

CITRIZORB[®]

The Truth About Mineral Supplementation

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THE NATURAL CHOICE FOR MINERAL SUPPLEMENTATION

When metallic minerals are presented to the body as supplementary nutrients in most cases they should be linked to an organic acid to form a "salt". In this form most of them are best absorbed and used. There has been much debate and many claims made as to which of these salts should be used. The tendency is for suppliers to sing the praises of their own products, often accompanied by much hype but little evidence. This newsletter has been written after teasing out the evidential value from 579 references in the scientific and medical literature. It comes down rather firmly in favour of the high value of citrates as mineral supplements. The prime reason is better absorption and usage. The high level of mineral absorption from mother's milk has been found to be due to its high citrate content. But citrates also have some key "add-on" advantages and these are very clear. Citrates are reported to combat calcareous kidney stones, even when the mineral being supplemented is calcium itself. Citrates have been reported to combat the absorption of lead. As lead is much higher than it should be in the environment and in foods that is an important advantage. Moreover there is a lot of confidence that intakes of citrates are completely safe. This is not true of all the different kinds of salts that are used for supplementing metallic minerals.

Metallic & Non-Metallic Minerals

The mineral components of our bodies and our food can be roughly divided into metallic and non-metallic ones. Sulphate, chloride and phosphate are examples of non-metallic minerals. They usually have to be combined with metallic ones to enter into our diet. Thus we may have potassium sulphate, sodium chloride or calcium phosphate. These enter into the composition of our foods as "salts". If these pairs were not combined together they would be strong acids or alkalis, quite incompatible with food, or in the case of the metallic minerals, they would be actual metals that would be either devastatingly reactive or else would be insoluble and lodge in tissues as insoluble metallic particles. Therefore metallic minerals need "something", some chemical entity to attach to in order to be in a fit state to take in and absorb. These attachments are called "ligands".

The metallic minerals mentioned above all occur commonly in foods and enter into the composition of

our bodies. Because sulphate, chloride and phosphate are widespread in foods also, our bodies contain potassium sulphate, sodium chloride and calcium phosphate in significant amounts, they are all examples of metallic minerals in an inorganic form. Sulphates, chlorides and phosphates are inorganic "salts" of these nutritionally required metals. In chemistry, substances that are referred to as "organic" are substances that contain both carbon and hydrogen. This definition arises from the fact that such substances are characteristic of life, i.e. of organisms. We now know that we can have such substances without having organisms, but the name has stuck. The metallic minerals, by this definition are all "inorganic". But they can be combined with "organic" substances, such as acetate, malate or citrate. These metallic minerals, although they are themselves inherently inorganic, can be said to be in an "organic form" through being combined with organic substances. For short we call these "organic minerals" even though this may appear a contradiction.

Inorganic & Organic Minerals

As soon as we concern ourselves with the nutritional need for the metallic minerals, and especially when we are seeking to use them as nutritional supplements, we learn to evaluate their different chemical forms according to how well absorbed they will be when we take them into our bodies. Based upon this criterion, the organic forms have come to be more valued nutritionally than the inorganic forms. This is not universally true, but it is commonly so.

Sodium chloride is inorganic, yet it is perhaps the commonest form in which to take the metal sodium into the body. It is not characterized by any lack of absorption. This is due to the special qualities of sodium itself, which is very soluble and diffusible, so it becomes absorbed very easily in most of its forms.

***“Let your food be your medicine!
Let your medicine be your food!”***

Hippocrates - the father of modern medicine



When we come to consider metallic nutrients that are harder to absorb anyway, such as iron or manganese, the choice of the chemical form becomes much more important. Where iron is concerned the sulphate (ferrous sulphate) is a commonly offered inorganic form in the hands of orthodox practitioners. Yet they know that ferrous fumarate (an organic form) can perform better, though it is more expensive. Amino chelated iron is three times better absorbed than ferrous sulphate (Ashmead, et al. 1974). Manganese is rarely offered as an inorganic form, mainly because orthodox practitioners rarely, if ever, use manganese at all. Organic forms such as manganese gluconate or citrate are much more often employed. In the case of calcium, calcium carbonate is almost invariably the "cheap-and-easy" form that is offered in cheap supplements. In the case of magnesium it is usually magnesium oxide. Both are reported to be relatively poorly absorbed and, worse still, both neutralize the acid of the stomach that is needed for proper digestion.

