

Short-term, high-dose iron supplementation to healthy pregnant women increases oxidative stress markers: Implications for use of phytonutrients

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Abstract

The National Nutritional Anemia Control Program of the Government of India prescribes a mandatory supplement of 100 mg elemental iron to all pregnant women for 100 days because of widespread iron deficiency anemia. However, such iron supplementation has been recently reported to cause oxidative stress (OS). The present study was undertaken to assess whether short-term supplementation to healthy pregnant women is a better strategy. Disease-free pregnant women, 20-35 years, blood hemoglobin (Hb) > 10 g/dL, 30 in each trimester (T1, T2, T3), were enrolled. T2+T3 respondents were divided into unsupplemented (UnS) and those receiving 100mg elemental iron with 500µg folic acid daily, for only 2-4 weeks (S) and compared with 50 matched non-pregnant (NP) controls. Supplemented (S) gained more weight than unsupplemented (UnS). Hb and hematocrit (Hct) declined in T2+T3 in UnS, but not in S. However, Hct remained lower than NP throughout pregnancy. Plasma ferritin declined through gestation in UnS, but S showed recovery of iron stores. OS marker, malonyldialdehyde (MDA) increased and antioxidant enzymes, superoxide dismutase (SOD) and catalase (CAT) declined through pregnancy. S showed statistically significantly more changes than UnS. Overall antioxidant capacity marker, Ferric Reducing Activity of plasma increased throughout pregnancy, but was only marginally higher in S compared to UnS. Thus, even short-term high-dose iron supplementation improved iron status marginally, but produced increase in OS in healthy pregnant women. We discuss the implications of these findings in the light of current knowledge regarding phytonutrients, especially iron and antioxidants which may provide a better strategy for supplementation of iron to pregnant women.

Key words: Iron supplementation, pregnancy, phytonutrients, iron status, oxidative stress

Introduction

Iron deficiency anemia is one of the most widespread pregnancy associated public health problems. To combat this problem, most countries have universal high dose iron supplementation programs. In India, the incidence of iron deficiency anemia during pregnancy has been reported to be

more than 59 per cent, with a 40 per cent incidence even among the richest two quintiles (National Nutrition Monitoring Bureau, 2002). Consequently the National Nutritional Anemia Control Program of the Government of India prescribes a mandatory supplement of folifer tablets, each providing 100 mg elemental iron with 500µg folic acid for 100 days to all pregnant women during the second and third trimester of pregnancy, without screening for their iron status (Kumar *et al.*, 2009).

This dose of iron is about three times the recommended allowance for iron during pregnancy: WHO recommends 27 mg/d (Institute of Medicine, 2001); the Indian Council for

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Medical Research (ICMR) recommends a substantially higher amount of 35mg/d for pregnant Indian women (Indian Council of Medical Research, 2010), in view of the poor absorption of iron from the predominantly vegetarian diets consumed by Indians. Most vegetable and fruit sources of iron do not provide it in doses sufficient to achieve the recommended levels. Heme sources contain higher, more easily absorbed amounts but these are present in animal foods which are expensive and generally beyond the reach of the common man in this country. Hence, inorganic supplements are the cheaper, common mode of supplementation widespread.

However, in recent years, the wisdom of such high dose universal supplementation has been questioned for several reasons. High doses of iron during pregnancy have been reported to lead to excessive levels of hemoglobin, hematocrit, and ferritin, resulting in hemoconcentration, known to create problems in child birth (Bedi *et al.*, 2001; Gomber *et al.*, 2002). They also reportedly lead to increased free radical generation and consequent increase in some indices of oxidative stress (Lachili *et al.*, 2001; Pryor, 2001). The problem is, further, complicated by the fact that, pregnancy itself promotes free radical formation due to the mitochondria rich placenta (Casaneva and Viteri, 2003).

Thus, the benefit of high doses of iron supplements for extended periods during pregnancy on iron status, needs to be assessed in relation to the possibility of concomitant increase in oxidative stress. It needs to be explored whether short-term supplementation can ameliorate associated problems, if any, while taking care of iron status. In view of the foregoing, the present study was undertaken to assess the impact of short-term, high-dose iron supplementation to non anemic / mildly anemic healthy pregnant women on their iron status and on selected markers of oxidative stress.

