



Labelled activity vs. *in vitro* β -galactosidase availability in commercial lactase supplements: impact of dosage form and formulation design

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ABSTRACT

Lactose intolerance is a highly prevalent condition commonly managed with oral lactase supplementation, although clinical efficacy remains variable. This study investigated whether labelled enzymatic activity (FCC ALU) reliably reflects β -galactosidase availability under gastrointestinal conditions, with particular emphasis on formulation-related factors.

A combined approach was adopted, including a systematic literature review (1979–2025), a market analysis of lactase supplements available in Italy, and *in vitro* characterization of eight selected products. Disintegration, enzyme release, and β -galactosidase activity were evaluated under simulated fasted and fed conditions.

Results showed that lactase performance was predominantly influenced by pharmaceutical form and formulation design rather than by labelled enzymatic activity alone. Orodispersible and chewable formulations provided rapid enzyme availability, whereas tablets and capsules showed delayed or incomplete release, particularly under fasted conditions. Normalisation of release data to FCC ALU revealed that lower-dose, fast-release formulations can achieve comparable effective enzyme delivery comparable to products with higher nominal activity but slower release kinetics. Differences among formulations were markedly reduced under fed conditions.

Overall, these findings demonstrated that formulation characteristics and release behavior are key determinants of lactase supplement performance, highlighting the limitations of relying solely on labelled FCC ALU values to predict effective enzyme availability.

1. Introduction

Lactose intolerance (LI) is a highly prevalent digestive disorder caused by a reduction in lactase-phlorizin hydrolase activity on the apical surface of enterocytes in the small intestine.

This enzymatic decline, which can be genetically programmed or secondary to gastrointestinal conditions, impairs the proper hydrolysis of lactose into glucose and galactose, leading to typical gastrointestinal symptoms, such as bloating, abdominal pain, flatulence, diarrhea, and constipation [1].

Following the establishment of a formal diagnosis, which is typically achieved through hydrogen breath testing or genetic testing, the clinical management of the patient shifts towards the implementation of

strategies that mitigate symptoms while ensuring nutritional adequacy and improving quality of life [2–4].

In the post-diagnosis phase, patients are commonly advised to adjust their diet by reducing or eliminating their lactose consumption. Furthermore, the utilization of exogenous lactase supplements has become a fundamental component of symptom management. These oral enzyme formulations facilitate the breakdown of lactose in the gastrointestinal tract, thereby enabling more flexible dairy consumption and enhancing patients' quality of life.

It is imperative to differentiate between lactase enzyme supplements and enzyme mixtures. In addition to lactase, these latter samples also contain other enzymes (e.g. amylase, maltase, sucrase, etc.) that aid and facilitate the overall digestion of food, specifically carbohydrates.

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