How to detect the gluten intake?

The only direct method to follow up the **Gluten Free Diet**

BIOMEDAL

1 What are our products about?

The iVYDAL In Vitro Diagnostics® product line are immunoassays based on G12 an A1 monoclonal antibodies, which react to peptides 33-mer-like of the α-gliadin, the most immunogenic fragment of gluten. These products allow very specific and sensible detection and / or quantification of the Gluten Immunogenic Peptides (GIP) in stool and urine samples as a direct marker of the adherence to a gluten-free diet.

2 What are the GIP?

Gluten Immunogenic Peptides are fragments of gluten resistant to gastrointestinal digestion. These peptides trigger a series of immunogenic reactions in celiac patients. The resistance of GIP to gastrointestinal digestion achieves that a significant part of it is excreted by any person that ingests gluten. Due to this fact, the presence of GIP in stool and urine samples is a reliable and direct marker for the accurate short and long-term control of the gluten-free diet.

3 GIP justification

The clinical utility of the detection of GIP in urine or stool samples has been proved by several clinical trials (Comino et al. 2016 and Moreno et al. 2017). In these trials, the results obtained reveal the limitations of the current methods for the follow-up of celiac patients as GIP were present in 30-50% of patients, showing that dietary transgressions are very frequent and cannot be correctly detected by serology, symptoms or dietary questionnaires (Figure 1). Additionally, analysis of duodenal biopsies revealed that most celiac patients with no villous atrophy had no detectable GIP levels (89%), while all patients with quantifiable GIP levels showed incomplete intestinal mucosa recovery. This correlation with the state of the intestinal mucosa was not observed with serology (Figure 2).

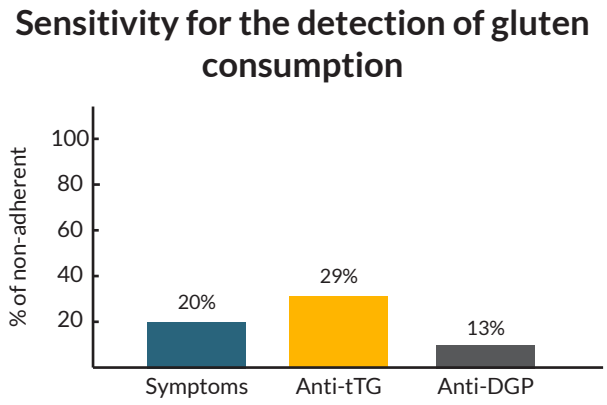

Figure 1. Sensitivity for the detection of gluten consumption in 56 celiac patients (positive GIP results) according to symptoms and celiac disease serologies: anti-DGP (anti-deamidated gliadin peptite antibody) and anti-tTG (anti-tissue transglutaminase antibody). GIP: gluten immunogenic peptides. Modified from Comino et al 2016.

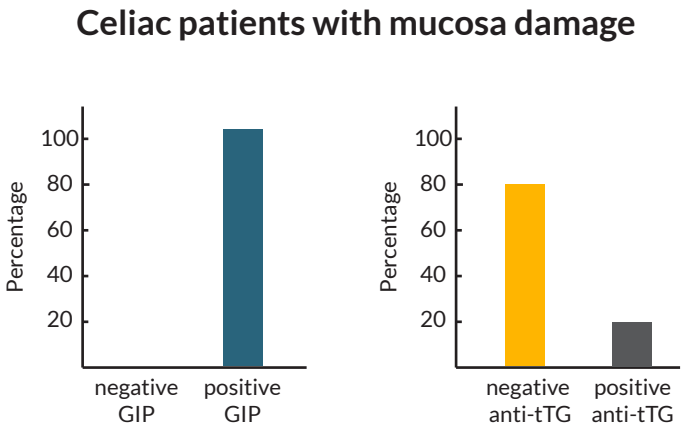

Figure 2. Correlation between the presence of damage in the small intestine and the GIP and anti-tTG results. Small intestine damage determined by the Marsh scale of the severity of mucosal lesion (Marsh I-III). GIP: gluten immunogenic peptides; anti-tTG: anti-tissue transglutaminase antibody. Modified from Moreno et al. 2017.

