

# ZINC PICOLINATE: ABSORPTION AND SUPPLEMENTATION

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## ABSTRACT

There is concern regarding the absorption of zinc, both from dietary intake and nutritional supplements, because of zinc's essential role in human nutrition and metabolism, and because of evidence that some population groups have a marginal to deficient intake of zinc. While oral zinc supplementation is efficacious in most zinc deficiency conditions, not all zinc preparations have equal bioavailability. Acrodermatitis enteropathica (AE), a rare genetic disorder characterized by a severe zinc deficit, provides an excellent model for understanding zinc deficiency and absorption in humans. Patients with AE have a defect in tryptophan metabolism which may predispose them to producing decreased levels of picolinic acid (PA). PA, a natural product of normal tryptophan metabolism in the body, has been shown to be an important, if not essential component of zinc absorption. Zinc picolinate appears to have the greatest efficacy in reversing the zinc deficiency of AE and is also absorbed to a higher degree in normal subjects than other zinc supplements. Unlike supplementation with many other mineral chelates, use of exogenous zinc picolinate may actually provide the compound normally created by the body in the intestinal tract to facilitate absorption.

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## INTRODUCTION

Concern regarding the absorption of zinc, both from dietary sources as well as from supplementation stems not only from its essential role in human nutrition and metabolism, but also from evidence that "some infants, pregnant women, teenage and college women, institutionalized individuals, and some living on low income diets have a marginal to deficient intake of zinc."<sup>1</sup> As a result, a significant amount of research has been aimed at determining the mechanisms of zinc absorption as well as the bioavailability of various forms of zinc. Among the trace elements, the abundance of zinc in biology is second only to that of iron. Zinc deficiency has been observed to cause infertility, fetal growth retardation, abnormal fetal development, and skin lesions in experimental animal studies.<sup>2-5</sup> In humans, zinc is considered to be an essential trace mineral, and deficiencies in zinc have been associated with endocrine changes, immune dysfunction, congenital malformations and prematurity, anorexia, and hypogeusia.<sup>6-9</sup> Zinc is also involved in the functioning of over 200 enzymes, including RNA and DNA polymerase, alcohol dehydrogenase and alkaline phosphatase, and plays a key role in genetic expression, cell division, and growth.<sup>10</sup>

## Acrodermatitis Enteropathica and Zinc Absorption

Acrodermatitis enteropathica (AE) is a rare genetic disorder which provides an excellent model for understanding zinc deficiency and absorption in humans. First described by Brandt in 1936,<sup>11</sup> AE is characterized by severe dermatitis, diarrhea and alopecia, and sometimes includes conjunctivitis and paronchia. In the acute stage, patients may also exhibit irritability and depression.<sup>12</sup> The disease affects males and females equally, and usually begins in early childhood, frequently at the time of weaning. The addition of even small amounts of mothers' milk to the diets of children with AE was adequate to reverse the disease, prompting Brandt to conclude that, "mothers' milk contains some substance which these children are not able to produce from ordinary food elements."<sup>11</sup> Subsequently, patients with AE have been shown to have a defect in tryptophan metabolism<sup>13</sup> and to respond to supplementation with zinc sulfate,<sup>14-16</sup> zinc picolinate, and picolinic acid without additional zinc.<sup>17,18</sup>

Due to the dramatic response of patients with AE to human milk, considerable research has been devoted to the analysis of the differences between human and cow's milk. Human milk, but not cow's milk, seems to contain a low-molecular-weight zinc-binding-ligand (LMW ZBL) which enhances zinc absorption in humans.<sup>19, 20</sup> Human milk may also contain a higher molecular weight, biologically active protein that increases zinc utilization and also establishes in part the basis for differences in zinc bioavailability between various species.<sup>21</sup>

Some controversy seems to exist over whether the LMW ZBL in human milk is picolinate,<sup>22</sup> citrate<sup>23,24</sup> or prostaglandins.<sup>25,26</sup> While the researchers may argue over which compound is the true ligand in breast milk, this is of less importance in adult nutrition,

since human milk is rarely consumed. In adults, other elements in the diet such as phytates,<sup>27</sup> casein,<sup>28</sup> and soy,<sup>29</sup> can all interfere with zinc absorption, making the more critical issue a question of how best to optimize zinc uptake in adult humans. Contrary to earlier reports, recent research indicates that dietary supplementation with either folic acid<sup>30</sup> or iron<sup>31</sup> does not impede zinc absorption.

