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Iron Bioavailability from its Complex with Sucrose

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ABSTRACT

The bioavailability of iron (^{55}Fe) and its incorporation into rat tissues were investigated after peroral administration of the iron–sucrose (Fe–Su) complex, which is proposed for the fortification of foodstuffs, especially of beverages. Iron bioavailability from Fe–Su reached 119–165% of that from $FeSO_4$, depending on the method of complex stabilization. The stabilization of Fe–Su by ascorbic acid increased the level of iron bioavailability in comparison with stabilization by citric acid. The bioavailabilities of the other metal ions (Mn, Zn, Cu and Co) from their complexes with sucrose were equal (Mn, Cu) or less (Co, Zn) than those of the equivalent inorganic salts.

INTRODUCTION

Iron is still often deficient in certain parts of the human population (Turnbull, 1974) and thus, new compounds are tested to provide iron bioavailability and good acceptability to the recipient (Cook & Reusser, 1983). Besides different iron compounds, adapted natural sources of iron are used also for food and fodder fortification (Picciano *et al.*, 1984; Johnson *et al.*, 1985).

Considerable attention has been paid to the enhancing nature of several organic acids, such as ascorbate, citrate, malate and ethylenediaminetetracetic acid, on iron absorption. Several studies have implicated fructose as an effective enhancer of iron incorporation by virtue of its iron chelating properties and the apparent ability of the ferric–fructose complex to cross the intestinal mucosa and be absorbed (Stitt *et al.*, 1962; Bates *et al.*, 1972).

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While sucrose has not shown appreciable iron enhancement properties, it has been successfully evaluated as an iron fortificant vehicle (Layrisse *et al.*, 1976; Nadeau & Clydesdale, 1987).

Čapek and Ranný (1983) have proposed iron complexed with sucrose (Fe–Su) as a suitable food additive for the fortification of beverages, bread, pastry, sweets, dietetic powdered food, milk products and some other foodstuffs. It may be also used in pharmaceuticals and fodder supplements. The preparations are dark-brown crystals of sweet taste.

The aim of this paper was to compare the bioavailability of iron administered to rats either in the form of Fe–Su or as $FeSO_4$ and to obtain information needed for the application of these preparations in iron supplementation of food and fodder. The favourable results with Fe–Su encouraged us to also test the sucrose complexes with some other metal ions (manganese, zinc, copper and cobalt).

MATERIALS AND METHODS

Materials

Radionuclides $^{55}FeCl_3$, $^{54}MnCl_2$, $^{65}ZnCl_2$, $^{64}CuCl_2$ and $^{58}CoCl_2$ were from the Institute of Nuclear Research, Swierck, Poland. Liquid scintillator

TABLE 1

^{55}Fe Incorporation into Organs of Rat 6 h after Peroral Administration of Different Complexes of Iron with Sucrose and $FeSO_4$ (control)

Investigated tissue[a]	*Administered compound*[b]			
	$FeSO_4$	*A*	*B*	*C*
	Incorporated radioactivity (Bq/g ± SD)			
Liver	780 ± 110	870 ± 120***	920 ± 130*	1 010 ± 180*
Kidney	290 ± 40	320 ± 30***	360 ± 40*	370 ± 60*
Heart	430 ± 80	470 ± 60***	480 ± 50***	500 ± 60*
Lung	340 ± 60	360 ± 40****	390 ± 50**	410 ± 80*
Spleen	970 ± 100	1 220 ± 130*	1 610 ± 300*	1 920 ± 380*
Blood	1 080 ± 120	1 380 ± 160*	1 840 ± 220*	2 200 ± 240*
Mean incorporation	648	770	933	1 072
Mean bioavailability (%)	100	119	144	165

[a] Number of experimental animals in each group ($n = 10$).

[b] Administered compounds: A = Fe–Su, citrate.
B = Fe–Su, ascorbate.
C = Fe–Su, ascorbate:ascorbate (1:1).

*, $p < 0{\cdot}01$; **, $p < 0{\cdot}02$; ***, $p < 0{\cdot}05$; ****, $p < 0{\cdot}1$.

Aquasol and tissue solubulizer Protosol were purchased from NEN Chemicals, Boston, USA. ^{55}Fe–Su was prepared according to Čapek and Ranný (1983) and adjusted either with citric (preparation A) or ascorbic (preparation B) acids to pH 7·4. Preparation C, pH 7·4 (Table 1), was prepared by mixing equal parts by weight of ascorbic acid and preparation B. $^{55}FeSO_4$ was adjusted to the same specific radioactivity, pH and ascorbic acid content as preparation B.

The complexes of the other metal ions with sucrose were prepared by the same procedure as used for the Fe–Su (preparation A).

All other chemicals of analytical grade were from Lachema, Brno, Czechoslovakia.