It is clear that if one is going to attend to the evidence about this rather than just follow dogmas, then one should be prepared to look at the merits of each chemical form of each metal element on its own merits. It has been reported sometimes that zinc sulphate can be a reasonably effective form in which to administer zinc. If so, then this should be looked at on a cost/efficiency basis. But the weight of the accumulated evidence tends to support the use of organic forms for most of the metallic minerals used as supplements. As much of this evidence is impressive, the use of organic forms has become the "norm", at least for use by "alternative"

nutritional practitioners, who place a much higher premium upon correcting the body status in metallic minerals than do most orthodox practitioners.

Different Organic Types

In this newsletter many more references are offered than in others in the series. This is because there is very substantial evidence available and because some solid science needs to be quoted to set aside some of the unsupported claims often made about other forms of supplementary minerals. No suggestion is made here that there is universal harmony of view about one particular form of supplement that is always superior to all others. Therefore, a careful appraisal of the literature has been needed. This is what is offered below. The merits of the citrate forms emerge with a very potent range of attractive properties.

The different types of metallic "salts" that are used or have been used include acetates, citrates, lactates, gluconates, fumarates, malates, aspartates, ascorbates, orotates, picolinates and amino acid chelates of the respective metallic minerals. These are, therefore, the different available common ligands. People concerned with buying supplements are familiar with most of these, especially practitioners, though they usually have little information available to help them choose between these different kinds. The usually accepted wisdom in "alternative circles" is that all these forms are much better than the corresponding inorganic forms. While this is most often true, scientific evidence does show there are a few exceptions.



The truth does appear to be that all the types previously mentioned are, indeed, quite good from a technical viewpoint. The choice between them can often be better justified on the basis of price, concentration (the amount of elemental mineral per gram of the salt) and lack of toxicity of the organic ligand. In Section 4 below we shall look at a new definition of "toxicity" in this connection. In any case, the orotates and perhaps the picolinate also may not be completely in the clear from the standpoint of even conventional definitions of toxicity (Jeejeebhoy, 1999). Picolinate is suspected of causing DNA damage in macrophage cells in vitro (Bagchi et al, 1997) and renal failure in humans at high intake (Cerulli et al, 1998).

The best concentrations of mineral (among "organic forms") of the metallic minerals are usually to be found in either acetates or citrates. Often these same forms may also give us the best relative prices per unit of elemental mineral being supplied. So that makes them cost-effective. What makes citrates special, beyond the properties of good absorption, high concentrations and freedom from any adverse effects, is their "add-on" good effects, in particular their benefits in discouraging the formation of kidney stones and inhibiting (or possibly simply "not enhancing") the absorption of toxic lead.

Some individual minerals have "special" forms that are indeed particularly valuable. These include the "GTF" form of chromium and the selenomethionine form of selenium. These may well be among the best available forms for presenting these individual minerals. Selenium could not in any case be presented as a citrate, since it is not a metal. These two minerals will not be further covered here.

Also included under "organic minerals" are those that have been specially "bioprocessed" through living organisms, usually yeast. Prominent among these are those products designated as "Food Form" or similar names. Basically these minerals are "fed" to the yeast and incorporated into

the yeast cells. The claim is then made that they are the same or similar to the same minerals that occur naturally in foods. No evidence was adduced that these possess any of the "extra" advantages possessed by the citrates. We examine their claims more closely in Section 13 below.

Potential Toxicity of Some Types

There has been no clear demonstration of orotate toxicity in humans, though it has come under some suspicion because high intakes cause fatty liver in rats. Humans do appear rather more tolerant of it. (Braverman & Pfeiffer 1986). Picolinate is related to the chromium GTF form but not identical with it. We are not yet completely assured that it is without harm. Even ascorbates in very large intakes (these are forms of Vitamin C as well as being mineral sources) have been alleged to encourage kidney stones or to inhibit the utilization of Vitamin B12. These observations show us that we should be critical of the non-mineral part (i.e. the ligand) of the salts we use as supplements. The toxicity problems referred to may be minor ones, applicable only at very high intakes, or simply be unproven and controversial. However, it is best when using supplements to be free from nagging doubts.

