

Evaluation of a Novel Autoinjector for Rapid Intramuscular Delivery of Sulfanegen as a Cyanide Antidote in a Porcine Model

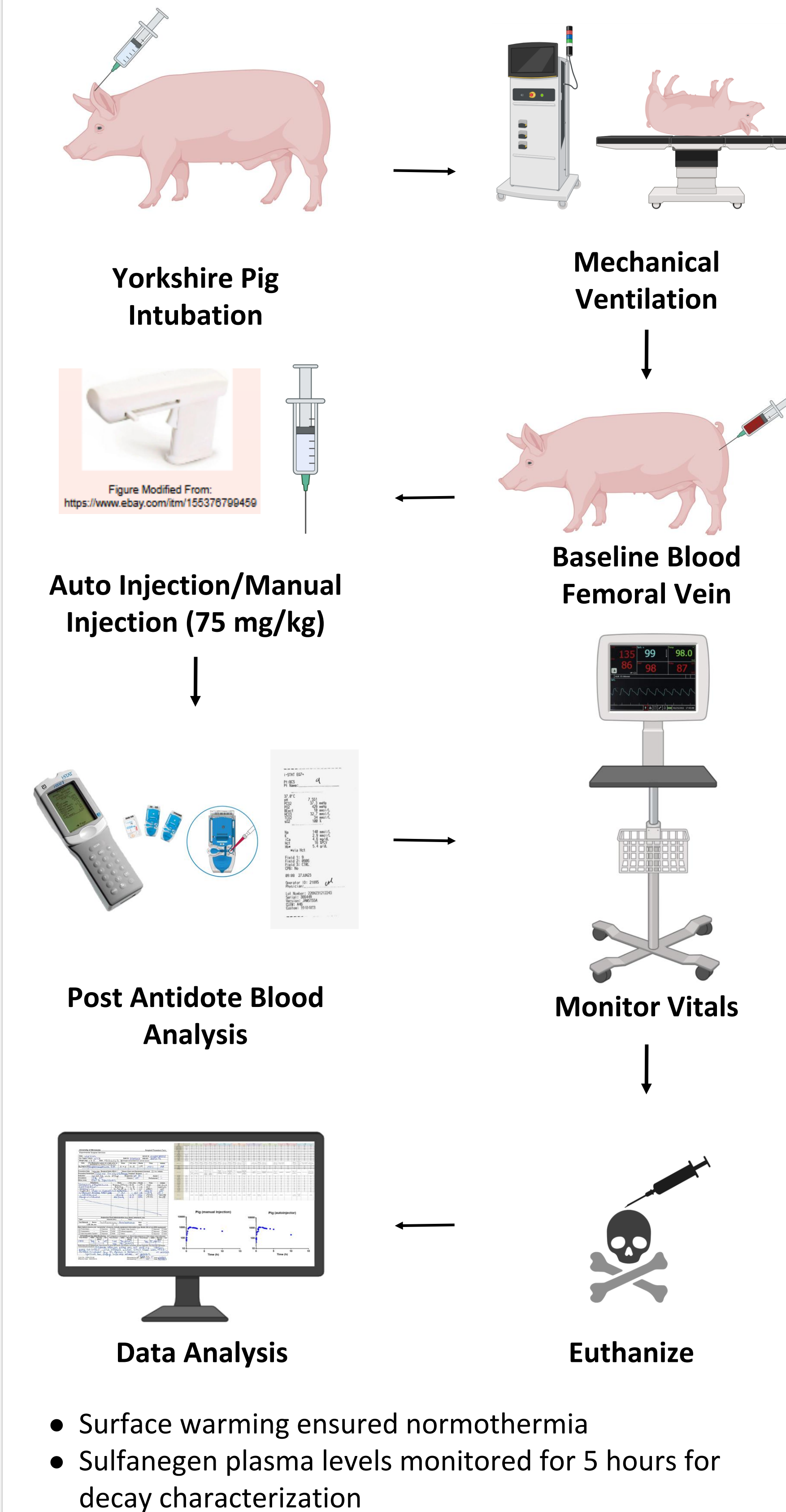
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Background, Aims, and Objectives

Untreated severe cyanide (CN) toxicity is fatal. Sulfanegen is rapid-acting within mitochondria and deactivates cyanide by using 3-mercaptopyruvate sulfurtransferase (3-MST). In this study, the autoinjector prototype performance was evaluated in juvenile domestic pigs, comparing both manual and autoinjector methods.