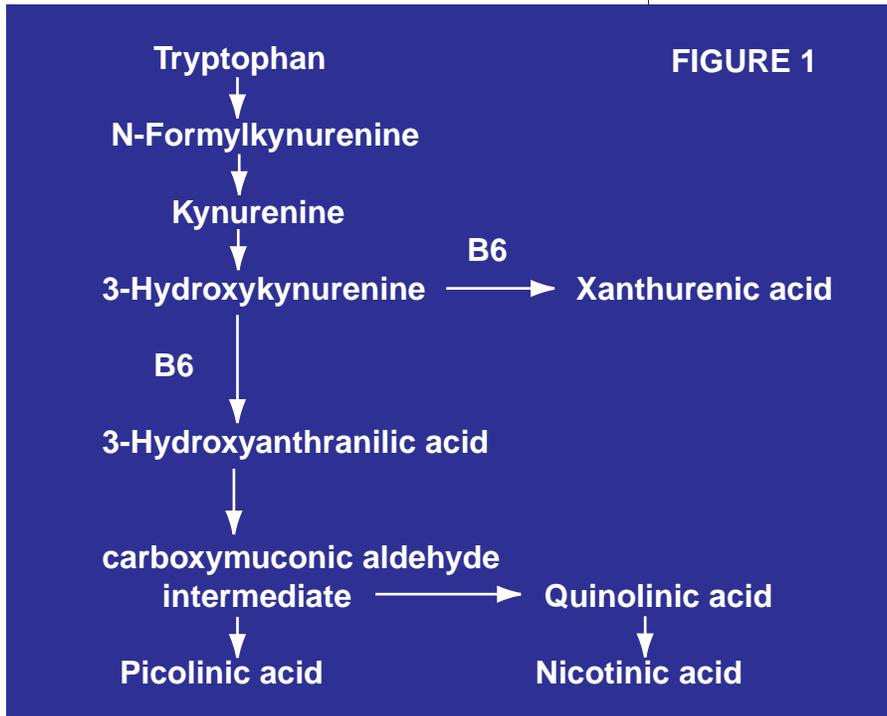
## The Role of Picolinic Acid in Zinc Metabolism

Evans et al have reported picolinic acid (pyridine 2-carboxylic acid, PA) to be the LMW ZBL in human milk,<sup>22</sup> and have demonstrated that zinc absorption is decreased in the absence of pancreatic secretions, which in rats have been shown to contain PA.<sup>32</sup> They propose the theory that picolinic acid release at the level of the hepatopancreatic duct binds to elemental zinc released during acid digestion in the stomach, facilitating absorption. In reviewing a series of studies on zinc absorption, Evans concludes "these results provide strong evidence that endogenous picolinic acid is essential for normal zinc absorption."<sup>19</sup>

Other studies on zinc metabolism lend credence to the concept that picolinic acid produced in the pancreas and released into the duodenum plays a critical role in zinc uptake. Researchers have observed low plasma zinc concentration in patients with cystic fibrosis, a disease known to produce pancreatic dysfunction, and concluded that the low zinc level was due to an impaired zinc absorption from the gut.<sup>33</sup> Enteric coating of zinc supplement tablets has also been shown to interfere with zinc absorption,<sup>34</sup> perhaps because delayed tablet dissolution resulted in the release of zinc in the small intestine at a point too distal to the hepatopancreatic duct to make use of endogenous picolinic acid.