The Extremely Safe Citrates: The Citric Acid Cycle

We now focus upon an issue that is close to the safety issue. Some of the organic ligands that are attached to nutritional



metals to make supplements have no chance of being toxic in the usual sense because they are "normal metabolites". That is to say that they are substances formed and destroyed during the normal operations of the body tissues in tissue respirations, protein synthesis etc. That comment would apply to lactates, gluconates, fumarates, malates and aspartates. No toxic properties can be adduced.

The question that now arises is, given that these are not toxic, to what extent might they alter normal metabolism? The biochemist's answer to this should be that fumarates and malates should not disturb metabolism. The reason is that they are intermediate substances in the pathway that oxidizes all the bulk nutrients of our foods - protein, carbohydrate and fat. Virtually all of the carbon in our food goes through this pathway that is called "The Citric Acid Cycle". This means that the amount of fumarate and malate formed and destroyed within our bodies each day is probably about 1 kilogram of each. If we take capsules that contain a gram or two of them, the degree of perturbation to normal metabolism is quite negligible. We can say, therefore, that there is no need for concern about their use. The same is true for acetates and citrates. They enter into the same important "bulk" pathway. The quantity of citrate formed and destroyed each day is probably 1.5 kilograms at a conservative estimate. Lactates may well be in the same category as fumarates and malates. This is because lactate can convert to a form called pyruvate that can then enter the citric acid cycle.

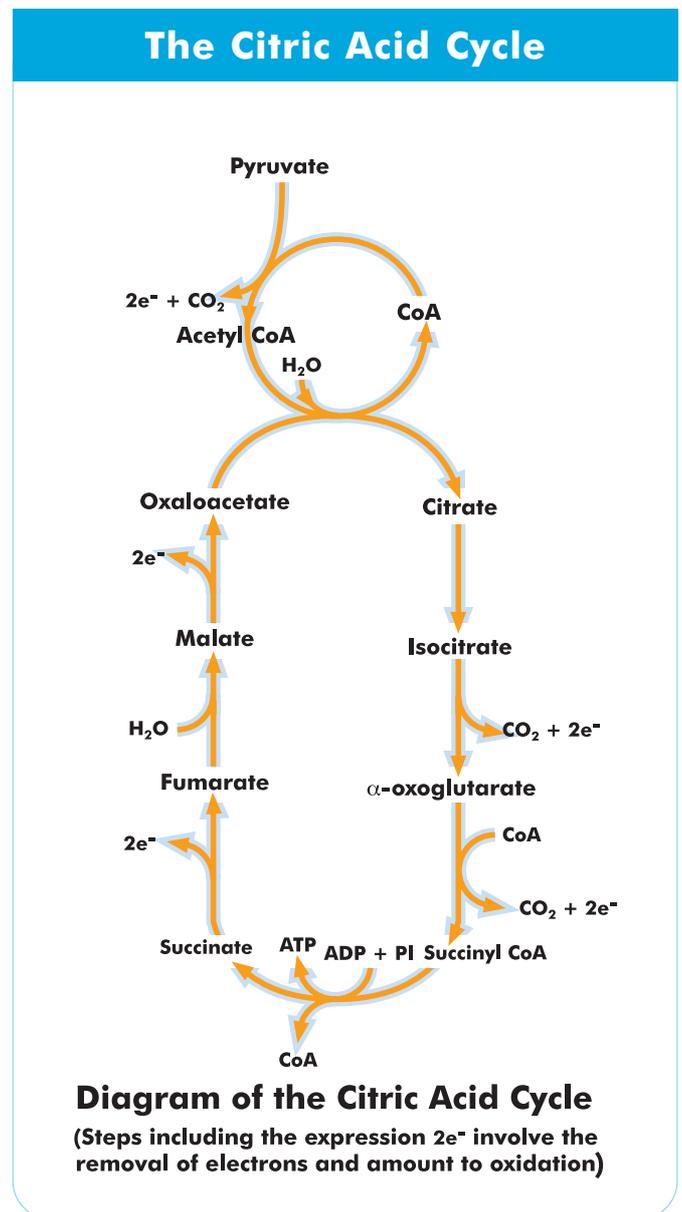
The conclusion to draw is that we can readily accept acetates and citrates; fumarates and malates, as very acceptable forms for nutritional minerals. Any resulting perturbation to metabolism is negligible. There are some differences in concentration and cost between them and the "add-on" properties of citrates are very telling also in the final choice. However, gluconates may be less favoured because the pathway in which gluconate participates in the body (one called the pentose phosphate pathway) is a more minor pathway and may be more easily perturbed by intakes of one of its metabolites. Hence the use of the gluconate forms of minerals may be free from any perturbation to metabolism at low intakes but suspect at higher intakes. They are also low scorers with regard to the question of their concentration. You need to take in a lot of the gluconate forms to obtain a given weight of elemental mineral. Hence the necessary intake of gluconate is pushed up if you want to access realistic amounts of mineral intake and the danger of perturbing metabolism has to be considered.

