Degradation of Glyoxylate and Glycolate by Human Gastrointestinal Microbes

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Introduction

An estimated 5-10% of the human population will develop a kidney stone in their lifetime (1, 2). Most stones consist of calcium oxalate and are formed when urinary oxalate levels are increased. Urinary oxalate is derived from the diet (i.e., the consumption of oxalate-containing foods) and from endogenous synthesis (**Figure 1**) (1). Recent studies have shown that intestinal oxalate-degrading bacteria limit the absorption of dietary oxalate and thus reduce urinary oxalate excretion and the risk for kidney stone formation (3). Relative to endogenous synthesis, glycolate and glyoxylate are direct precursors of oxalate in the human body and are found in most fruits and vegetables (1, 4, 5). Increased consumption of these oxalogenic precursors increases endogenous oxalate synthesis, which in turn leads to increased urinary oxalate excretion (4, 5). Given the importance of these precursors in oxalate metabolism, it is interesting that little, if anything, is known about the factors which limit the absorption of dietary glyoxylate or glycolate from the gut in humans.

References

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- Allison, M. J., Daniel, S.L., and Cornick, N. A. 1995. Calcium Oxalate in Biological Systems 7:131-168.
- Harris, K.S., and Richardson, K.E. 1980. Glycolate in the Diet and Its Conversion to Urinary Oxalate in the Rat. Investigative Urology 18:106-109.
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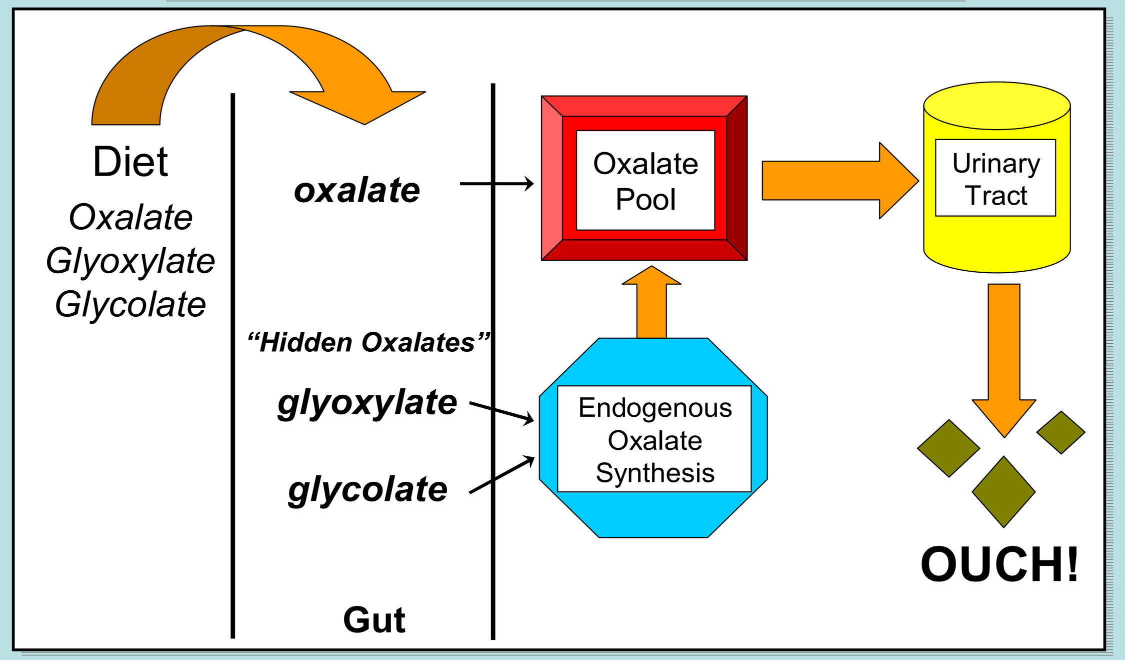
Figure 1. Metabolism of Oxalate and Oxalate Precursors in the Human Body



Objectives

The objectives of this study were to:

- Determine if glyoxylate-, glycolate-, and oxalate-degrading bacteria are present in the gastrointestinal tracts of humans
- Isolate and characterize the bacteria that are responsible for the turnover of these important two-carbon compounds in the mammalian body

