RAPESEED DERIVED PEPTIDES – POTENTIAL ANTIHYPERTENSIVE AGENTS: EFFECTS ON BLOOD PRESSURE AND METABOLIC PARAMETERS IN CONSCIOUS SPONTANEOUSLY HYPERTENSIVE RATS (SHR)

Iwona Baranowska, Olga Gawrys, Bozena Badzynska, Elzbieta Kompanowska-Jezierska

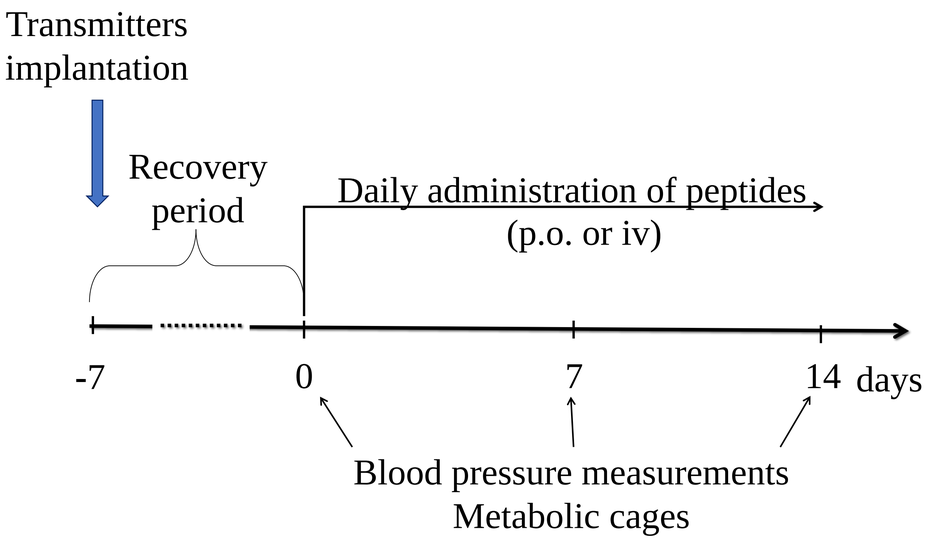
Department of Renal and Body Fluid Physiology Mossakowski Medical Research Centre, Polish Academy of Sciences, Warsaw, Poland

Introduction and objectives

Chymase is an essential enzyme of the local angiotensin II (Ang II) production, which is an independent of the angiotensin converting enzyme (ACE) process. Chymase expression is increased in pathological conditions such as hypertension. It is known to form Ang II in cardiovascular and renal tissues independently of ACE and it is responsible for remodeling of the vasculature. To block the local pathways of Ang II formation we employed novel, synthetic analogs of peptides obtained from rapeseed: VWIS (Valine-Tryptophan-Serine-Tyrosine) and RIY (Arginine-Tyrosine-Isoleucine). The antihypertensive activity of these peptides was previously confirmed *in vitro* and *in vivo* (single oral administration to spontaneously hypertensive rats, SHR). In the present study we wanted to evaluate the impact of chronic administration (intravenous and intragastric) of VWIS and RIY on blood pressure and metabolic parameters of SHR in established phase of hypertension.