In the case of orotates the risk of disturbing metabolic patterns is probably considerable. This is because the pathway leading to formation and removal of orotate in the body is a minor pathway leading towards nucleic

acids. Minor pathways can be much more readily overloaded than major ones. Even if one does not accept that orotate might cause fatty liver in humans, as it does in rats, then one might choose to avoid it on the grounds of likely perturbation of metabolism.

Citrates, in common with acetates, fumarates, malates and probably lactates, are supremely safe to use as supplements because they are normal metabolites on really major pathways in the body. None of them seem likely to perturb the balance of metabolism in any significant way. The choices between them then depend on other factors. Some of these factors relate to the "extra" physiological benefits of citrates and some to availability and economics.

We conclude this Section by showing, in Figure 1, an illustration of the citric acid cycle for the oxidation of bulk food substrates in the body. This shows the sequence of the reactions that lead from citrate and then back to citrate again with each "turn" of the cycle. Virtually the whole of our oxidative metabolism depends upon this process.



What We Know About Absorption of Metal Citrates

Here we examine the scientific evidence that shows how well metal citrates are absorbed from the alimentary canal. Lindberg et al (1990) did work on magnesium absorption. This study compared magnesium oxide and magnesium citrate with respect to gastrointestinal absorbability. Magnesium oxide was virtually insoluble in water. It was only 43% soluble in hydrochloric acid at concentrations adjusted to the peak acid secretion level within the stomach. Magnesium citrate had high solubility even in water (55%) and was substantially more soluble than magnesium oxide in all states of acid secretion. Solubility is the first step to bioavailability.

Approximately 65% of magnesium citrate was complexed as soluble magnesium citrate, whereas magnesium complex formation was not found in the case of magnesium oxide. Complexing is another important step towards bioavailability.

They measured magnesium absorption from the two forms of magnesium in vivo in normal volunteers by assessing the rise in urinary magnesium following oral magnesium load. The increase in urinary magnesium after taking magnesium citrate was significantly higher than that obtained from magnesium oxide. The figures (in units of mg/mg creatinine) were 0.035 for citrate versus 0.008 for the oxide, a factor of 4 to 4.5 times. Thus, magnesium citrate

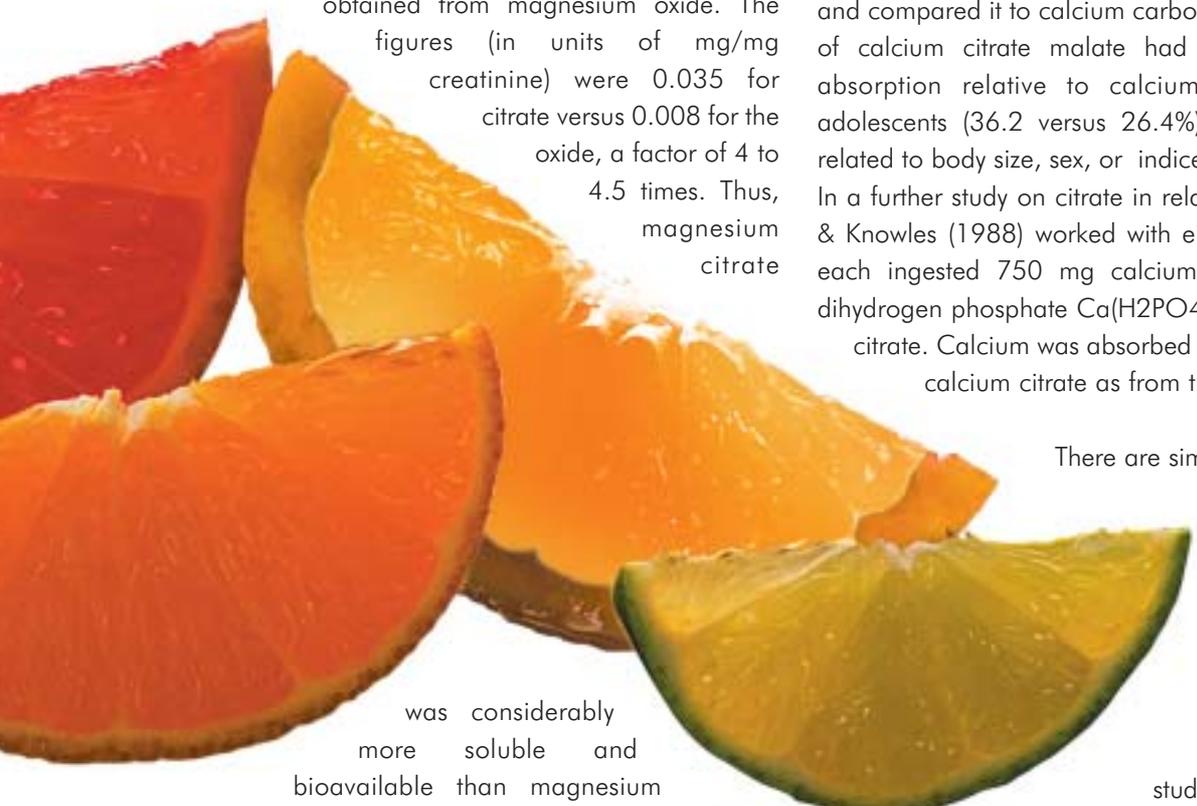
was considerably more soluble and bioavailable than magnesium oxide. Hence, the "cheap and cheerful" magnesium oxide approach to supplementation is rather ineffective, while magnesium citrate was shown to be an excellent magnesium source. Similar results were obtained by Nicar