Methods

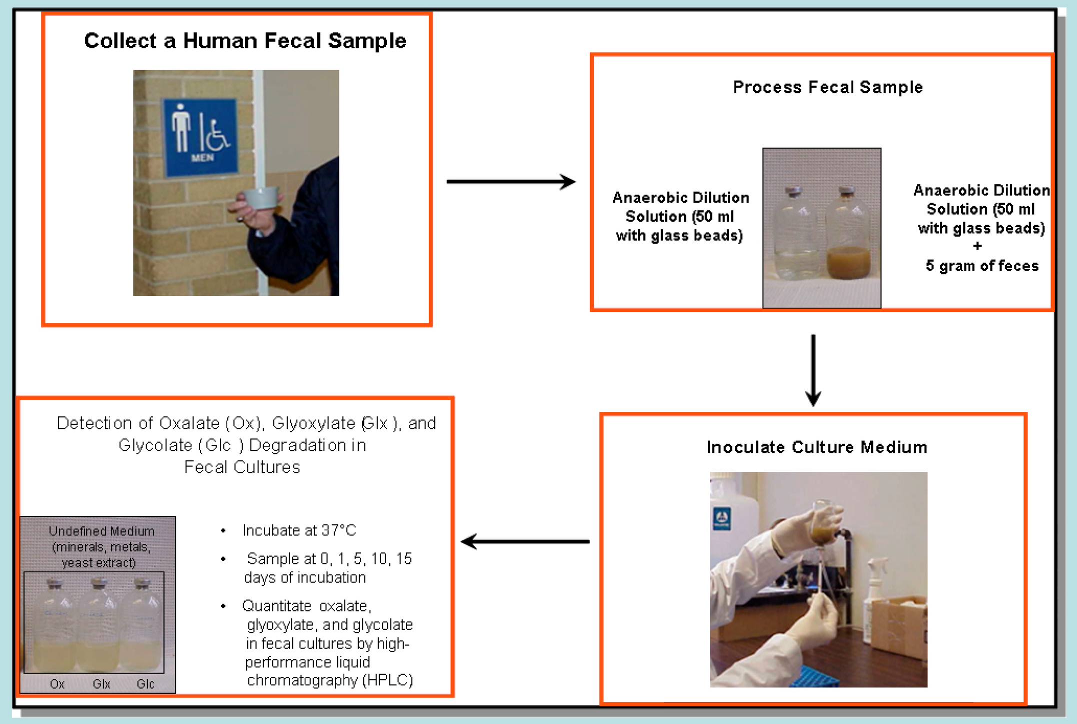
Fecal samples were collected from ten human subjects and processed immediately (**Table 1**).

Fecal samples were processed by adding five (5) grams of a fecal sample to a serum bottle containing 50 ml of anaerobic dilution solution. Bottles were sealed and shaken at room temperature for 15 minutes at 175 rpm. From each fecal slurry, 1-ml aliquots (90 mg) was added to an anaerobic enrichment medium (50 ml) containing 10 mM oxalate, glyoxylate, or glycolate. Fecal cultures were incubated at 37°C, and, during incubation, oxalate, glyoxylate, and glycolate utilization was monitored by high performance liquid chromatography; samples were considered positive if oxalate, glyoxylate or glycolate concentrations in fecal cultures were reduced to less than 1 mM during the 15-d incubation period (**Figure 2**).

Table 1. Human Subjects Examined in This Study

Subject	Age	Gender	Ethnicity	Stone former (SF)	Servings of Fruit per Day	Servings of Vegetables per Day
1	15-20	Male	Caucasian	No	4-5	2-3
2	41-50	Female	Caucasian	No	2-3	2-3
3	41-50	Female	Caucasian	No	0-1	0-1
4	21-30	Male	Caucasian	No	0-1	2-3
5	41-50	Male	Caucasian	No	0-1	0-1
6	21-30	Male	Caucasian	No	0-1	0-1
7	21-30	Male	Afr. Amer.	No	0-1	0-1
8	21-30	Female	Afr. Amer.	Yes	0-1	2-3
9	41-50	Male	Caucasian	Yes	0-1	3-4
10	41-50	Female	Caucasian	No	4-5	2-3

Figure 2. Collection and Processing of Human Fecal Samples



Results

- Of the 10 humans examined (**Table 2, Figure 3**):
  - 30% were positive for oxalate-degrading bacteria
  - 100% were positive for glyoxylate-degrading bacteria
  - None tested positive for glycolate-degrading bacteria
- Human fecal bacteria also transformed glyoxylate (**Figures 4 and 5**):