Materials and Methods



Results

Parameter	Autoinjector (Mean ± SD)	Manual Injection (Mean ± SD)	t-statistic	p-value	Significant (p < 0.05)
Venous Blood pH	7.5 ± 0.1	7.5 ± 0.1	N/A	N/A	No
PaO2 (mmHg)	482 ± 42	513 ± 12	-0.0015	0.999	No
PaCO2 (mmHg)	42 ± 7	46 ± 7	-0.0763	0.946	No
PvO2 (mmHg)	41 ± 6	55 ± 19	-0.538	0.645	No
Heart Rate (beats/min)	115 ± 23	116 ± 30	-0.0635	0.955	No
Mean Arterial Pressure (mmHg)	67 ± 16	59 ± 6	0.245	0.829	No
SaO2 (% Saturation)	97 ± 2	97 ± 2	0	1	No

Table 1: Statistical Analysis of Hemodynamic and Blood Gases Data

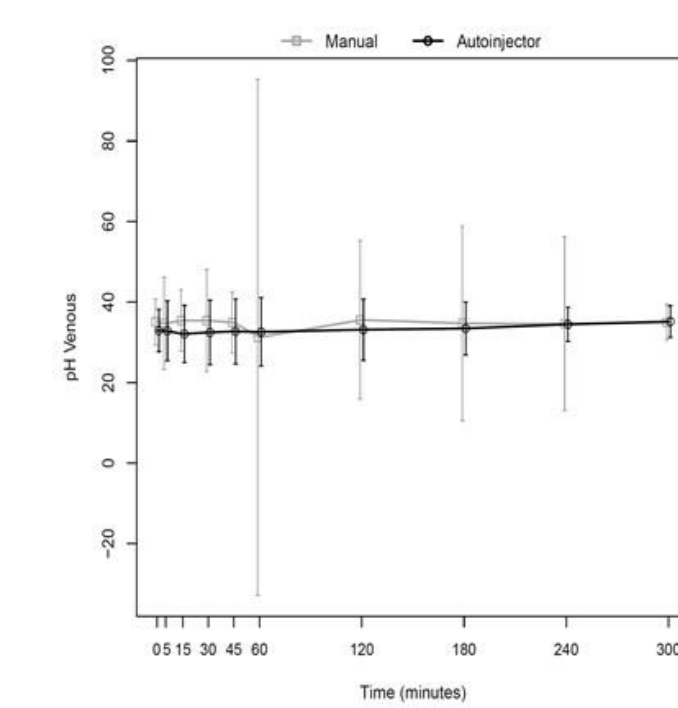


Figure 1: Venous Blood pH

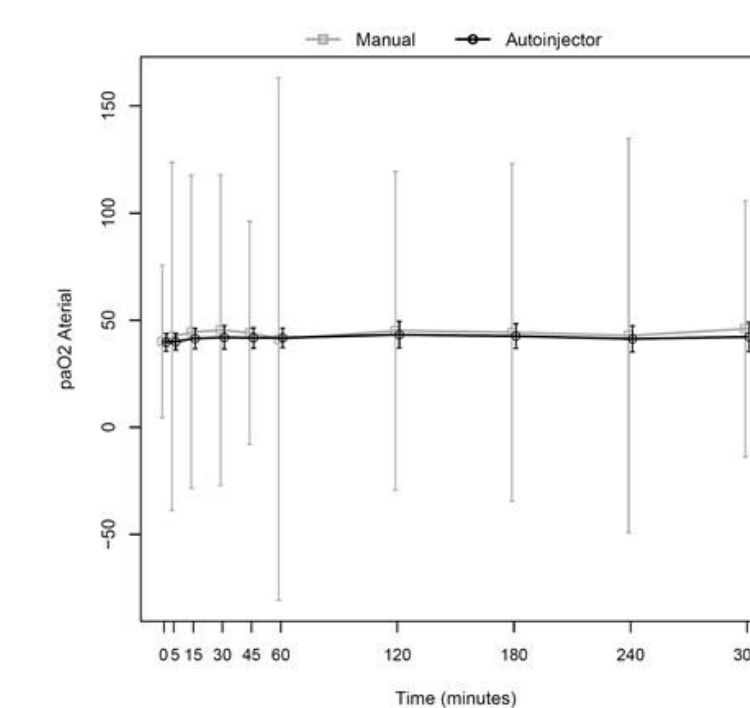


Figure 2: PaO2 (mmHg)

