NON-CANONICAL ROLE OF MK-7 IN VASCULAR SMOOTH MUSCLE CELLS

1 Introduction:

Antagonism of vitamin K pathway by warfarin induces oxidative stress in vascular smooth muscle cells. This contributes to pathological phenotype perpetuating vascular calcification and cardiovascular disease.

2 Hypothesis:

Menaquinone-7 (MenaQ7®) can counter induced oxidative stress in vascular smooth muscle cells.

3 Key Findings:

- Interference with vitamin K metabolism by Warfarin results in increased intracellular oxidative stress and EV secretion
- MK7 counteracts intracellular oxidative stress, both under normal conditions as well as warfarin induced
- MK7 counteracts the effect of CoCl2 induced ROS production whereas UQ10 has no such effect
- Warfarin does not affect ATP levels, suggesting that warfarin does not affect mitochondrial function
- MK7 increases ATP production, even in the presence of warfarin.

4 FINAL CONCLUSION

Our experiments with human VSMCs demonstrate that MK7 lowers oxidative stress and increases ATP production.

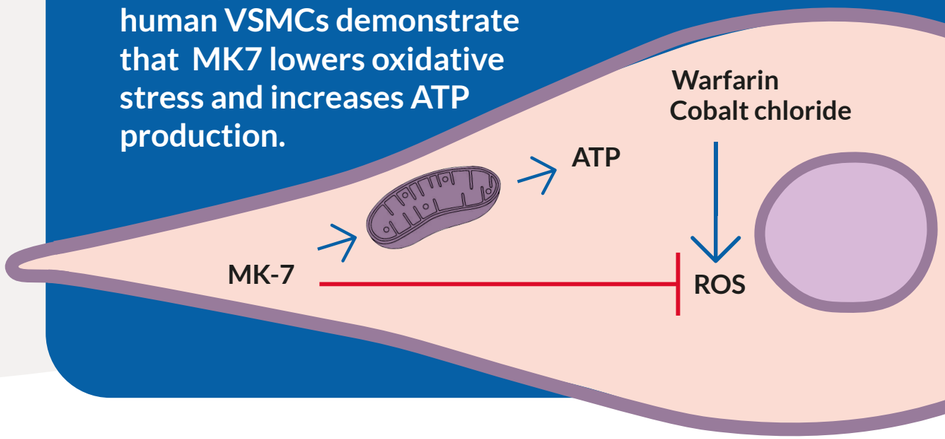


Figure 1. Warfarin exposure (6 hr) affects Reactive oxygen species (ROS) production in VSMC in a dose dependant manner.

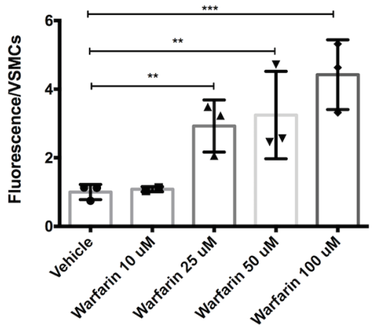


Figure 2. Warfarin treatment increases extracellular vesicle (EV) secretion.

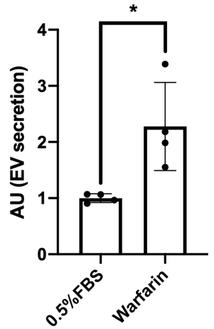


Figure 3. MK-7 treatment decreases ROS production in VSMCs compared to control and warfarin. The cells in all 3 experiments were pretreated for 24 hrs with 100 µM Warfarin.

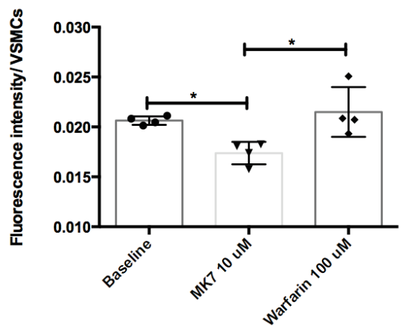


Figure 4. MK-7 may counteract effect of Cobalt chloride (CoCl2) on ROS production unlike Ubiquinone-10 (UQ10).

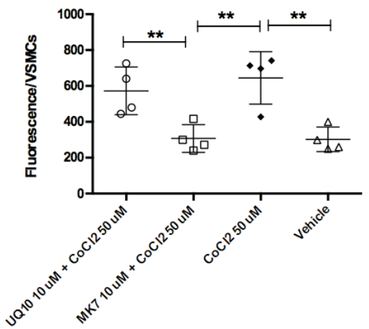
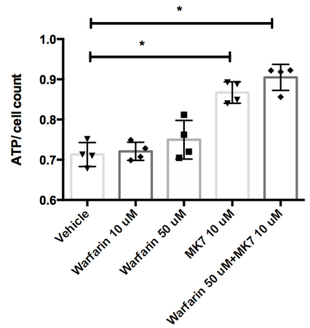


Figure 5. Warfarin does not affect VSMC ATP production; however, MK-7 improves ATP production independent of warfarin action.



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