Interspecies Comparison of Pro-oxidant Stress Response: Bovine Versus Human Red blood Cell Survival

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Background

- **Anemia** is a common problem among cattle, caused by nutritional deficiencies and vector-borne pathogens.[1]
- Eryptosis, the form of programmed cell death in red blood cells (RBCs), is associated with the pathophysiology of various **systemic diseases**, including anemia.[2]
- Bovine RBCs have a **unique membrane** phospholipid organization and a **longer lifespan** in circulation compared to humans.[3]
- These differences are hypothesized to influence their **survival** in circulation.
- Mechanisms of **cell death** are well studied in human RBCs, but this process has not been widely explored in cows.

Objective: To assess parameters of cell death and lipid signaling patterns of bovine RBCs in response to pro-oxidants such as hemin and menadione (Vitamin K_3).

Methods

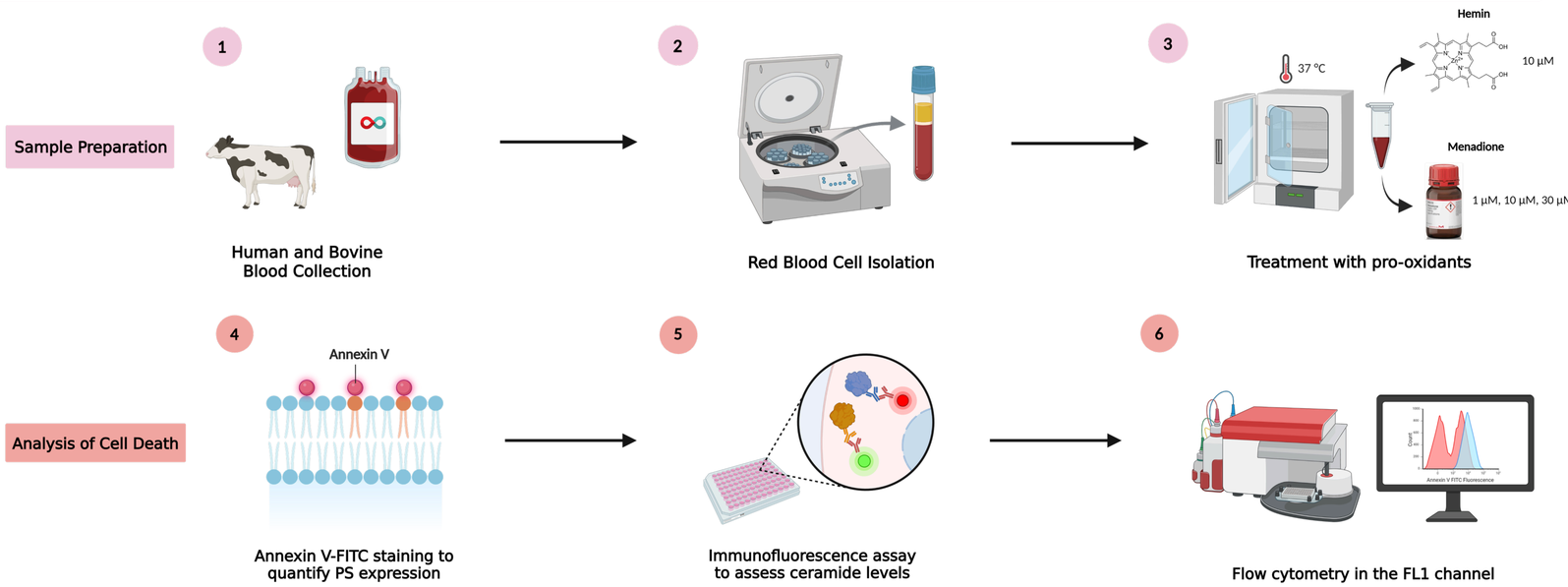


Figure 1. Red blood cell collection, isolation, and incubation for *in vitro* analysis. Created in BioRender.