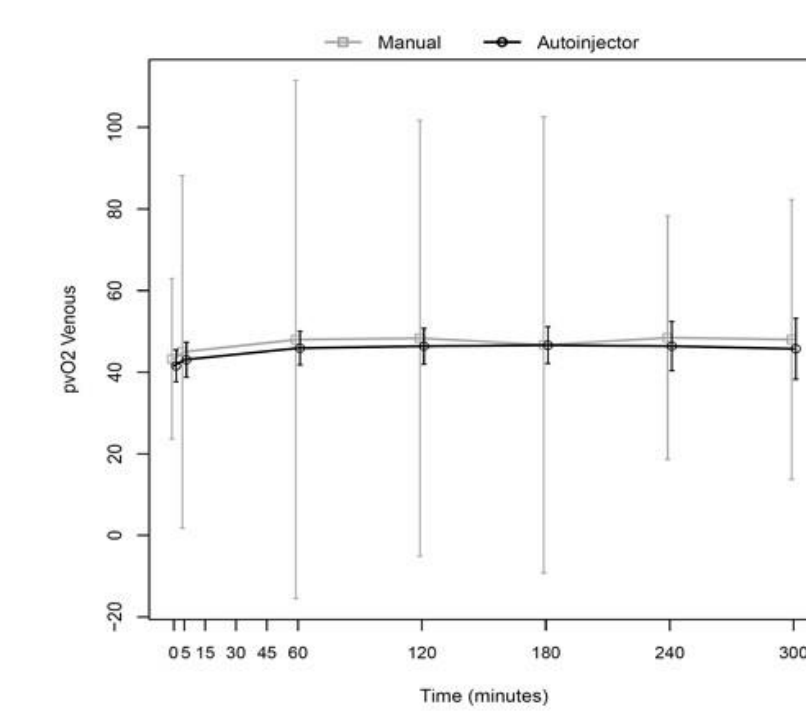


Figure 4: PvO2 (mmHg)

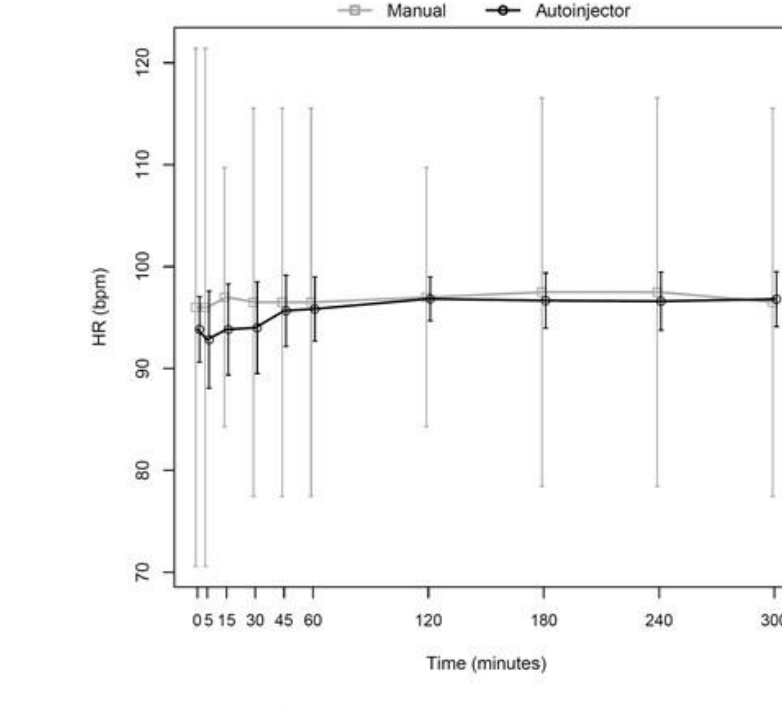


Figure 5: Heart Rate (beats/min)

Hemodynamic changes observed after sulfanegen i.m. injection (all values are mean±SD)										
Group	Baseline	5 mins	15 mins	30 mins	45 mins	60 mins	120 mins	180 mins	240 mins	300 mins
Heart Rate (beats/minute)										
Autoinjector	123±16	113±16	114±22	104±14	102±17	101±15	109±15	109±18	110±16	115±23
Manual injection	112±11	111±18	113±23	116±28	117±28	117±27	117±38	111±37	112±40	116±30
Mean Arterial Blood Pressure										
Autoinjector	81±20	85±13	82±13	81±22	77±19	76±14	74±16	70±11	70±12	67±16
Manual injection	78±6	74±1	75±1	73±6	71±9	71±8	68±1	65±2	62±1	59±6
CVP (mm Hg)										
Autoinjector	5±3	5±4	5±3	5±3	5±3	4±3	5±2	5±3	5±4	5±3
Manual injection	4±2	5±1	3±1	3±1	4±2	3±1	2±0	3±1	3±1	4±1
SaO2 (%)										
Autoinjector	94±3	93±5	94±4	94±4	96±3	96±3	97±2	93±3	97±2	97±2
Manual injection	96±3	96±3	97±1	97±2	97±2	97±1	98±2	98±2	97±2	97±2