Iron status was assessed by circulating hemoglobin (Hb), hematocrit (Hct) because they are the most common and ubiquitous measures of anemia, and ferritin levels because it is a fairly good indicator of iron stores. Metallozyme superoxide dismutase (SOD), which removes the superoxide oxygen radical by conversion to hydrogen peroxide (H_2O_2), the heme protein, catalase (CAT), which converts some of this H_2O_2 to water and oxygen, and malonyldialdehyde (MDA) formation, which is an index of lipid peroxidation, resulting from free radical mediated attack on cell membranes and lipoproteins were selected to assess OS, because they form the first line of defence against reactive oxygen species in erythrocytes. Blood is suitable for studies of oxidative stress, because erythrocytes are a target for oxidative reactions. They have a relatively high oxygen tension, a plasma membrane rich in polyunsaturated fatty acids (PUFA), and an effective mechanism to prevent and neutralize OS induced damage by the presence of antioxidant enzymes. Since measures such as SOD and CAT are interdependent, and may compensate

each other, the ferric reducing ability of plasma (FRAP) assay was included to give an assessment of the overall OS levels.

Material and Methods

Participants

A case-control study was designed to assess the effect of iron supplementation to pregnant women who were non-anemic / mildly anemic. A large number of pregnant women attending outpatient departments of Swaroop Rani Nehru Hospital and Kamala Nehru Memorial Hospital, Allahabad, India, were screened for blood Hb levels. According to the World Health Organization (WHO), during pregnancy, normal Hb has been defined as >11 g/dL and mild anemia as Hb 10- 11 g/dL blood (WHO, 2001). Inclusion criteria was that the respondent was a disease-free woman with blood Hb > 10 g/dL, aged 20 to 35 years, pregnancy parity not more than 3. Those suffering from obesity, hypertension, dyslipidemia, hyperglycemia, addiction to alcohol and smoking, as well as other systemic disorders of cardiovascular, central nervous and respiratory systems were excluded.

Only those meeting these inclusion and exclusion criteria were, further, screened for their iron supplementation status. The final respondents comprised of a cross-section of 90 pregnant women, 30 in each trimester, matched for socio-economic status. No iron supplementation was being given in Trimester 1 (T1), as it is known to aggravate symptoms of nausea and anorexia, often reported during this trimester. Trimester 2 and 3 (T2+T3) respondents comprised of two groups, one comprising of women who had visited the gynaecologist for the first time, and had not received any supplement (UnS) and the other of those who had received the mandatory iron supplement of 100 mg elemental iron with 500 μ g folic acid per day, for about 2-4 weeks (S). The control group comprised of 50 healthy age matched non-pregnant (NP) women. The protocol of the study was approved by the Institutional Ethical Committee of the PRCC, Allahabad and informed consent to participate in the study was obtained from all participants.

The age, parity and gestational age of all respondents was recorded and their body weight was measured using standard techniques ensuring reliability as far as possible. The ages of respondents were : 26.4 ± 4.3 , 25 ± 3.1 , 24.6 ± 3.6 and 24.7 ± 3.1 , respectively for NP, T1, T2 and T3. Obstetrical examination to assess fundal height ensured that only normal pregnancies were enrolled. Blood was collected by trained technicians for biochemical analyses as described below.

Biochemical analyses

Assessment of iron status

5 ml of venous blood was drawn into Acid-Citrate-Dextrose (ACD) vials and kept on ice for not more than 1 hour before

processing. Whole blood aliquots were used to determine Hb by the cyanmethemoglobin method and Hct (packed cell volume, PCV) by the Wintrobe method. Ferritin was estimated in plasma by solid phase ELISA.

Assessment of oxidative stress

SOD, CAT and MDA were estimated in red cell hemolysate, prepared from fasting intravenous blood, as described by Beutler (Beutler, 1984), and activity expressed per g Hb. SOD was estimated by the modified method of Marklund and Marklund (1974), which utilizes the inhibition of auto-oxidation of pyrogallol by superoxide dismutase. SOD activity was expressed as units per gHb, where a unit of SOD is described as the amount of enzyme required to cause 50% inhibition of pyrogallol auto-oxidation. CAT was estimated

by the method as described by Beutler (1984), which utilizes the reduction of dichromate acetic acid to chromic acetate in the presence of hydrogen peroxide. CAT activity was expressed as units per g Hb, where a unit is described as the amount of enzyme required to decompose 1 mole of H₂O₂. MDA, the index for lipid peroxidation, was estimated in hemolysate, by the thiobarbituric acid (TBA) method (Niehaus and Samuelsson, 1968). MDA was expressed as n moles per g of Hb. Plasma was used to measure ferritin by solid phase ELISA and FRAP, an index of the total oxidative stress, by the method of Benzie and Strain (1996), where plasma reacts with 2, 4, 6-tripyridyl-s-triazine (TPTZ) and the Fe²⁺-TPTZ complex is measured at 593 nm with time scanning, done at 30 second intervals for 4 minutes. Quantification was done by regression analysis and result expressed as μmol/ml.

