrous sulfate iron. This equation was used to predict the iron that would be gained as hemoglobin if an identical amount of iron were consumed as ferrous sulfate. Relative bioavailability was then calculated as the observed value for iron gained as hemoglobin relative to the value predicted for ferrous sulfate. The respective relative bioavailabilities of WGM, WCM, SGM, and SCM are 54, 14, 28, and 14% for this study.

Futher studies are necessary to define the mechanism and scientific basis for superior iron availability from goat milk compared with cow milk observed in this study.

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