(1985). Wood & Serfaty-Lacrosniere (1992), working with the elderly, also found that "a highly soluble source" of calcium was clearly preferable to calcium carbonate.

Obviously, comparisons between different organic forms of the metals do not show such large differences. This is because most organic sources are far superior to the inorganic forms. One such comparison between alternative organic forms was that done by the German researchers Hansen et al (1996). They compared the bioavailability of calcium citrate with that of calcium lactogluconate/carbonate from a therapeutic dose of 500 mg elemental. The study was done in men between 45 and 60 years of age. Their purpose was to provide adequate calcium supplementation for the prophylaxis and therapy of osteoporosis. There was a significantly higher absorption of 29% from the citrate solution than from the lactogluconate/carbonate solution (25%).

Patrick (1999) chose a route involving a combination of both citrate and malate for calcium supplementation and showed that "calcium citrate malate has high bioavailability" and "positive effects have been seen in prepubertal girls, adolescents, and postmenopausal women". The results were evaluated in terms of the effect of calcium citrate malate on bone density and reduction of the risk of fractures. Miller et al (1988) also looked at calcium citrate malate absorption and compared it to calcium carbonate. Calcium in the form of calcium citrate malate had an increased fractional absorption relative to calcium carbonate in healthy adolescents (36.2 versus 26.4%). This increase was not related to body size, sex, or indices of calcium metabolism. In a further study on citrate in relation to calcium, Schuette & Knowles (1988) worked with eight normal subjects who each ingested 750 mg calcium as solution of calcium dihydrogen phosphate $\text{Ca}(\text{H}_2\text{PO}_4)_2$ (inorganic) or calcium citrate. Calcium was absorbed at least twice as well from calcium citrate as from the phosphate form.

There are similar studies performed on the citrates of other minerals. Examples are those of Grassmann & Kirchgessner (1969) on copper citrate and iron, zinc, copper and manganese have all been studied in connection with the role of citrate in human milk (see below). Manganese citrate was also studied by Garcia-Aranda (1984). There is a hint in the literature of involvement of citrate in vanadium absorption (Kiss, 2000).



All these direct studies upon the absorption of metallic mineral nutrients have clearly established the credentials of citrates as a generally attractive organic form in which to supply these minerals. Of course, not all experimenters reach the same conclusions all the time. The citrate form undoubtedly offers more special features for some minerals than others. There again, for some individual minerals alternative forms do exist that appear to vie with citrates. One example is picolinate, much favoured for chromium because it is rather close to the GTF form, but which has also been recommended on occasion for zinc. Picolinate, however, is a highly specialized chemical form and we cannot necessarily rely upon it not to "perturb" the metabolic pathways. It is an intermediate on the rather minor pathway of tryptophan breakdown. What is impressive also about the citrates is their wide range of applicability among many minerals, their special "extra" advantages and also the way in which they are prone to have their bioavailability performance enhanced by certain accompanying substances.

