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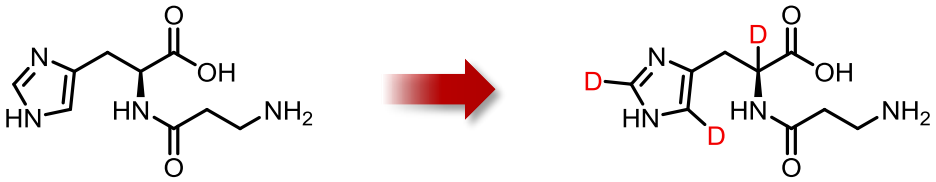
SYNTHESIS AND APPLICATION OF ISOTOPE-LABELED CARNOSINE IN LCMS/MS

Maspero, M.;[a] Gilardoni, E.;[a] Regazzoni, L.;[a] Aldini, G.;[a] Carini, M.;[a] De Amici, M.;[a] Dallanoce, C. [a]

[a]*Department of Pharmaceutical Sciences, University of Milan, via L. Mangiagalli 25, 20133 Milano, Italy*
E-mail of the presenting author: marco.maspero@unimi.it

Carnosine is an endogenous dipeptide, composed of β-alanine and L-histidine, and is highly concentrated in skeletal muscle and other excitable tissues. Its physiological roles, based on its biochemical properties, include pH-buffering, metal-ion chelation and antioxidant capacity as well as the ability to protect against the formation of advanced glycation and lipoxidation end-products.[1] For these reasons, besides its nutritional ergogenic application in the sport community,[2] carnosine supplementation offers a therapeutic potential for the treatment of numerous diseases in which ischemic or oxidative stress is involved.[1] Quantitation of carnosine in biological matrices appears to be crucial for these applications, and LC-MS procedures with isotope-labeled internal standards are the state-of-the-art approach for this analytical need.[3] The use of these standards allows to account for variations during the complex sample preparation process, different matrix effects between patient samples, and variations in instrument performance.



Carnosine **Carnosine-d$_3$**

Figure 1

In this work, we present a fast and highly efficient synthetic route to obtain a deuterated carnosine analogue (Figure 1) starting from the trideuterated L-histidine (α-d$_1$, imidazole-2,5-d$_2$). Moreover, the use of Carnosine-d$_3$ in the validation of a multiple reaction monitoring (MRM) LC-MS/MS method for the analytical quantitation of carnosine in a biological matrix will be reported.

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