PA is a product of tryptophan metabolism, as is nicotinic acid (vitamin B3). It is interesting to note the similarity between the symptoms of AE and the classic symptoms of pel-

nutrition. Studies utilizing piglets<sup>36</sup> and cattle<sup>38</sup> have shown that picolinate does not enhance zinc absorption, while studies in rats have shown both negative<sup>29,37</sup> and positive results.<sup>39-42</sup> Initially, the only research on the use of zinc picolinate in humans was in patients with AE, whose metabolism was admittedly abnormal,<sup>17,18</sup> or in patients with pancreatic insufficiency.<sup>43</sup> Barrie et al,<sup>44</sup> in a double-blind, placebo-controlled cross-over trial with healthy human volunteers, showed that, "in humans zinc picolinate appears to be absorbed significantly better than zinc gluconate or zinc citrate."



lagra, vitamin B3 deficiency - diarrhea, dermatitis, and neuropsychiatric disturbances.<sup>17</sup> One step in the common pathway of PA and nicotinic acid requires vitamin B6 as a cofactor.<sup>17-19</sup> (See Figure 1) Patients with a vitamin B6 deficiency, as well as patients with AE (whose defect in tryptophan metabolism is one step higher in the pathway) could both be expected to develop a zinc deficiency due to a lack of PA,<sup>13,17</sup> and might also develop signs of vitamin B3 deficiency if dietary intake of that vitamin is inadequate. Dietary deficiency in vitamin B6 has been shown to alter zinc metabolism.<sup>35</sup>

Since various species have differing mechanisms for zinc absorption,<sup>21</sup> experimental studies on zinc absorption using animal models are less than desirable when attempting to determine factors relating to human

each supplementation period. In this study, supplementation with zinc picolinate showed significant increases in zinc levels of the hair, urine and erythrocytes, but not in the serum. (Changes in serum zinc have been found to be an inaccurate reflection of zinc nutritional status.<sup>45</sup>) The use of both zinc citrate and zinc gluconate showed no such change. In 1995, Sakai and associates also demonstrated the effectiveness of zinc picolinate supplementation in subjects with taste disorders.<sup>46</sup>

A few dietary supplementation studies have implied that the use of unbound PA increases fecal and urinary zinc excretion,<sup>41,42</sup> and some researchers have theorized that this may therefore compromise zinc status.<sup>47</sup> However, in a study using radio-labeled zinc in rats, Seal and Heaton have demonstrated that even

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though there was an increase in the fecal excretion of zinc when PA was present, this was “balanced by greater intestinal absorption of the metal,” since overall zinc excretion was not increased.<sup>42</sup> They also demonstrated that the use of PA enhances the general turnover and mobilization of zinc from the deeper pools of the body. In an earlier, 1983 study, Seal and Heaton reported that, “2-picolinic acid has the potential to enhance the absorption of dietary Zn in the rat whereas [sic] citric acid does not, irrespective of their occurrence in milk.”<sup>41</sup>

## CONCLUSION

Even if citrate is the naturally occurring LMW ZBL in human milk, it is an unlikely candidate for a major role in adult zinc metabolism. Even Hurley and Lonnerdal, the primary proponents of citrate’s role in human milk, agree that, “there is no evidence at the present time that [citrate] plays a general role in intestinal zinc absorption.”<sup>23</sup> “Even at supplemental levels, citrate is apparently not a major regulator of zinc absorption, and normal intakes of citrate-containing foods do not influence zinc status significantly.”<sup>47</sup> Barrie et al also found “that picolinic acid promotes absorption of zinc in humans and further that it is superior to citrate or gluconate.”<sup>44</sup> Unlike supplementation with many other mineral chelates, use of exogenous zinc picolinate may actually provide the compound normally created by the body in the intestinal tract to facilitate absorption.

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