Table 1: Effect of iron supplementation during pregnancy on biochemical indicators of iron status and oxidative stress

Biochemical Indicators	NP (controls)	Trimester 1	Iron Supplementation Status	Trimester 2+3
Sample size (n)	50	30	UnS	27
			S	33
Body Weight	51±3.91	51.36±3.9	UnS	55.85±3.74
			S	60.73±4.24***
Hb(g/dL)	11.13±0.12	11.2±0.17	UnS	10.46±0.08
			S	11.15±0.17***
Hct (%)	35.2±0.3	33.2±0.55	UnS	29.7±0.46
			S	31.94±0.43***
Plasma Ferritin (μg/l)	45.32±4.98	20.63±4	UnS	16.5±2.50
			S	37.3±5.56**
MDA (nmol/g Hb)	4.11±0.12	6.42±0.17	UnS	8.89±0.27
			S	9.76±0.05*
SOD (μg/g Hb)	1307±25.7	1047±15.8	UnS	857.36±13.35
			S	811.62±14.10*
CAT (μg/g Hb)	9.89±0.11	311±7.93	UnS	8.22±0.13
			S	7.77±0.14*
FRAP (μmol/ml)	207±6.12	311±7.93	UnS	352±13.10
			S	380±13.29

All values are expressed as Mean ± SE.

p values: All UnS values compared with corresponding S values. Values marked with one*, two** and three*** asterisks are statistically significantly different at p<0.05, p<0.001, p<0.0001 respectively.

Abbreviations: UnS: unsupplemented, S: supplemented, NP: non pregnant, OS: oxidative stress,

SOD: Superoxide dismutase, CAT: catalase, MDA: malonyldialdehyde, FRAP: ferric reducing ability of plasma.

Statistical analysis

All parameters were expressed as Mean \pm S.E.M and differences between groups assessed using Student's t-test. Pearson's correlation coefficients (r) were also calculated to study the relationships between various factors.

Results and Discussion

The main issue addressed by this study was to assess the effect of short-term, high-dose iron supplementation on iron status and oxidative stress status of healthy, non- anemic / mildly anemic pregnant women. Table 1 presents the effect of iron supplementation during pregnancy on body weight, biochemical indicators of iron status, Hb, Hct and ferritin; and oxidative stress markers, SOD, CAT, MDA and FRAP in non-anemic /mildly anemic respondents.

Supplemented (S) women gained more weight than those who were unsupplemented (UnS). There was a decline in Hb and Hct in T2+T3 in the UnS, which was arrested by iron supplementation in S group. However, Hct remained lower than NP throughout pregnancy even as the values remained lower than those in non pregnant women. This was as expected, because of normal, physiologically desirable plasma volume expansion during pregnancy, detectable as early as 6-8 weeks of gestation (Centers for Disease Control, 1989). Plasma ferritin declined significantly and dramatically in T1, and, further, in T2+T3 in the UnS group, but not in the S group, which showed some recovery of iron stores. Ferritin levels in T1 and T2+T3 remained lower than non pregnant levels in UnS women as expected, but even in iron supplemented women despite the high dose supplement. This is known to occur because stored iron begins to shift to hemoglobin early during the second trimester and continues till term (Bothwell, 2012).

Thus, it is generally agreed upon that marginal decline in Hb, Hct and ferritin during pregnancy, should not be attributed to iron deficiency, and the pattern of iron status indices in the present study even in the UnS does not signal any harm. Moreover, high dose iron supplements during pregnancy have been reported to lead to hemoconcentration, indicated by increased levels of hemoglobin, hematocrit, and ferritin, known to create problems in child birth (Bedi *et al.*, 2001; Gomber *et al.*, 2002; Graves and Berger, 2001).

Yet, as described earlier, in view of wide spread iron deficiency (National Nutrition Monitoring Bureau, 2002), a mandatory supplement providing 100 mg elemental iron is recommended by the National Nutritional Anemia Control Program of the Government of India to all pregnant women during the second and third trimester of pregnancy, irrespective of whether they are anemic or not, and without screening for hemoglobin or hematocrit. In the present study, this dose was consumed by the non-anemic/ mildly anemic pregnant women.

