# TOTUM•854 reduction of blood pressure is associated with tissue remodeling in aorta and heart of SHR rat

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Arterial Hypertension (AHT) is a major cause of premature death worldwide, with an estimated global prevalence of 1.13 billion people. Polyphenolic compounds have been shown promising effects in the context of AHT management. We have developed TOTUM•854 (T-854), a polyphenol-rich botanical composition to reduce the risk of developing AHT.

## Study 1. Acute effect of T-854 on blood pressure in SHR

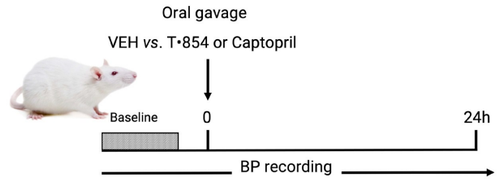



Figure 1. Experimental design (Study 1): Effects on blood pressure of acute supplementation with T-854 (1250 mg/kg) or Captopril (50 mg/kg) *vs.* vehicle (VEH) in hypertensive SHR rats. BP: Blood Pressure.

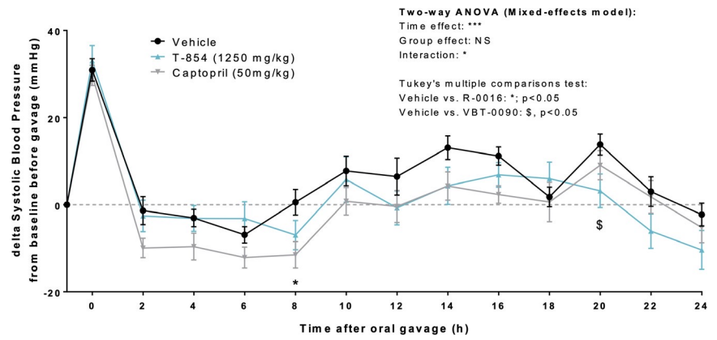



Figure 2. Acute effect of T-854 and Captopril administration on systolic blood pressure difference from baseline along 24h-post gavage.

## Study 2. Effect of T-854 chronic administration on change in blood pressure in SHR rats

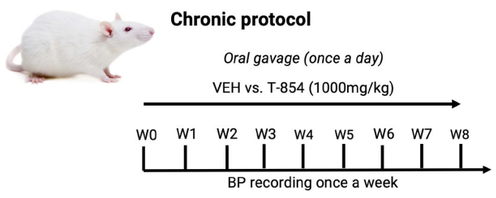
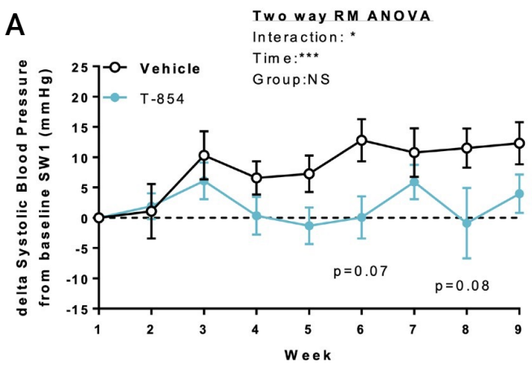



Figure 3. Experimental design: Effects on blood pressure of chronic supplementation with T-854 (1000 mg/kg) *vs.* vehicle (VEH) in hypertensive SHR rats. BP: Blood Pressure.



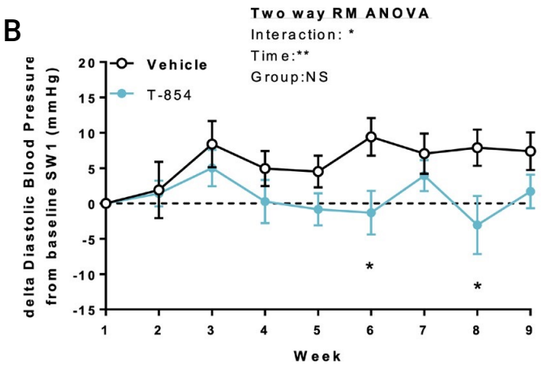




Figure 4. Chronic effect of T-854 on blood pressure difference from baseline, along 8 weeks of supplementation. SBP: Systolic Blood Pressure. DBP: Diastolic Blood Pressure. SW: Study week.