Citrates in Mother's Milk

The bioavailability of the trace elements iron, zinc, copper and manganese from human milk is high compared to cow's milk and infant formulas. For example Sandstrom et al. (1983) found that absorption of zinc was 41% from human milk and 28% from cow's milk. Absorption was 22% from a cereal-cow's milk formula, and 14% from soy formula.

It has long been questioned why this should be so. What component or components of human milk are responsible for this much better performance? A protein called lactoferrin in human milk may facilitate iron and manganese uptake. However, high concentrations of citrate are thought to facilitate specifically uptake of trace elements from human milk (Lonnerdal et al 1980, Lonnerdal, 1989). Bratter (1997) found that the principle binding agent for zinc in human milk is citrate. Bratter also found that zinc citrate was clearly prominently involved in the absorption of zinc from human milk. He knew this because when mothers took in excessive amounts of selenium (well in excess of usual nutritional intakes) the citrate content of mother's milk was diminished and zinc absorption was inhibited as a result. Lonnerdal et al 1980 suggested that the known therapeutic value of human milk for patients with the genetic disorder of zinc metabolism acrodermatitis enteropathica (AE) derives from a greater content of bioavailable zinc citrate in human than in cow's milk. Peaker et al (1975) refer to citrate as "the harbinger of lactogenesis". Copper citrate has been carefully studied in human milk by Martin et al (1981).



Citrates in Prostatic Fluid and Seminal Plasma

Seminal fluid contains an especially high concentration of zinc, a fact that indicates a strong association of that metal with the generation of new life. The fact that prostatic fluid and seminal plasma is also rich in citrate is also extremely interesting. The reason for this is, of course, not known, but it is certainly tempting to think that the role of the citrate is to make it easier for the sperm to take up (or "absorb") this zinc. It was an investigation by Arver (1982) that concluded that "citrate is the major low molecular weight zinc ligand in prostatic fluid, seminal plasma and breast milk". The zinc citrate in prostatic fluid and seminal plasma are accompanied by the sugar fructose, a known enhancer of the pro-absorption properties of citrate.

How to Augment Even Further the Availability of Citrates

The research literature is studded with references to the absorption of metallic minerals from the citrates being accelerated by certain "helper" substances that may exist in foods along with the citrate minerals themselves. These include apple juice, gum arabic, and the sugar fructose (fruit sugar). There is at least a hint that ascorbate (Vitamin C) may play a role in this also. Finally, it is apparently a benefit to absorption if extra free citric acid is present along with the mineral citrate (Pak et al, 1987). For those who understand the chemistry of mineral-citrate interaction, the recommendation made by these authors was that the "mineral / citrate molar ratio" should be 1.25.

“No illness that can be treated with diet should be treated by any other means!”

Moses Maimonides (12th Century Monk)



The discovery of the "add-on" value of apple juice and fructose is due to Andon et al (1996). They reported that calcium retention in dogs was 15% for calcium-fortified orange juice and 29% for calcium fortified apple juice. Calcium retention was significantly different in rats. Calcium fortified orange juice gave (52%) absorption, calcium fortified apple juice (61%). By manipulating the carbohydrate and organic acid concentrations of test solutions to mimic the composition of calcium fortified juices, they found that the greater fructose and lower organic acid content of apple juice accounted for its greater calcium absorption.

Citrates and Kidney Stones: (Nephrolithiasis)

One of the most exciting findings about using mineral supplements based upon citrate is the potential for inhibiting the formation of kidney stones. Typical of the research reports on this topic is that by Fardella et al (1994). They reported that patients with nephrolithiasis did not differ from controls in urinary calcium, uric acid or magnesium whereas urinary citrate was much lower than the normal value. Schwille et al (1987) and Herrmann (1999) have therefore suggested employing citrates in the treatment of the condition.

Citrates Do Not Enhance Absorption of Lead

Zerwekh et al, (1998) reported upon the lack of skeletal lead accumulation during calcium citrate supplementation. This is good news because one might have expected that citrate would bring about

the absorption of extra lead, just as it enhances the absorption of nutritional minerals. However, there is no such good news in respect of aluminium, which is also toxic. Aluminium absorption is enhanced by citrate, so when citrates are employed as supplements it will be best to ensure that aluminium saucepans and aluminium antacids are not in use (Slanina et al 1986; Testolin et al 1996). However, this is another example of the powerful absorption promoting action of citrate.