Results

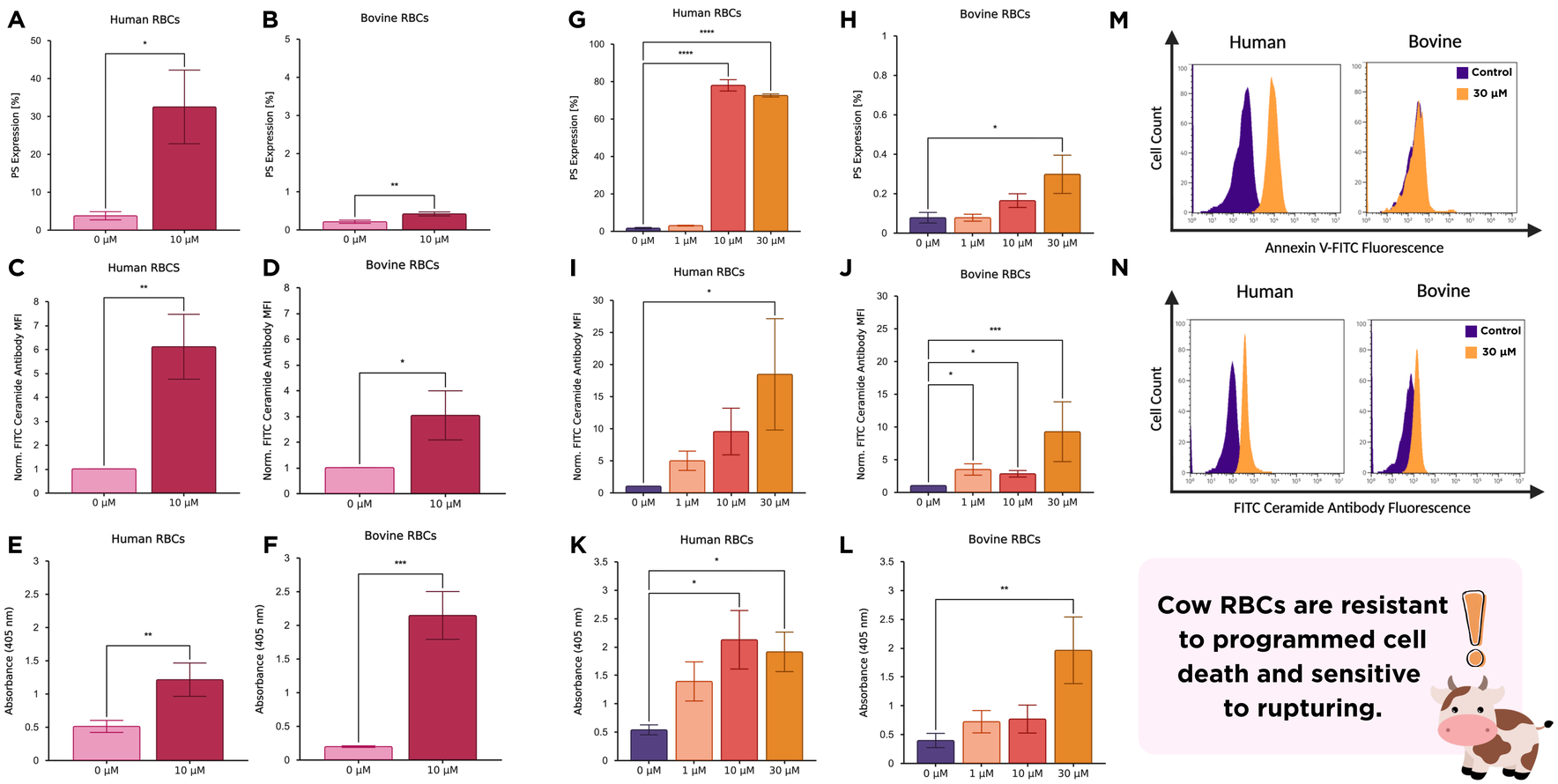


Figure 2. Effect of hemin on PS expression, ceramide formation, and hemolysis in human and bovine RBCs. Percentage of PS expression (A,B; n=8), means ± SEM of FITC Ceramide Antibody Mean Fluorescence Intensity (MFI) normalized to control (C,D; n =9), and means ± SEM of relative hemolysis (E,F; n=4; 405 nm absorbance) in human and bovine RBCs following 48-hour incubation in Ringer's solution at 0 µM (control) and 10 µM hemin chloride. *, **, and *** indicate significant difference ($p < 0.05$, $p < 0.01$, $p< 0.001$, respectively, ANOVA) from the control.

Figure 3. Effect of menadione on PS expression, ceramide formation, and hemolysis in human and bovine RBCs. Percentage of PS expression (G,H; n=3), means ± SEM of FITC Ceramide Antibody Mean Fluorescence Intensity (MFI) normalized to control (I,J; n =6), and means ± SEM of relative hemolysis (K,L; n=4; 405 nm absorbance) in human and bovine RBCs following 48-hour incubation in Ringer's solution at 0 µM (control), 1 µM, 10 µM, and 30 µM menadione. *, **, ***, and **** indicate significant difference ($p < 0.05$, $p < 0.01$, $p < 0.001$, $p< 0.0001$, respectively, ANOVA) from the control. Representative histogram overlays (M, N).

Cow RBCs are resistant to programmed cell death and sensitive to rupturing.

Discussion

- Bovine RBCs displayed subtle phosphatidylserine (PS) expression compared to human RBCs, indicating minimal eryptosis.
- Menadione and hemin induced significant increases in ceramide formation in bovine and human RBCs, demonstrating the potential role of ceramide-mediated cell death in bovine RBCs.
- Greater hemolysis in bovine RBCs was observed after treatment with hemin and menadione, demonstrating greater membrane fragility.

Conclusion

- This study provides insight into sphingolipid-mediated alterations in bovine RBCs, with potential applications to targeting RBC dysfunction in cattle and improving livestock productivity.
- Future avenues of study should explore downstream pathways of sphingolipid signaling in bovine RBCs.

References

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