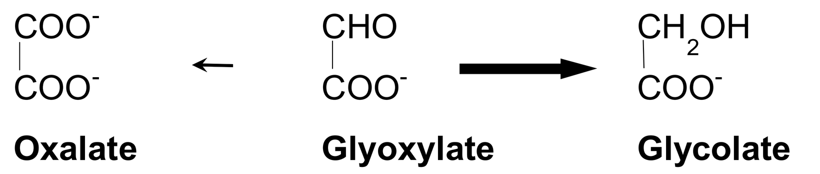


Table 2. Detection of Anaerobic Oxalate-, Glyoxylate-, and Glycolate-Degrading Bacteria in Human Feces

Subject	Age	Gender	Oxalate	Glyoxylate	Glycolate
1	15-20	Male	-	+ (15)	-
2	41-50	Female	-	+ (10)	-
3	41-50	Female	+ (5)	+ (10)	-
4	21-30	Male	-	+ (10)	-
5	41-50	Male	+ (1)	+ (15)	-
6	21-30	Male	-	+ (10)	-
7	21-30	Male	-	+ (5)	-
8	21-30	Female (SF)	-	+ (5)	-
9	41-50	Male (SF)	+ (10)	+ (5)	-
10	41-50	Female	-	+ (10)	-

Figure 3. Anaerobic Degradation of Oxalate, Glyoxylate, and Glycolate by Human Fecal Bacteria