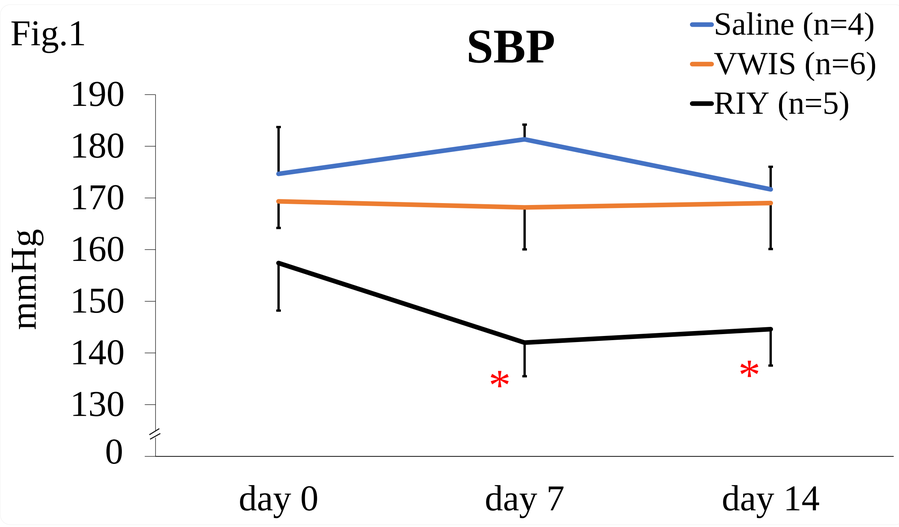
Methods

Conscious, male SHR (age: 16 weeks) were treated daily for two weeks with peptides VWIS (12.5 mg/kg) or RIY (7.5 mg/kg) both dissolved in 1 ml of 0.9% saline; control group received saline. Substances were administered either intravenously (iv; through femoral vein cannulated prior to the experiment) or intragastrically (p.o.) in consecutive groups. Systolic blood pressure (SBP) was measured by telemetry technique. Once a week observation in metabolic cages (food and water intake, feces and urine excretion) were performed; blood and urine samples were collected.



Results

Fig.1



Systolic blood pressure (SBP) changes after iv administration of peptides VWIS and RIY

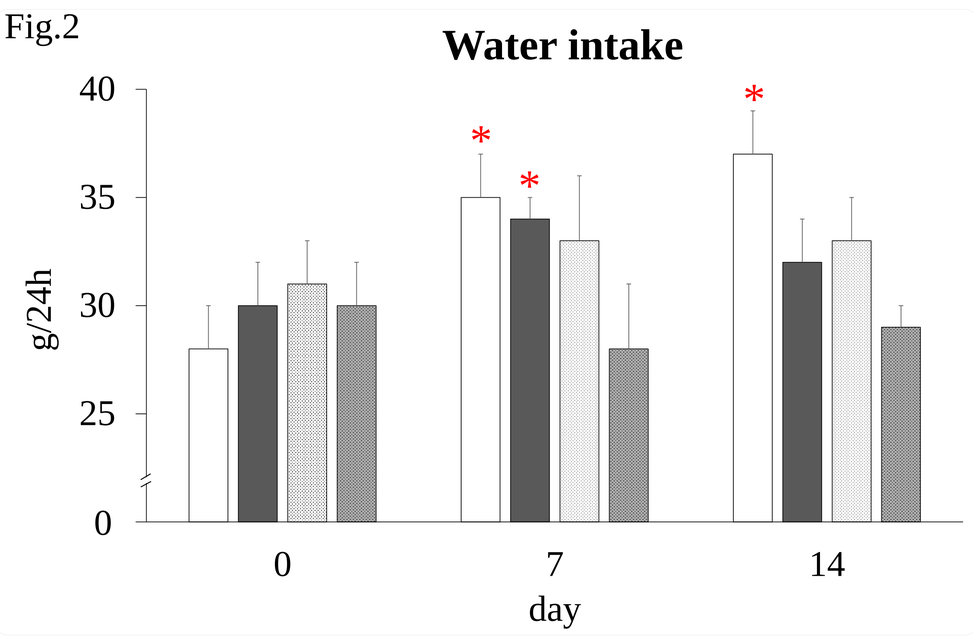
Only peptide RIY caused a significant decrease in SBP after one week of treatment and this antihypertensive effect lasted till the end of the experiment (**p<0.05 vs.* day 0)

Water intake changes after iv and p.o. administration of peptides VWIS and RIY

Increase in water intake was observed only after intravenous administration: for RIY significant after 7 and 14 days, for VWIS only after 7 days (**p<0.05 vs.* day 0)

Water intake and diuresis did not differ within the control group, which received saline, hence the values for this group on Fig. 2 and 3 were omitted for clarity