OS marker, MDA, which is the measure of lipid peroxidation, increased throughout pregnancy in both UnS and S groups. The increase was statistically significantly more in the S group as compared to the UnS. Antioxidant enzymes, SOD and CAT declined steadily throughout pregnancy in both UnS and S groups, but the decline was statistically significantly more in the S as compared to UnS group, respectively. Marker of overall antioxidant capacity, FRAP increased steadily throughout pregnancy in both UnS and S groups, but was only marginally but not significantly higher in the S group as compared to the UnS group. These findings are supported by other recent studies, which report increased oxidative stress following iron supplementation to pregnant women. Devrim *et al.* (2006) reported increased MDA levels in maternal plasma and placenta in iron supplemented pregnant women. Lachili *et al.* (2001) found that a daily supplement of 100mg iron with vitamin C in the third trimester of pregnancy resulted in increased lipid peroxidation and decreased vitamin E but did not change antioxidant micronutrients and antioxidant metallozymes, RBC Cu-Zn SOD and Se-GPX. Pryor (2001) reported that ingestion of iron supplements enhanced free radical production through glycation and elevated non-transferrin bound iron (NTBI), as measured in plasma and umbilical cord blood. Anetor *et al.* (2010) reported weight loss, higher serum iron, and decreased levels of the antioxidants ascorbic acid, copper, zinc, and bilirubin, following iron supplementation during pregnancy. In our study the duration of supplementation is shorter than reported in the above studies, yet increase in OS is indicated, accompanied with mild increases in Hb, Hct and ferritin. The benefits of which are not clearly established in the non-anemic / mildly anemic women of the present study.

The changes in all parameters with gestational age were assessed by studying the correlation coefficients between gestational age and the biochemical indicators. The relationships are presented in Table 2.

Results indicated that almost all parameters have a significant correlation with gestational age. Iron status indices Hct, and ferritin declined, and OS markers MDA and FRAP increased, and SOD and CAT declined with progression of pregnancy. Iron supplementation did not change the relationship, except in the case of FRAP, where it became more pronounced with supplementation.

The issue of iron supplementation must be analyzed in relation to the requirements of this trace element. The actual requirement of iron to achieve positive iron balance during pregnancy is 130, 320 and 310 mg in trimester 1, 2 and 3, respectively, totaling 760 mg through pregnancy, that is about 3.5 mg/day during the second and third trimester. The ICMR RDA (Indian Council of Medical Research Expert Group, 2010) of iron in trimester 2 and 3 has been computed to be 35 mg per day,

Table 2: Correlations between gestational age and biochemical indicators

Correlation coefficient (r) between		Trimester 1	Iron supplementation	Trimester 2+3
	Biochemical Indicators			
Gestational age	Hct	-0.01	UnS	-0.50*
			S	-0.27
	Ferritin	-0.38*	UnS	-0.40*
			S	-0.36*
	MDA	0.65*	UnS	0.63*
			S	0.64*
	SOD	-0.60*	UnS	-0.87*
			S	-0.86*
	CAT	-0.5*	UnS	-0.82*
			S	-0.84*
	FRAP	0.1	UnS	0.22
			S	0.38*

All values are correlation coefficients (r). Values marked with an asterisk are statistically significantly different at $p < 0.05$

Abbreviations: UnS: unsupplemented, S: supplemented, NP: non pregnant, OS: oxidative stress, SOD: superoxide dismutase, CAT: catalase, MDA: malonyldialdehyde, FRAP: ferric reducing ability of plasma.

up from 21 mg per day for nonpregnant women. Iron absorption is need based because iron is a heavy metal, and its excretion is limited because its salts have low solubility in the aqueous medium of urine. Iron absorption has been assumed to be 8 per cent for computation of ICMR RDA, even though it is reported to be higher during pregnancy, increasing from 7 per cent at 12 weeks to 36 per cent at 24 weeks and 66 per cent at 36 weeks (Barrett *et al.*, 1994), so the recommended allowances for trimester 2 and 3 are on the higher side.

Moreover, the methodology adopted to compute RDA adds averages to cover 2 standard deviations, *i.e.* 97.5 per cent of the population, so lower dietary intakes may be sufficient to meet requirements of about half of the population even in the absence of supplementation. Yet the mandatory supplement is three times in the ICMR RDA, and about 30 times the actual iron needs of pregnancy, across all pregnant women, including those who are non-anemic, without screening for iron deficiency.