White male rats, weighing about 170 g, were supplied from the Experimental Animal Farm at Lysolaje near Prague, Czechoslovakia. Before the experiment the rats were starved for 24 h and received water *ad libitum*.

Methods

All preparations of the same specific radioactivity were administered to the rats by stomach tube, giving 100 μl of 10% aqueous solutions of the above sucrose complexes per rat. The animals were kept in metabolic cages (Rauch *et al.*, 1983). The incorporation of the biogenic metals tested was measured 6 h after the administration of the preparations. Then the rats were killed by decapitation. Tissues were collected, cut into small pieces and thrice washed in 0·8% sodium chloride. The radioactivity was measured in the tissue samples solubilized by Protosol according to the Mahin and Lofberg (1966) procedure as modified by Rauch and Káš (1983). Radioactivity of the iron and copper was measured by liquid scintillation counting using Aquasol as the scintillator (Rauch & Káš, 1984), while the radioactivity of the cobalt, manganese and zinc was counted in the solubilized tissue with a well-type scintillator.

The results were evaluated using the Student's *t*-test.

RESULTS AND DISCUSSION

Iron bioavailability was tested on rats suitable for this purpose (Mahoney & Hendricks, 1983). Iron administered perorally to the rat as iron–sucrose complex (Fe–Su) was incorporated into important organs significantly better ($p < 0·05$) than iron administered in the dissociated form of $FeSO_4$ (Table 1). The highest incorporation of ^{55}Fe was achieved after the peroral administration of Fe–Su with ascorbic acid in weight ratio 1:1 (preparation C).

Incorporation of ^{55}Fe from the other preparations decreases in the following order: Fe–Su adjusted with ascorbic acid to pH 7·4 (preparation B), Fe–Su adjusted with citric acid to pH 7·4 (preparation A) and $^{55}FeSO_4$ with ascorbic acid, pH 7·4 (control). Ascorbic acid was also added to the control preparation because it is known that it increases the bioavailability of iron (Clydesdale & Nadeau, 1985).

The increased incorporation of iron after administration of Fe–Su was not caused only by the presence of citric or ascorbic acid (control consisted of iron ions with ascorbic acid). Evidently, increased iron absorption is caused either by increased incorporation of intact complex Fe–Su or by the synergistic effect of sucrose and citric or ascorbic acid, as indicated also by other authors (Stitt *et al.*, 1962; Bates *et al.*, 1972; Layrisse *et al.*, 1976; Nadeau & Clydesdale, 1987).

Table 1 shows the mean incorporation of ^{55}Fe (Bq/g) into five most important organs and blood. The incorporation is also expressed in percent occurrence related to those obtained with administration of $FeSO_4$. The highest ^{55}Fe incorporation was always found in blood and then it decreased in the order: spleen, liver, heart, lung and kidney. Much lower levels of ^{55}Fe were found in the other organs of the experimental animals.

Therefore Fe–Su preparations are a suitable form of iron supplementation due to its high bioavailability and very good uptake into tissue. The conjugation of iron with sucrose in the proposed iron supplement improved the uptake of iron in the organism in comparison with iron sulphate.

Complexes of sucrose with other ions Mn, Zn, Cu and Co were also prepared and their bioavailability was tested in a similar manner (Table 2). The incorporation of the metal tested was measured in liver, kidney, heart, spleen and blood. The mean incorporation of the metals from the individual

TABLE 2

Comparison of the Mean Bioavailability of Chosen Metal Ions Administered either as Complex with Sucrose or as Corresponding Inorganic Salt

Administered form of metal ion[a]	*Mean bioavailability of metal ions (Bq/g ± SD)*			
	Co	*Mn*	*Zn*	*Cu*
Metal–Su (C)	140 ± 18	840 ± 100	530 ± 70	390 ± 80
Inorganic salt (I)	165 ± 25	880 ± 90	590 ± 80	430 ± 70
C/I in %	85 ± 13	95 ± 12	90 ± 14	91 ± 22
p	<0·01	>0·3	<0·05	<0·1

[a] Number of experimental animals in each group ($n = 10$).

preparations was calculated. Metal incorporation from its complex was related to that of the corresponding inorganic salt, and expressed in percentage (Table 2). The bioavailability of manganese and copper from Mn–Su and Cu–Su did not differ significantly from that achieved after administration of the corresponding inorganic salts. In constrast, the bioavailabilities of zinc and cobalt from Zn–Su and Co–Su were significantly lower in comparison with inorganic ions; however, the 85–90% control bioavailability may be considered as satisfactory, especially when the decreased bioavailability is compensated by better acceptability of the sucrose preparation in the organism.

The advantage of this type of preparation is that complexes of different metal ions with sucrose may be prepared in different forms and used either for food or fodder fortification for human or veterinary treatments.

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