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Editorial
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Orotic Acid: Why it is Important to Understand Its Role in Metabolism.

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The molecule orotic acid was originally thought to be a vitamin that was essential to animal nutrition. Vitamin B_{13} was originally postulated to be present in distillers dried soluble from grains. It was later determined that vitamin B_{13} or orotic acid was synthesized by mammals during the synthesis of pyrimidines using the *de novo* pyrimidine biosynthetic pathway [1,2]. In humans and other organisms, orotic acid is synthesized by the enzyme dihydroorotate dehydrogenase which converts dihydroorotate to orotic acid [3]. It has been found that orotic acid improves the metabolism of folic acid and vitamin B_{12}. Orotic acid is found in milk produced by cows and other commercial dairy products derived from milk. The presence of orotate in mammals is important to the development of the central nervous system [1]. The importance of orotic acid in human metabolism can be witnessed in individuals afflicted with orotic aciduria. Orotic aciduria is detected in humans by virtue of affected individuals excreting excess orotic acid. This autosomal recessive disorder has been associated with developmental retardation.

Two forms of orotic aciduria have been distinguished in humans. Type I form of orotic aciduria is caused by the loss of uridine 5'-monophosphate synthase activity. The other form of orotic aciduria is associated with megaloblastic anemia [4-6]. Megaloblastic anemia results due to DNA synthesis inhibition in human red blood cells. Recently, it was noted that the administration of orotic acid in humans improved the condition of hearts with hypertrophy. It was concluded that the positive effect of administering orotic acid to humans with hypertrophic hearts was caused by the release of pyrimidine nucleosides into the blood stream blocking adenine nucleotide depletion in the myocardium [7]. It has also been observed that salts of orotic acid, including zinc or magnesium orotate, can be used in metal ion substitution therapy [5]. Negative effects have also been observed with respect to orotic acid since insulin resistance and hypertension or fatty livers can be induced in rats when orotic acid is included in their diet [8,9]. The hypertension observed in orotic acid-fed rats was thought to be the result of impaired endothelial nitric acid synthesis [8]. With respect to gene transcription, it has been speculated that orotic acid may influence the synthesis of genes involved in cell proliferation in eukaryotes [1]. In prokaryotes, the supplementation of orotic acid to *Pseudomonas fluorescens*, *Pseudomonas putida* and *Pseudomonas lundensis* cells was shown to increase the transcription of the pyrimidine biosynthetic pathway enzyme dihydroorotase, orotate phosphoribosyltransferase or orotidine 5'-monophosphate decarboxylase [10-12].

It is clear that orotic acid can affect gene transcription in both prokaryotes and eukaryotes. In summary, the importance of orotic acid, previously identified as vitamin B13, in metabolism has been known since its discovery in 1905 [1] but recent research findings have demonstrated that orotic acid likely has additional roles in metabolism. Only recently has a more intensive effort been made to learn the relationship between orotic acid levels and its cumulative effect upon metabolism. Further analysis of the role that this pyrimidine base occupies in metabolism needs to be elucidated to more fully understand its overall importance.

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