Citrates and the Absorption of Other Substances

One other action of citrate, which you may class as a benefit or not as you see fit, is to enhance the absorption of drugs. This is true of the antibiotics chlortetracycline (Pollet et al, 1983, Pollet et al 1985) and oxytetracycline (Luthman & Jacobsson, 1985). A paper by Wanner et al, (1991) reported that chlortetracycline absorption was improved 65% with 1.5% or 3.0% dietary citric acid supplementation. Most alternative nutritional practitioners prefer, where feasible, to avoid administration of antibiotics and apply other methods. Hence this effect upon their absorption is only of interest within orthodox medicine. Once again the powerful absorption promoting effect of citrate is highlighted.

How Do Citrates Compare With the "Food Form" Minerals?

There are a number of mineral supplement products, including metallic minerals that are processed biologically by feeding the inorganic mineral to living organisms or living tissue and then harvesting the

resulting biomass. Such products are usually marketed on the basis of a claim that the minerals have been converted in the process into a form that is comparable with the same mineral as it occurs in foods. It is usually either implied or claimed that this conversion is advantageous in respect of the nutritional availability of the minerals. Firstly there is fairly good evidence that the mineral content in these products is bound to cellular constituents. Since they are then in an organically bound form, they definitely tend to be superior to straight-forward low-cost inorganic minerals, like calcium carbonate or magnesium oxide. The same is likely to apply to the low-cost sulphates of iron, zinc and manganese, even though zinc sulphate sometimes shows up quite well in bioavailability tests.

However, to give a fair comparison these products (they are usually more expensive than most chemical forms) need to be compared to the very best chemical forms available. No research study seems to have addressed directly the question of comparing "food form" varieties with pure mineral citrates. The published evidence in favour of the "food form" minerals is, in the opinion of this writer, rather sketchy and incomplete. On examination, what the researchers actually wrote has been vulnerable to misinterpretation. Moreover, most of the "food form" research has been conducted by the same group of US researchers. Independent, peer-reviewed research supporting the view that "food form" can out-perform the best organically combined chemical forms appears to be lacking.

Citrates have been subjected to extensive research as is testified by the bibliography of this newsletter.

Moreover, although "organic binding" is generally good in the sense that it makes nutrients more bioavailable, this is not always the case. One has only to cite the case of Vitamin C in cabbages, part of which is converted into a bound, yet inactive form, called "ascorbigen". To be effective in promoting nutrient absorption the binding must be of the correct kind. To be bound to a substance that is itself inherently unabsorbable is obviously a disadvantage.

Most of the nutritional metallic minerals are known to be largely in a "bound" state in the living cell and there is even quite a lot of information about how they are bound. They are principally cofactors of enzymes. In many cases most of the cellular content of the mineral is bound to the enzymes concerned or else with the other cofactors involved in the reaction. A good example is magnesium. Magnesium is mainly involved in reactions in the body that also involve ATP (adenosine triphosphate). Hence some 80% of the cell's magnesium is held in the form of an "ATP-magnesium complex". This is a way of saying that the true "food form" state of magnesium is mainly this complex. If an

alleged "food form" magnesium supplement is made by adding inorganic magnesium to yeast cells and allowing them to metabolize it, then the added magnesium is only in the true "food form" in the product if it has been converted by the yeast into "ATP-magnesium complex". The question is "is it so converted and can it be?" The answer is that most of it is almost certainly not so converted.

The reason for this is connected with the concentration of different components within the cell. Normally the concentrations of both magnesium and ATP within the cells are low. To make a food supplement out of the yeast, one that contains enough magnesium to make it into an effective magnesium supplement, a far higher concentration of inorganic magnesium has to be added. It is almost inevitable that this high level (usually several percent of the entire weight of the yeast) so floods the cells with magnesium that there cannot be enough ATP to go round to complex with it. Most of the added magnesium will become bound nonetheless, because there are many cell constituents available to bind with magnesium, but the binding will not be able to occur, to any substantial extent, with the ATP that is its normal cellular binding ligand. Therefore we shall end up with cells that contain bound magnesium but this will not be the usual form of binding that occurs within the normal function of the yeast cell. Whether the form of bound magnesium that is created by the method for manufacturing so-called "food form" magnesium products has good absorption properties or not is a matter for conjecture. No one seems to have published research that clearly shows what this bound form is.