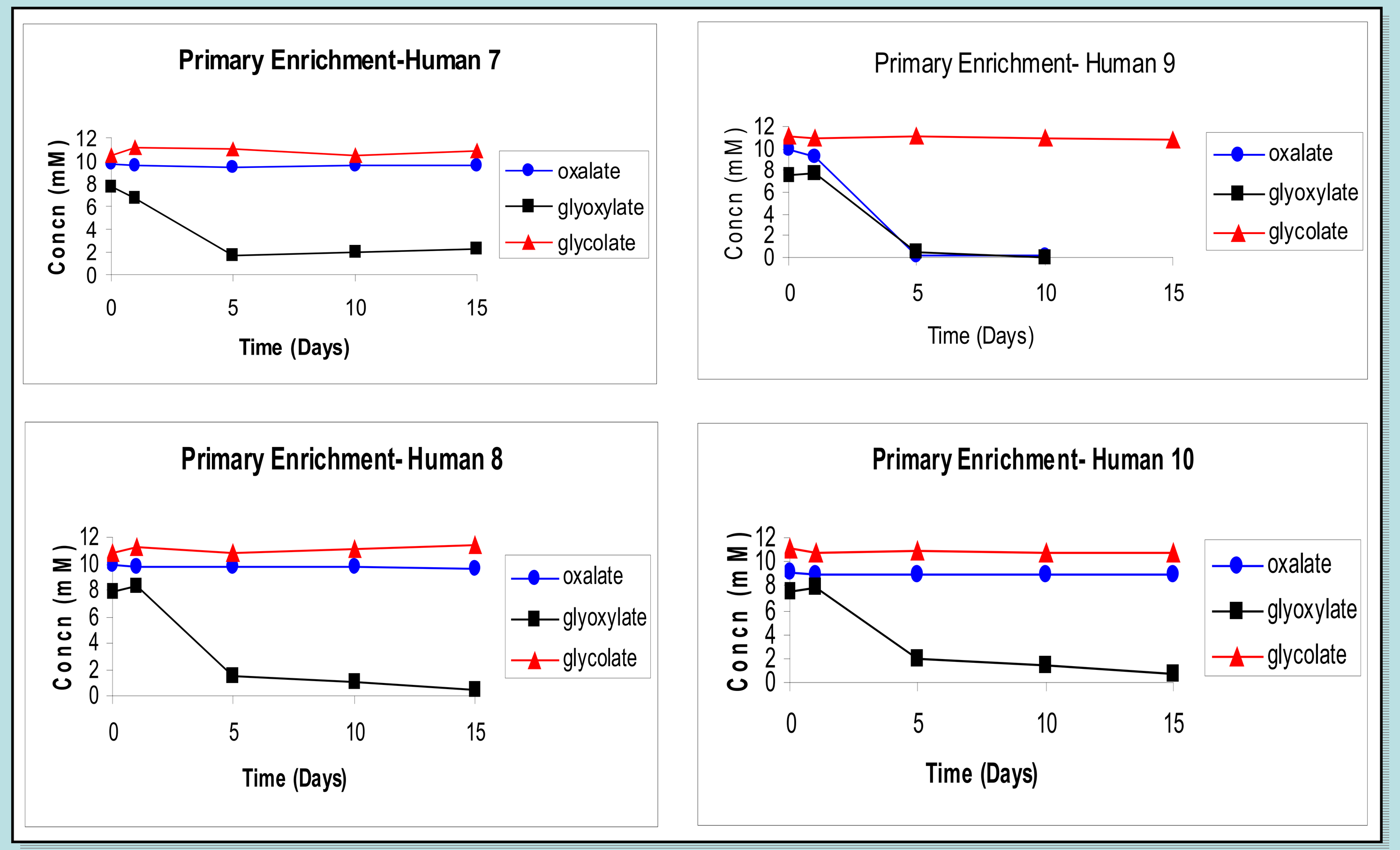


Figure 4. Product Profiles during Glyoxylate and Oxalate Degradation by Human Fecal Bacteria (Human 9)