Fig.2



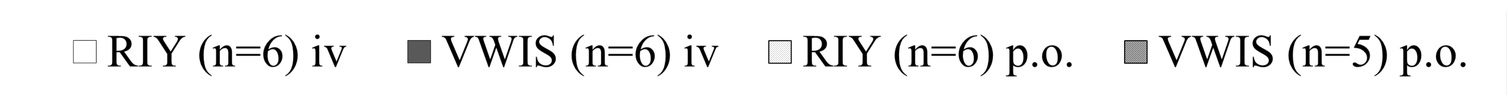
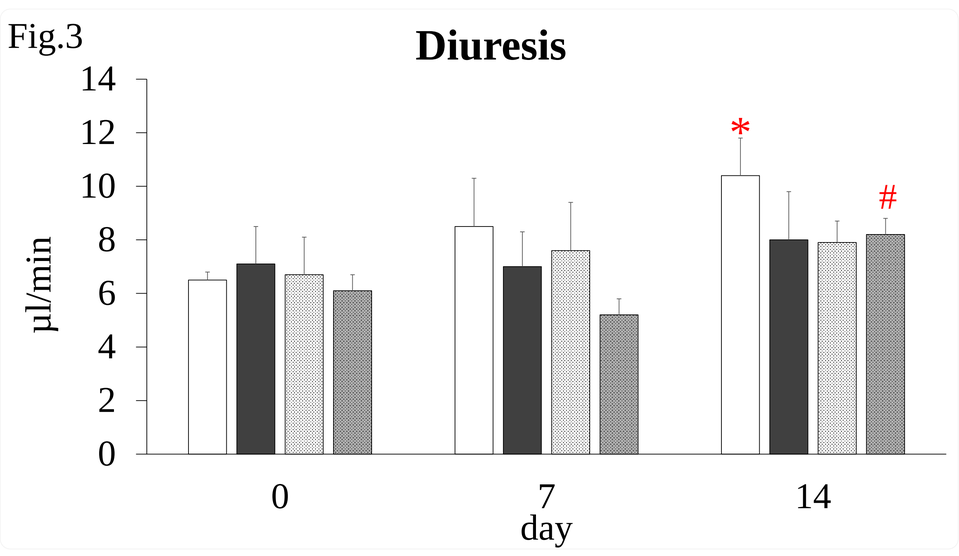


Fig.3



Diuresis changes after iv and p.o. administration of peptides VWIS and RIY

Significant increase in diuresis was observed in rats which received peptide RIY (iv). Also after p.o. administration of VWIS significant increase in diuresis was observed (**p≤0.05 vs. day 0, #p≤0.05 vs. day 0&7*).

VWIS (Valine-Tryptophan-Isoleucine-Serine)
RIY (Arginine-Isoleucine-Tyrosine)

Summary & Conclusions

- Obtained results suggest that peptide RIY possesses antihypertensive activity and it seems greater than the one exhibited by VWIS. This observation is in accordance to previous study by Marczak *et al.* The authors showed that RIY is more resistant to enzymatic degradation, therefore it is very slowly degraded by enzymes like ACE. Its greater stability could translate into longer and/or stronger inhibition of chymase, resulting in higher antihypertensive activity.
- Additionally, in rats receiving VWIS (iv), a significantly higher water intake without higher diuresis was observed, which may indicate water retention. This could partially account for the lack of hypotensive effect in this group.

In conclusion, peptide RIY may be of a great value as a potent antihypertensive agent, especially useful in cases when ACE blockers are not effective

References:

Kirimura K, Takai S, Jin D, Muramatsu M, Kishi K, Yoshikawa K, Nakabayashi M, Mino Y & Miyazaki M (2005). Role of chymase-dependent angiotensin II formation in regulating blood pressure in spontaneously hypertensive rats. Hypertens Res 28, 457–464.

Marczak ED, Usui H, Fujita H, Yang Y, Yokoo M, Lipkowski AW & Yoshikawa M (2003). New antihypertensive peptides isolated from rapeseed. Peptides 24, 791–798.

Yamada Y, Iwasaki M, Usui H, Ohinata K, Marczak ED, Lipkowski AW & Yoshikawa M (2010). Rapakinin, an anti-hypertensive peptide derived from rapeseed protein, dilates mesenteric artery of spontaneously hypertensive rats via the prostaglandin IP receptor followed by CCK1 receptor. Peptides 31, 909–914.

The study was funded by Polish National Science Centre, Grant No 2011/01/B/NZ4/05703 and project was implemented under the program KNOW-MMRC

*"**The search for new biomarkers of civilization diseases using high-throughput techniques and modern diagnostic imaging**"*