We have to conclude that whatever the merits or demerits of these "food form" products, they almost certainly do not correspond in most cases to the natural form of binding that exists within the normally functioning cell. To promote such products along the lines that this is what they contain appears unjustified. In the absence of any clear evidence that they can out-perform, in terms of absorption and utilization, the best of the organic chemical forms (viz. citrates) this author prefers to use mainly citrates as the principal mineral form for supplementation. As already stated, chromium and selenium are exceptions.

In discussing these forms of supplementation, we do not imply reference to any particular manufacturer's products or brands but generally to those products that claim the mineral is in a form or state resembling that of the same mineral in foods.

Concentrations in Citrates and the Intakes Required for the RNI's

In the following tabulation the weight of mineral citrate required to deliver the UK daily "Reference Nutrient Intake" (RNI) has been calculated. This has assumed that the citric acid is fully saturated with the mineral (i.e. no "sub-citrates" have been included) and that the citrate salts used are anhydrous (i.e. no water of crystallization).

| ELEMENTS | ADULT RNI (mg) | | % OF MINERAL IN THE CITRATE | CITRATE INTAKE GIVING RNI (mg) | |
|-----------|----------------|--------|-----------------------------|--------------------------------|--------|
| | MALE | FEMALE | | MALE | FEMALE |
| CALCIUM | 700 | 700 | 24.1 | 2904 | 2904 |
| MAGNESIUM | 300 | 270 | 16.0 | 1875 | 1687 |
| IRON | 8.7 | 14.8 | 30.8 | 28.2 | 48.1 |
| ZINC | 9.5 | 7.0 | 34.2 | 27.8 | 20.5 |
| MANGANESE | 1.4* | 1.4* | 30.4 | 4.61 | 4.61 |
| COPPER | 1.2 | 1.2 | 33.5 | 3.58 | 3.58 |

* Not identified as a true RNI value.

The figures in the two right hand columns can be used to indicate the amount of the appropriate mineral citrates required to give a daily intake of the metal equivalent to its the UK RNI value.

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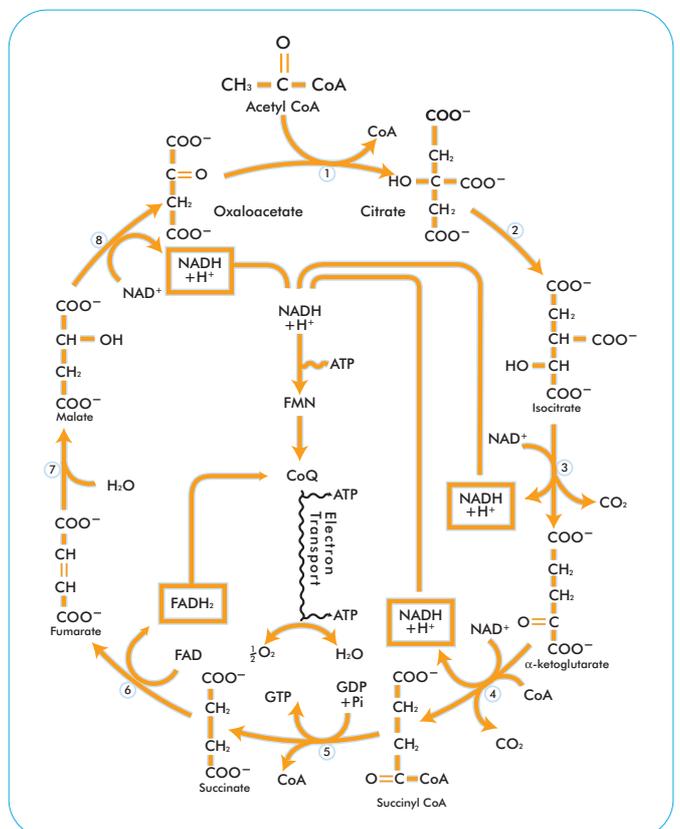
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16 Appendix 1

Complete Diagram of the Krebs or Citric Acid Cycle showing the formulae of the participating metabolites. It also shows the principal cofactors involved in this cycle.



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