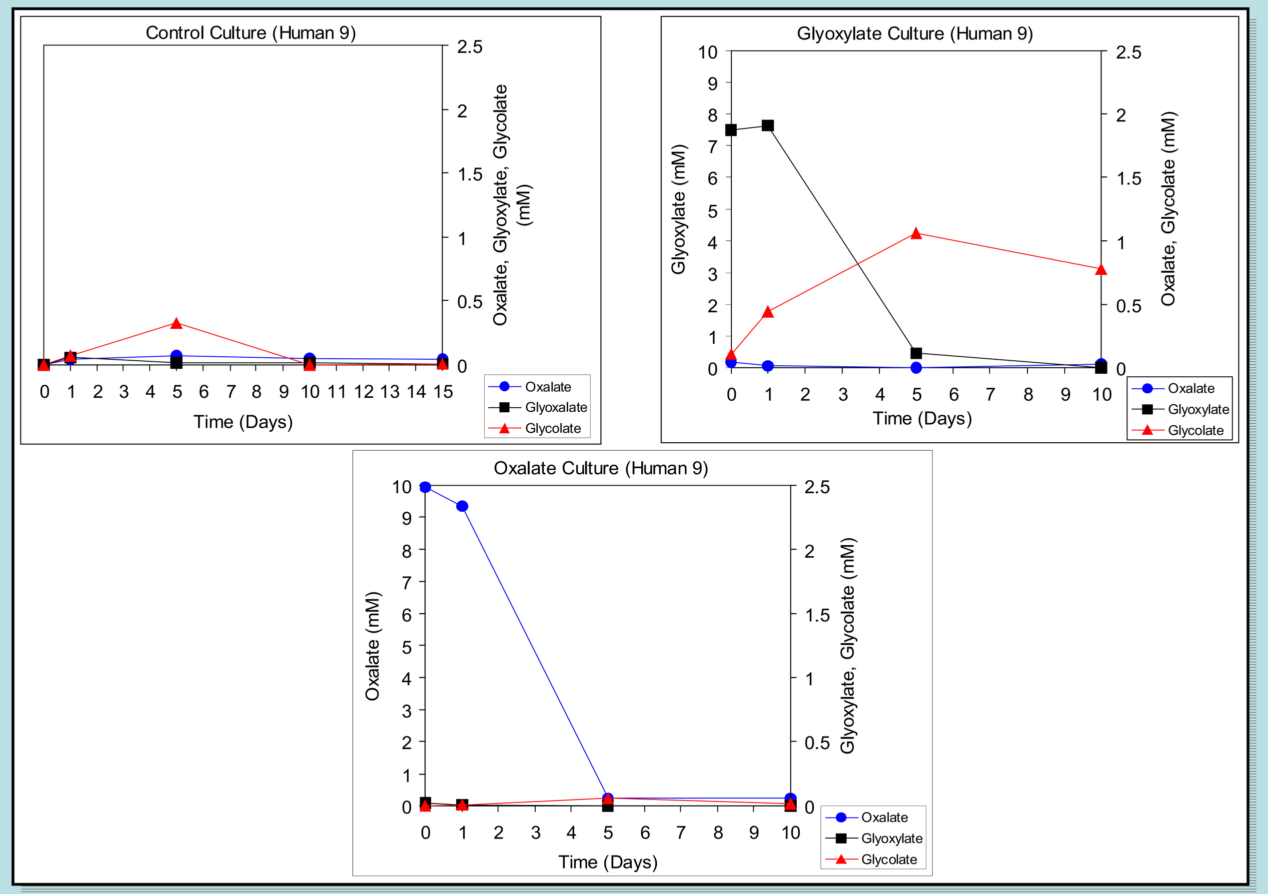
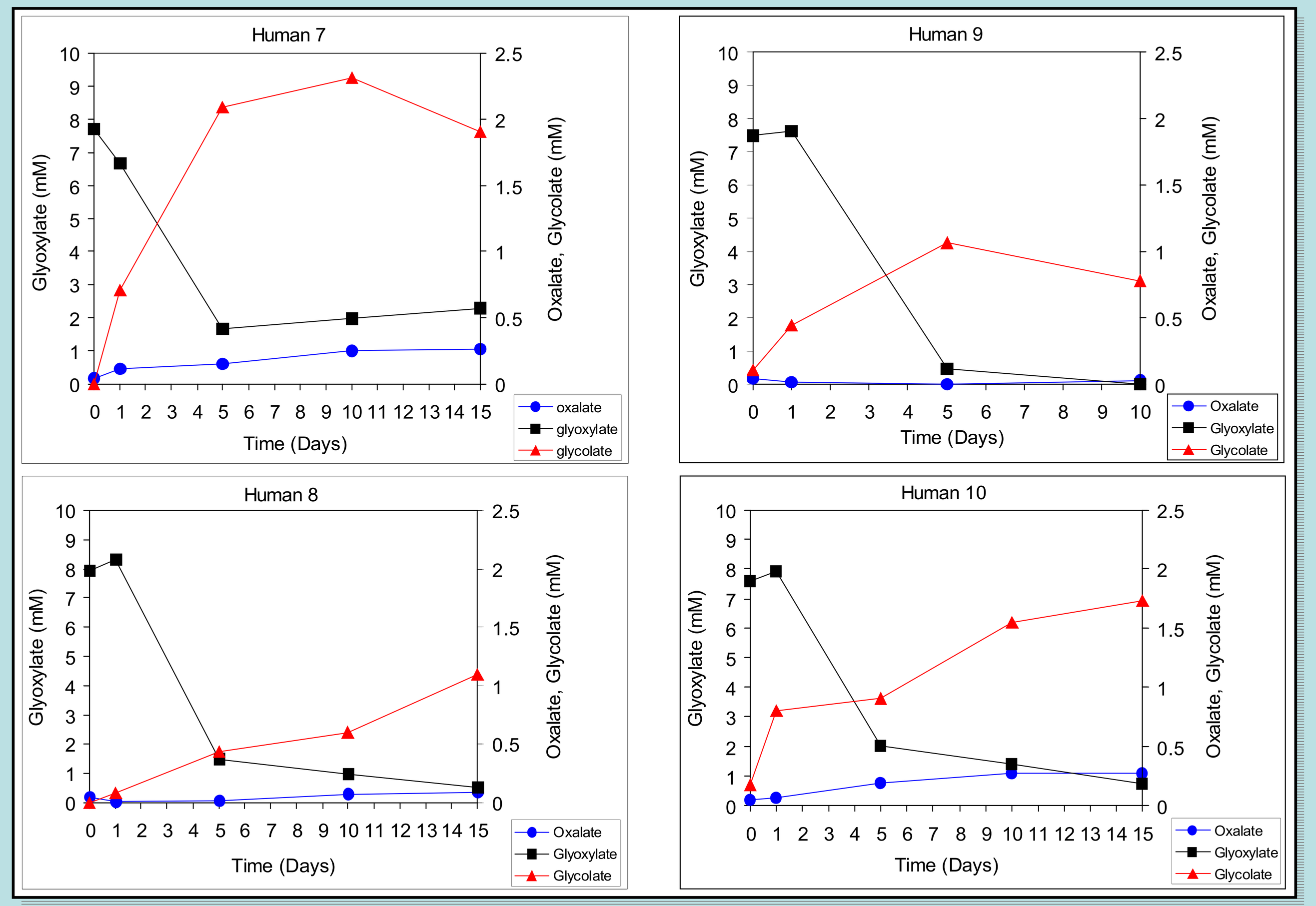


Figure 5. Oxalate and Glycolate Production During Glyoxylate Metabolism by Human Fecal Bacteria



Summary

Understanding the gut ecology of oxalate-, glyoxylate-, and glycolate-degrading bacteria will provide valuable information on the roles that these organisms play in human oxalate metabolism.

Potential risk factor for kidney stone formation?

Increased absorption of "hidden oxalates" due to the absence of glyoxylate- or glycolate-degrading bacteria in the gut