Table 2: Hemodynamic changes after Sulfanegen Injection

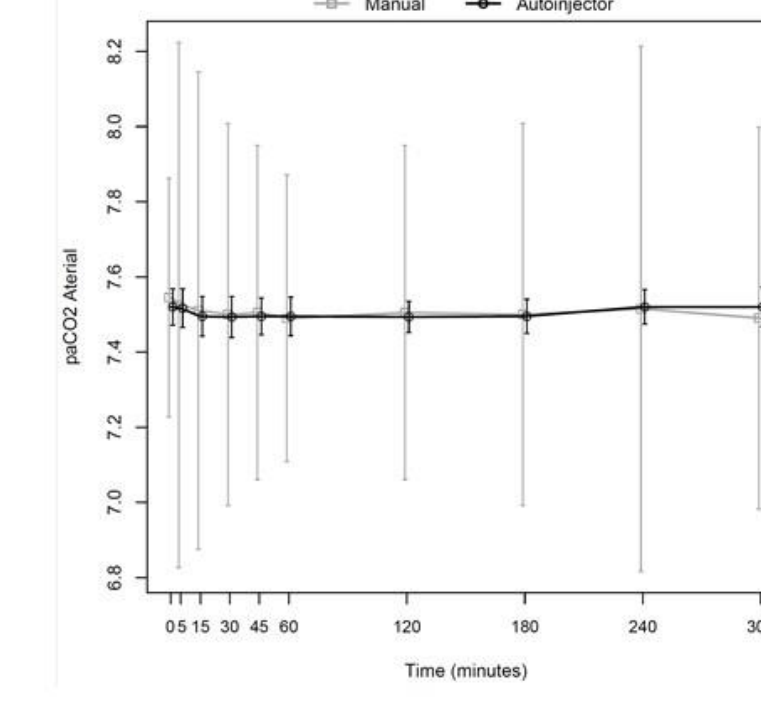


Figure 3: PaCO2 (mmHg)

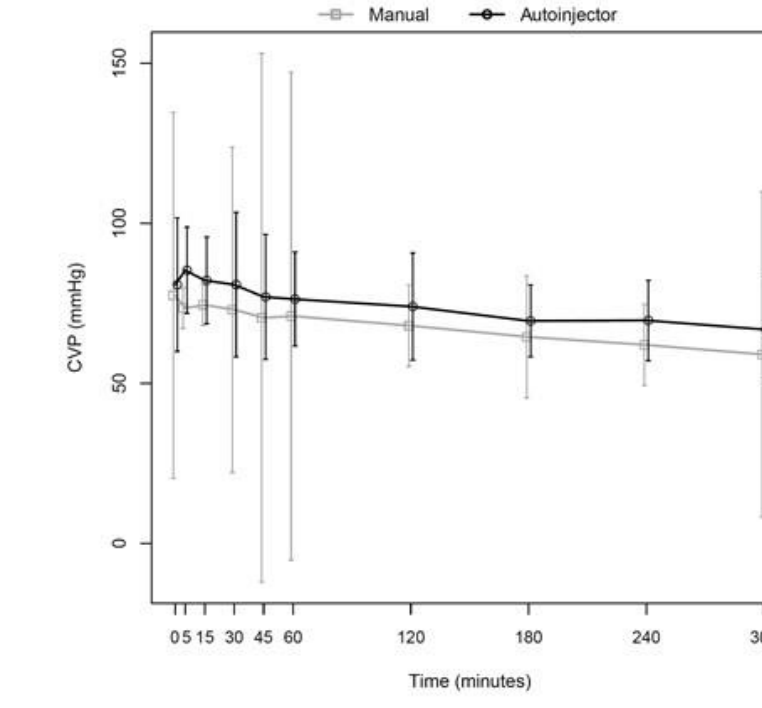


Figure 7: CVP (mmHg)