From the foregoing, it is illustrated that iron supplementation can have potentially harmful effects, when prescribed only on the assumption of anemia and not on the basis of biological criteria. It has been pointed out (Graves and Berger, 2001) that trimester-specific norms are not based on an

unsupplemented healthy, well-nourished population, but on women who were supplemented with doses that are unachievable through diet. It has been assumed that higher is better, hematologic changes in pregnancy have been regarded as pathologic, rather than a physiological adaptation to the normal state of pregnancy. Due to the physiological hemodilution, the criteria to classify women as anemic during pregnancy remains an unresolved issue, and hematocrit and hemoglobin are imperfect measures of anemia, but they remain the most ubiquitous test in all areas of the world because of their low cost and ease of measurement. The question also arises whether our metabolic machinery is designed to handle amounts, that are larger than can be obtained from diet.

Recent studies have suggested that using smaller doses of supplement may be as effective in removing iron deficiency where it exists, but the harmful effects would be ameliorated. A lower dose of 20 mg per day from week 20 of pregnancy until delivery has been found to be an effective strategy for preventing iron deficiency without the side effects of higher doses (Makrides *et al.*, 2003). Other studies have found intermittent iron supplementation preferable over daily supplementation for non-anemic pregnant women (Casanueva and Viteri, 2003; Mukhopadhyay *et al.*, 2004). However, in the present study, just 2-4 weeks of supplementation was found to result in higher oxidative stress.

However, studies not providing iron to pregnant women in India are not available, because of the mandatory nature of iron supplementation. All gynecologists are advised to prescribe at least 60 mg of elemental iron once or twice daily from the second trimester onwards to all pregnant women (Federation of Obstetric and Gynecological Societies of India, 2011), while 100 mg tablets are recommended by National Nutrition Monitoring Bureau (2002) as discussed earlier, and are supplied to public health centres for free distribution. Hence, studies providing iron in smaller doses or iron from other sources such as nutraceuticals or functional foods are not likely to get ethical approval.

Finally, the healthy non-anemic or mildly anemic unsupplemented women also showed a markedly increased lipid peroxidation and decreased SOD and catalase with progression of pregnancy. Thus, the impact of pregnancy itself on OS markers in healthy unsupplemented controls was quantitatively very significant, even as iron supplementation increased oxidative stress. The former could be a physiological phenomenon, attributed to the placenta which produces oxidative stress due to the high concentration of mitochondria (Palm *et al.*, 2009; Toescu *et al.*, 2002).

It is hypothesized that there may be a component of increased oxidative stress which may be a physiological phenomenon, which increases to pathological proportions in the high dose iron supplemented women. Reactive oxygen species have been reported to have useful functions in cells, such as redox signalling, and the function of antioxidant systems is not to remove oxidants entirely, but to keep them at an optimum level (Rhee, 1999; Valko *et al.*, 2007). More studies are required to study the role of free radical markers in healthy pregnant women.

Increasing the intake of antioxidant foods is increasingly recognized to result in reduction of oxidative stress. Since all vegetables, especially green leafy vegetables, and fruits have been found to be good sources of antioxidants, they should be the preferred source of iron. However, as summarized in Tables 3 and 4, the iron content of commonly consumed green leafy vegetables and fruits, generally perceived as good sources of iron do not provide the amounts prescribed during pregnancy. Some spices contain high amounts of iron (Table 5) but these are consumed in very small amounts, just a few grams per day, hence cannot be expected to contribute significantly to the increased iron intake of pregnancy. Moreover, they are traditionally used after parturition, but not during pregnancy because of the perception that they can induce labor.

Table 3: Iron content of commonly consumed green leafy vegetables

	Green leafy vegetable	Iron mg per 100 g edible portion
1.	Bengalgram leaves*	22.23
2.	Mint leaves	5.1
3.	Spinach raw	2.71
4.	Beet greens	2.57
5.	Amaranth leaves (boiled)	2.26
6.	Fenugreek leaves**	1.93
7.	Coriander leaves	1.7
8.	Sarson leaves	1.63
9.	Turnip greens (frozen)	1.51
10.	Bathua (<i>Chenopodium album</i>) ***	1.2

All values are as given by US Department of Agriculture available at <http://ndb.nal.usda.gov/ndb/nutrients/report/> except those marked with asterisks as follows:

*Bisla, G.; Archana and Pareek, S. Asian J. Plant Sci. Res., 2012, 2(4):396-402.

