

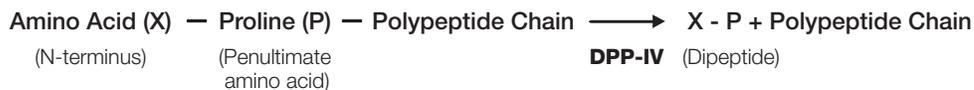
DPP-IV Enzymes: Clearing Up the Confusion about Activity Units

Klaire Labs™ was the first nutritional supplement company to introduce a vegetarian enzyme formulation with dipeptidyl peptidase IV (DPP-IV) activity to assist in the complete breakdown of allergenic proteins such as gluten (wheat, rye, barley) and casein (milk and dairy products). Since then a number of other companies have introduced their own versions of enzyme products with DPP-IV activity. Unfortunately, some of these companies are now creating confusion in the minds of consumers and healthcare professionals by attempting to quantify the amount of DPP-IV activity in their products using potency units that are not applicable to DPP-IV. Some have even gone so far as to invent potency units not recognized within the scientific community or the nutritional products industry. As a leader in the field of enzyme formulation, Klaire Labs™ would like to clear up the confusion surrounding DPP-IV and how to assess its activity.

DPP-IV Background

Dipeptidyl peptidase IV (DPP-IV) belongs to the exopeptidase class of proteolytic enzymes. Exopeptidases cleave the N- or C-terminal amino acid residues from peptides and proteins. Exopeptidases that cleave N-terminal residues are referred to as aminopeptidases, while those that cleave C-terminal residues are called carboxypeptidases. DPP-IV has the very uncommon capacity to cleave the peptide bond following a penultimate proline thereby releasing proline-containing dipeptides from the N-terminus of polypeptide chains. DPP-IV is technically referred to as a prolyl-amino-dipeptidase. It is one of the few enzymes able to facilitate the digestion of proline-rich proteins and polypeptides. The specific activity of DPP-IV is depicted below.

DPP-IV Activity



DPP-IV is normally expressed by the cells of the intestinal brush border and is essential for the complete breakdown of proline-containing dietary proteins such as gluten and casein. These allergenic proteins are highly resistant to hydrolysis by other proteolytic enzymes and have been implicated in a number of serious adverse food reactions including the enteropathic manifestations of celiac disease. All of the toxic and immunogenic peptide sequences of gliadin contain proline. Prolyl peptides are also believed to act as exorphins, or opioid receptor agonists, that may mediate or exacerbate neurobehavioral symptoms in people with autism spectrum disorders (ASD).

Interestingly, studies show intestinal DPP-IV activity is abnormally low in children and adults with celiac disease. Moreover, persons with ASD actually produce antibodies against DPP-IV. Supplementation with DPP-IV may thus be of value for reducing levels of pathogenic prolyl peptides in the intestinal tract.

Studies Supporting the Use of DPP-IV

In vitro, DPP-IV efficiently degrades the immunodominant, proline-containing epitope of gliadin, the primary allergenic protein in gluten. DPP-IV has also been shown to markedly enhance the gluten- and casein-degrading capacity of other proteolytic enzymes. In rats, functional expression of DPP-IV in intestinal and kidney cells is a requirement for proper digestion of gliadin and for renal filtration of the dairy exorphin beta-casomorphin. Research on the use of supplemental DPP-IV in humans is limited, but one clinical trial examined the effects of a multi-enzyme preparation with DPP-IV activity in a group of 22 children and young adults with ASD. In this open-label trial, 12 weeks of supplementation with the enzyme blend led to significant improvements in most of the clinical parameters measured including attention, comprehension, digestion, eye contact, hyperactivity, mood, perseverance, sleep, socialization, and speech. A growing body of evidence thus suggests exogenous DPP-IV can be of substantial benefit for managing the digestive and neurobehavioral symptoms associated with reactivity to gluten, casein, and other allergenic and neuroactive dietary proteins.

Expressing DPP-IV Activity

Currently, there are no scientifically accepted potency units that describe DPP-IV activity. Assays have been developed that can measure the type of prolyl peptide hydrolysis achieved by DPP-IV, but these tests are not yet listed in any official compendium of enzyme analyses such as the Food Chemicals Codex (FCC). Some manufacturers of enzyme supplements have been using a proteolytic enzyme unit called HUT (hemoglobin unit on the tyrosine basis) to express DPP-IV activity in their products. This is a misapplication of enzyme potency nomenclature as HUT units reflect the generalized capacity of a protease to

degrade hemoglobin. HUT units do not convey any meaningful information about the specific hydrolysis of prolyl peptides or DPP-IV activity. In fact, it is possible to have a protease/peptidase product with exceptionally high HUT units and no DPP-IV activity whatsoever. Other manufacturers have been using units such as “DPPU”, “CFAU”, “CTGU”, and “LAPU” to describe DPP-IV activity in their enzyme formulas. Unfortunately, these units are not listed in the FCC or any other official monograph and thus provide no objective means by which to quantify DPP-IV activity in a particular product or compare DPP-IV activity between different products.

DPP-IV Formulas from Klaire Labs™

Klaire Labs™ has a long history of developing professional-quality enzyme products and offers a number of formulas with DPP-IV activity including:

- [SerenAid®](#)
- [InterFase®](#)
- [InterFase Plus®](#)
- [Vital-Zymes™ Complete](#)
- [Vital-Zymes™ Chewable](#)

Our SerenAid® was the first vegetarian enzyme formula to combine the specific, patented blend of proteolytic and peptidolytic enzymes capable of cleaving the prolyl peptides found in gluten and casein. We also hold 4 separate patents on DPP-IV-active enzyme formulations designed to break down exorphin dietary proteins that can trigger neurobehavioral problems in children. At Klaire, we formulate to high DPP-IV activity levels based on independent laboratory analyses of specific DPP-IV activity that guarantee the potency of our products. However, high DPP-IV activity is only a part of the complete breakdown of proline-rich proteins and peptides. Of equal importance is an effective blend of proteases and peptidases with exo- and endopeptidase activities. This allows enzymes with DPP-IV activity to do their job by hydrolyzing proline-rich proteins into peptide fragments with proline in the second position from the N-terminus. Klaire Labs™ enzyme formulations with DPP-IV activity contain enzymes with a broad spectrum of exo- and endopeptidase activities for which HUT units are an appropriate measure of proteolytic ability. We conform to the internationally recognized scientific standards set forth in the FCC and never use inappropriate or unrecognized potency units on our products. Klaire Labs™ experience for almost 15 years in producing enzyme formulations with DPP-IV activity have made SerenAid® and Vital-Zymes™ Complete the products of choice for doctors and their patients looking to most effectively support gluten and casein digestion.

References and further information available on request.

Copyright ©2010 ProThera, Inc. All rights reserved. No part of this publication may be reproduced, stored, or transmitted in any form by any means, including electronic, mechanical, photocopying, or otherwise, without prior written permission of the copyright owner.

The information contained in this publication is intended for educational purposes only. It is not provided in order to diagnose, prevent, or treat any disease, illness, or injured condition of the body, and the copyright owner accepts no responsibility for such use. Non-medical professionals should consult with their healthcare provider regarding their health condition. It is the responsibility of the healthcare provider to make his or her own determination of the usefulness and applicability of any information contained herein.