

Abstract

# Natural Brewing Peptides with Enhanced Inhibitory Effects on Angiotensin I-Converting Enzyme <sup>†</sup>

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**Abstract:** Angiotensin-converting enzyme (ACE) inhibitors are anti-hypertensive drugs associated with several side effects. Natural compounds, namely bioactive peptides from brewing by-products—brewer’s spent grain (BSG) and yeast (BSY)—are promising alternatives, as they can inhibit ACE in vitro and are less likely to cause severe side effects, while maintaining therapeutic efficacy. However, the impact of oral administration on peptides’ bioavailability has not been assessed so far. Thus, the aim of this study was to understand in vitro the impact of the oral route on the effectiveness of BSG/BSY peptides as ACE inhibitors. Extracted BSG/BSY proteins were hydrolysed and sequentially subjected to simulated gastrointestinal digestion (INFOGEST), intestinal absorption and liver metabolism (co-culture of Caco-2 and HepG2 cells). MTT assay was used to assess BSG/BSY peptides’ safeness. The ACE-inhibitory potential of initial and final products (BSY, BSG and a mixture 50:50—MIX) at an identical concentration (0.857mg/mL) was measured (fluorometric assay) and compared with Captopril (1 µM, a clinically used ACE-inhibitory drug). Simulation of oral administration increased brewing peptides’ ACE-inhibitory capacity. When comparing the final peptides with captopril, BSY demonstrated identical potency, while BSG showed 22% greater efficacy; the new tested product MIX presented 30% higher inhibition. In conclusion, the current study shows that BSG, BSY and MIX natural peptides derived from the brewing industry enhance their bioactive properties as ACE-inhibitors after oral administration, validating the usefulness of these peptides to reduce the risk of, ameliorate or treat primary hypertension.

**Keywords:** hypertension; bioactive peptides; brewer’s spent grain; brewer’s spent yeast; ACE; ACE inhibitor; anti-hypertensive drug



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