Key publications

Comino et al., Am J Gastroenterol (2016). Fecal Gluten Peptides Reveal Limitations of Serological Tests and Food Questionnaires for Monitoring Gluten-Free Diet in Celiac Disease Patients. The American journal of gastroenterology, 111: 1456-1465

Moreno et al., (2017). Detection of gluten immunogenic peptides in the urine of patients with coeliac disease reveals transgressions in the gluten-free diet and incomplete mucosal healing. Gut, 66(2): 250-257

Ludvigsson JF et al. (2018). Outcome measures in coeliac disease trials: the Tampere recommendations. Gut, 0: 1-15

4 Intended use of GIP

- For the general follow-up of celiac and non-celiac gluten sensitivity.
- When symptoms have not been completely eliminated after following a gluten free diet.
- During the first months after diagnosis to verify good habits.
- To evaluate gluten intake during Celiac Disease and Refractory Celiac Disease diagnosis.
- To prove Gluten Free Diet adherence or gluten challenge intake in clinical trials.

5 iVYDAL product range

iVYLISA GIP Stool

iVYLISA GIP Stool is a quantitative Sandwich ELISA kit designed for the detection and quantification of GIP in stool samples. High analytic sensitivity and specificity allow high quality quantification of GIP that are present in the sample, furthermore this method is easy scalable and automatable.

- CE marked ELISA Sandwich test
- For the analysis of stool samples
- High sensitivity (98.5 %) and specificity (100%)
- For professional use, have to be done in laboratory
- Storage at 4-8 °C
- 96 wells (40 samples in duplicate or 80 in simple analysis)

iVYCHECK GIP

The iVYCHECK GIP products are lateral flow immunochromatographic assays (LFIA) that detect the absence or presence of GIP in urine or stool samples, simplifying the evaluation of the patient in a few minutes.

iVYCHECK general characteristics:

- CE marked lateral flow test
- For the analysis of stool (iVYCHECK GIP Stool) or urine (iVYCHECK GIP Urine) samples.
- 10 or 25 tests
- Room temperature storage

	iVYLISA GIP Stool	iVYCHECK GIP Stool	iVYCHECK GIP Urine
Technics	ELISA	LFIA	LFIA
Antibodies	G12/G12	G12/A1	G12/A1
Sample	Stool	Stool	Urine
Sensitivity	78 ng/g	150 ng/g	2.2 ng/mL (LOD)
Maximum detection peak of GIP[1]	0-2 days	0-2 days	6-9 hours
Time range of detectable GIP[2]	1-7 days	1-7 days	1-24 hours
Minimum detectable levels of gluten intake	>50 mg/day	>50 mg/day	>50-500 mg/day
Diagnostics sensitivity	98,5%	97%	91%
Diagnostics specificity	100%	100%	99%
References	KT-5739	KT-6410 (10 test) KT-5737 (25 test)	KT-6412 (10 test) KT-6411 (25 test)

[1] The time depends on individual factors such as the composition of the diet, the gluten matrix, the gastrointestinal transit time, the intestinal permeability, and the intestinal microbiota.
[2] The ingestion of 50 mg of gluten per day can be detected in the urine with a sensitivity of 15%, and the ingestion of 500 mg of gluten per day can be detected with a 91% sensitivity.

Pros and cons of the methods to evaluate adherence to the **Gluten Free Diet**

Dietary and symptoms questionnaires	Serology	Biopsy	GIP
✗ Subjective, often inaccurate information based on patients' report.	✗ Low correlation with presence of symptoms and the state of the intestinal mucosa	✗ Invasive, costly and uncomfortable method	✓ Non-invasive. It only requires stool or urine samples
✗ The majority of transgressions are asymptomatic. The questionnaires can not detect them	✗ Not sensitive to contamination or modest transgressions, so it is not suitable to evaluate the adherence to a gluten free diet	✗ High variability of interpretation among pathologists	✓ High specificity and sensitivity for the detection of gluten intake
✗ Voluntary and involuntary omissions	✗ Requires blood extraction	✗ Detects mucosal damage which has already occurred, without the possibility of preventing it	✓ Detects gluten intake instead of its consequences, enabling immediate dietary habit modification to prevent intestinal damage
✓ Does not require specific technology	✓ Specific for the diagnosis of celiac disease	✓ Direct assessment of mucosal recovery or damage	✗ The dynamics of the GIP excretion varies among subjects

iVYDAL In Vitro Diagnostics

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