



## ORIGINAL ARTICLE

# Antihypertensive effect of Valyl-Tyrosine, a short chain peptide derived from sardine muscle hydrolyzate, on mild hypertensive subjects

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The present study was conducted to determine whether Valyl-Tyrosine (VY) has an antihypertensive effect on high-normal blood pressure and mild essential hypertension, as well as spontaneous hypertensive rats (SHR). A randomised double-blind placebo-controlled study was carried out on 29 volunteers. A 100-ml drink containing 3 mg of VY and a 100-ml placebo drink were prepared. The subjects were grouped as VY(16M/1F, 45.5 ± 3.2 years, 146.4 ± 2.3/90.5 ± 1.8 mm Hg) and the placebo (P) (11 M/1F, 48.8 ± 3.0 years, 145.5 ± 2.4/92.3 ± 1.8 mm Hg). At 3 weeks of the control (C) period, a VY- or P-drink was administered twice a day for 4 weeks in the experimental (E) period and during the 4-week recovery period, neither drink was given to either group. Blood pressure (BP) was measured every week in the morning in the sitting position. Blood specimens were

taken on the last day of the C and E periods. In the VY-group, reduction in systolic (S) and diastolic (D) BP was 9.7 and 5.3 mm Hg ( $P < 0.001$ ) at 1 week, and 9.3 and 5.2 mm Hg ( $P < 0.001$ ) at 4 weeks, following the start of the E period, respectively. Neither SBP nor DBP changed in the P-group. BP in the VY-group increased gradually by the end of the recovery period. Plasma angiotensin (Ang) I and VY concentrations significantly increased while Ang II and aldosterone significantly decreased after VY administration in the VY-group. VY appeared to have a significant antihypertensive effect on mild hypertensive subjects via Ang I-converting enzyme inhibition, as well as SHR, but no adverse effects could be detected at all.

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**Keywords:** randomised double-blind placebo-controlled study; Valyl-Tyrosine; sardine muscle; antihypertensive effect; mild hypertensive subjects; angiotensin I-converting enzyme inhibitor

## Introduction

The angiotensin I-converting enzyme (ACE) has a significant role in increasing blood pressure (BP) and maintaining hypertension. In the renin-angiotensin system, ACE acts on angiotensin (Ang) I to hydrolyze His-Leu from its C-terminal to produce Ang II, ACE activates bradykinin in the kinin-kallikrein system. Various ACE inhibitors, such as captopril, enalapril and so on, have been synthesized and presently are widely used as effective antihypertensive drugs.<sup>1</sup> But these ACE inhibitors have been found to lead to a high number of incidences of dry coughing as one adverse effect due to the activation of bradykinin.<sup>2</sup>

Several ACE inhibitory peptides have been isolated and identified from food materials.<sup>3–5</sup> The anti-

hypertensive effect of food materials on humans via ACE inhibition appears in a few papers.<sup>6–8</sup> Valyl-Tyrosine (VY) derived from sardine muscle hydrolyzate by *Bacillus licheniformis* alkaline protease, was confirmed in our previous study to have a remarkable antihypertensive effect in SHR via ACE inhibition.<sup>9</sup> This study was conducted to determine whether VY has an antihypertensive effect on human subjects with high-normal BP and mild hypertension, as does SHR.

## Subjects and methods

### Subjects

Thirty-four clinically healthy and active volunteers participated in this study. They initially underwent a medical examination, the results of which indicated no significant disorders such as cerebrovascular, renal, endocrine, or metabolic disease, though mild hypertension, hyperlipidaemia, hyperuricaemia or mild glucose intolerance were noted. Casual BP showed high-normal blood pressure<sup>10</sup> or stage I or II hypertension during the control

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