** (Gopalan, C; Ramasastry. B.V. and Balasubramaniam, S.C. Nutritive value of Indian food. National Institute of Nutrition, ICMR, Hyderabad.)

***http://en.wikipedia.org/wiki/Chenopodium_album

Table 4: Iron content of commonly consumed fruit

	Fruit	Iron mg per 100 g edible portion
1.	Grape	0.36
2.	Gooseberry (Amla)	0.31
3.	Guava	0.26
4.	Banana	0.26
5.	Water melon	0.24
6.	Melon, Honeydew	0.17
7.	Mango	0.16
8.	Apple	0.12
9.	Orange	0.10
10.	Lemon juice	0.08

All values are as given by US Department of Agriculture available at <http://ndb.nal.usda.gov/ndb/nutrients/report/>

Table 5: Some commonly consumed spices with high iron content

	Fruit	Iron mg per 100 g edible portion
1.	Cumin seed	66.36
2.	Turmeric	55.0
3.	Fenugreek seed	33.53
4.	Chilli powder	17.30
5.	Coriander seed	16.32

Replacement of currently prescribed high dose inorganic iron supplements by functional foods or nutraceuticals is a strategy that has not received the attention that it merits. The field of nutraceuticals and functional foods is new, and many gaps exist in the knowledge base. Functional foods are products produced using scientific data to provide specific nutrients, and are consumed as food, while nutraceuticals are healthful products formulated and taken in dosage form as capsules or tablets. Functional foods are a mix of several nutrients which work together and help each other in absorption or metabolism, thus they are different from the pharmaceuticals which are single component therapeutic agents and, thus, are more likely to create nutrient imbalances (El Sohaimy, 2012).

A functional food containing a smaller dose of inorganic iron with various antioxidants may be a good choice as replacement for the iron tablets currently being used the world over. In this regard, Puyfoulhoux *et al.* (2001) reported that *Spirulina platensis*, blue-green algae, contains a highly available form of iron. 20-25 g of this is sufficient to provide the ICMR RDA for iron. Due to its high iron content, *Spirulina* is commercially available for human consumption. Presence of antioxidant compounds in *Spirulina* has also been reported (Miranda *et al.*, 1998), which could be used by the body to combat the harmful effect of oxidative stress. In the light of these studies, and our finding that even short-term supplementation of inorganic iron increases oxidative stress during pregnancy, *Spirulina* promises to be a good candidate for source of iron, possibly without the associated increase in oxidative stress levels. We suggest that controlled trials under supervision of gynecologists, exploring the effect of *Spirulina* as an alternative to inorganic iron supplementation during pregnancy should be undertaken, with simultaneous monitoring of its effect on oxidative stress. Other herbs and phytosources (Table 6) are used during pregnancy for various purposes such as to improve liver function, tone the reproductive system and calm the nerves (http://www.sacredearth.com/ethnobotany_remedies/childbirth1.php). Therefore, it is suggested that these should be assessed for their iron and antioxidant content.

Table 6: Phytosources used in pregnancy to improve liver function, tone the reproductive system and calm the nerves:

	Phytosources used during pregnancy
1.	Dandelion (<i>Taraxacum officinale</i>)
2.	Burdock Root (<i>Arctium lappa</i>)
3.	Yarrow (<i>Achillea millefolium</i>)
4.	Lady's Mantle (<i>Alchemilla vulgaris</i>)
5.	Raspberry leaves (<i>Rubus idaeus</i>)
6.	Chaste berry (<i>Vitex Agnus Castus</i>)
7.	False Unicorn Root (<i>Chamaelirium luteum</i>)
8.	Chamomile (<i>Matricaria chamomilla</i>)
9.	Valerian (<i>Valeriana officinale</i>)
10.	St. Johnswort (<i>Hypericum perforatum</i>)

Available at http://www.sacredearth.com/ethnobotany_remedies/childbirth1.php

Conclusion

To conclude, it is submitted that the desirability of universal high-dose iron supplementation to all pregnant women is far from settled. As the high oxidative stress resulting from high iron doses may be harmful, it is hypothesized that iron supplements from natural phytosources, preferably also providing antioxidants be explored as alternative therapy or prophylaxis for iron deficiency during pregnancy.

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Conflict of interest

We declare that we have no conflict of interest.

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