## Effects of T-854 chronic administration on tissue remodeling in SHR rats

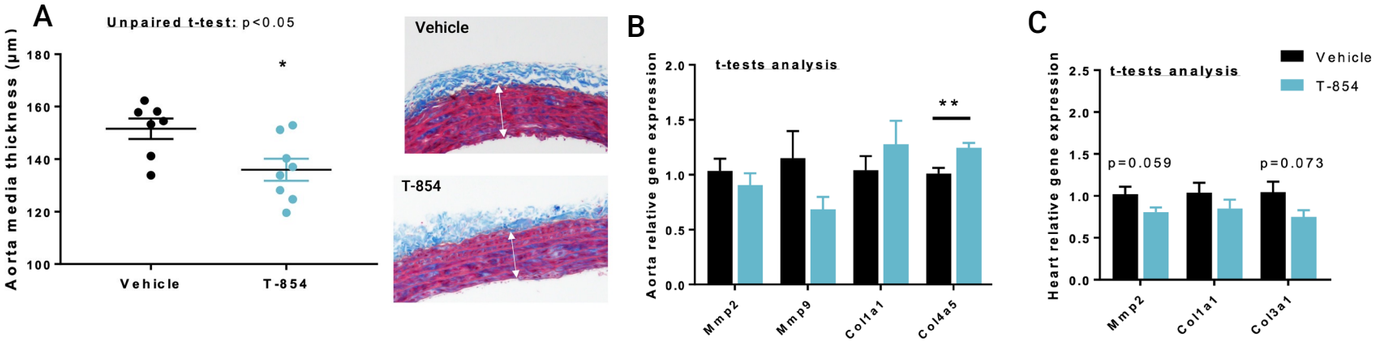



Figure 5. Chronic effect of T-854 administration on tissue remodeling after 8 weeks of supplementation in aorta and heart. A) Aorta media thickness values obtained by measuring of Trichrome Masson staining (x40). B) and C) Gene expression profile in aorta (B) and in heart (C).

## Anti-oxidative effects of T-854 chronic administration in SHR rats

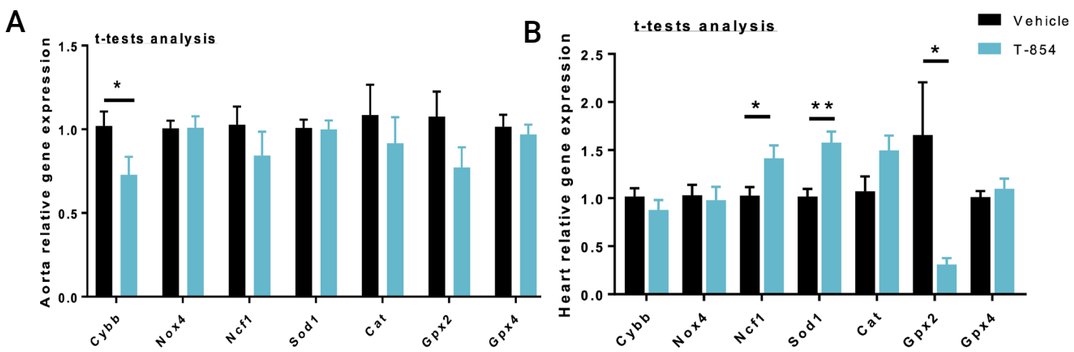
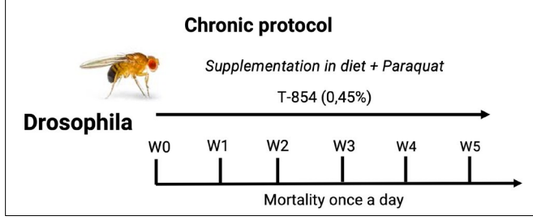



Figure 6. Chronic effect of T-854 administration on oxidative stress gene expression after 8 weeks of supplementation in aorta (A) and in heart (B).

## Validation of T-854 anti-oxidative effect on paraquat drosophila model



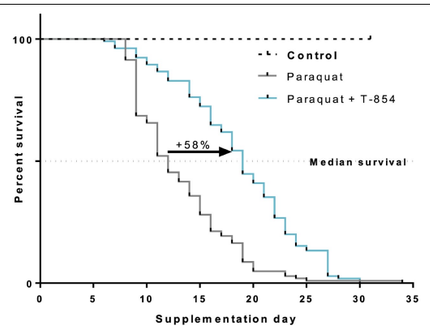




Figure 7. Effects on drosophila survival of chronic supplementation with T-854 (0.45%) in oxidative stress-induced drosophila with Paraquat. Log-rank (Mantel-Cox) test Paraquat *vs.* Paraquat + T-854: p<0.0001 (Bonferroni corrected p-value = 0.017).

T-854 24h-post-gavage acute effect on blood pressure in hypertensive SHR rats suggests a rapid effect, with a decrease in blood pressure few hours after oral administration and maintained during the time of the experiment. T-854 prevents the development of AHT after eight weeks in SHR rat, with improved aortic and cardiac tissue structure. These effects could be due in part to anti-oxidative role of T-854 in aorta and heart. Finally, T-854 supplementation in paraquat drosophila model validated anti-oxidative effect of this product by improving fly survival.