

Title: Prolidase Deficiency *GeneReview*- Information on laboratory methods used to detect imidodipeptiduria

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Recognition of imidodipeptide peaks (Table 1) requires experienced laboratory staff, as these peaks have been missed by different clinical laboratories in patients with prolidase deficiency [Wang et al 2006].

- An untreated (i.e., unhydrolyzed) urine sample analysis will exhibit several unknown peaks (which correspond to imidodipeptides). When properly treated *, the unknown peaks disappear and marked increase in the imidodipeptides proline, hydroxyproline, and glycine is evident. Glycylproline, the main imidodipeptide, comprises 15-35% of excreted imidodipeptides.

* Note: Mixing urine sample with an equal volume of 6N hydrochloric acid and hydrolyzing by heating at 100°C for 20-24 hours.

- The relative abundance of hydroxyproline-containing imidodipeptides varies from undetectable [Wysocki et al 1988] to up to one-quarter of all imidodipeptides [Powell et al 1974].
- The relative abundance of the N-terminal amino acids is as follows: Gly > Asx ≈ Glx > Leu > Ile ≈ Ala ≈ Thr ≈ Ser > Val ≈ Phe ≈ Tyr [Hechtman 2014].

Table 1. Position of Imidodipeptide Peaks with Ion-Exchange Chromatography

Imidodipeptide	Peak
Gly-Pro ¹	Coelutes with leucine ^{2,3} or elutes between leucine and tyrosine ^{4,5,9}
Glx-Pro ¹	Elutes with isoleucine ⁶ or between isoleucine and leucine ⁹
Asx-Pro	Elutes between alanine and valine ^{2,5} or between valine and isoleucine ⁹
Leu-Pro	Elutes between phenylalanine and ammonia ^{6,9} or coelutes with ammonia ²
Ile-Pro	Elutes soon before ⁹ or soon after ammonia ² (thus soon after Leu-Pro ⁷)
Ala-Pro ¹	Elutes between leucine and tyrosine ^{2,4,6} (soon after Gly-Pro ^{2,7}) or coelutes with tyrosine ⁹
Thr-Pro ¹ and Ser-Pro ¹	Elute between isoleucine and leucine ² or between leucine and tyrosine ⁹
Val-Pro	Elutes after phenylalanine ⁸ , between phenylalanine and ammonia ^{2,9}
Phe-Pro	Elutes between lysine and histidine ²
Tyr-Pro	Elutes soon after ammonia ⁹

1. In untreated urine of patients with prolidase deficiency, the presence of these imidodipeptides can obscure the peaks of isoleucine, leucine, and tyrosine [Wysocki et al 1988].

2. Powell et al [1974]

3. Duran [2008]

4. Heathcote et al [1975]

5. Lemieux et al [1984]

6. Lou & Hamilton [1979]

7 Nusgens & Lapiere [1973]

8 Goodman et al [1968]

9 Buist et al [1972]

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