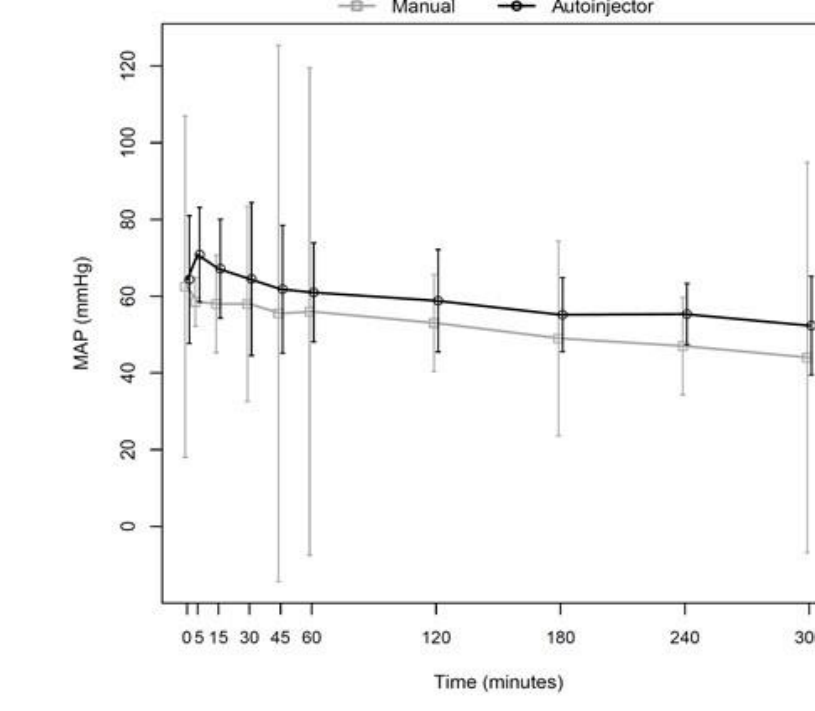


Figure 6: Mean Arterial Pressure (mmHg)

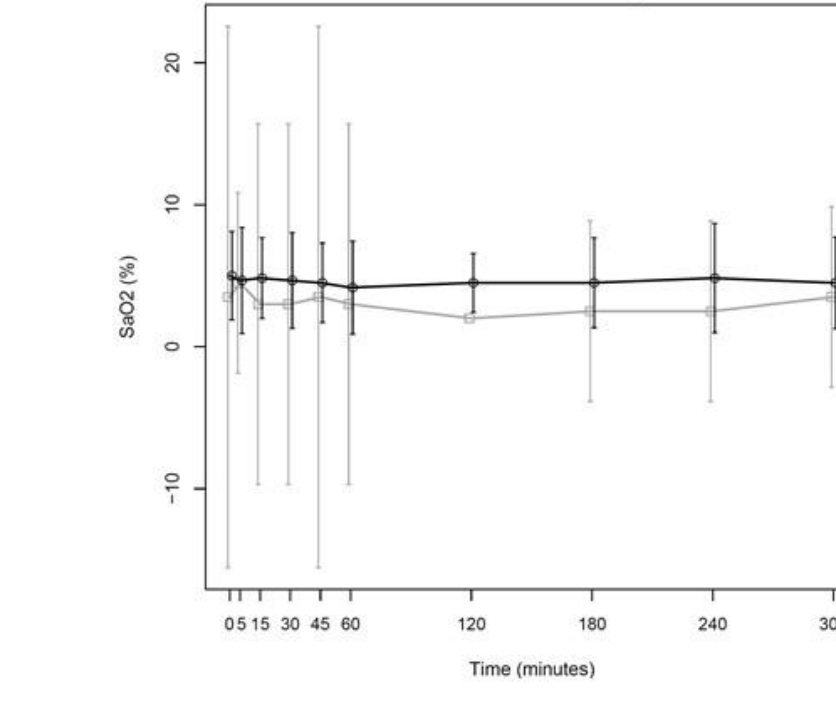


Figure 8: SaO2 (% Saturation)

Parameter	Auto-injector	Manual Injection
Time to Maximum Concentration	0.9 ± 0.1 h	1.1 h
Half Life	4.4 ± 0.3 h	4.6 ± 0.3 h
Time to 50% Peak Concentration	0.42 h	0.48 h
Vd	0.199 L	0.201 L
Clearance	0.176 L/h	0.179 L/h

Table 3: Sulfanegen Uptake in Plasma Pharmacokinetics

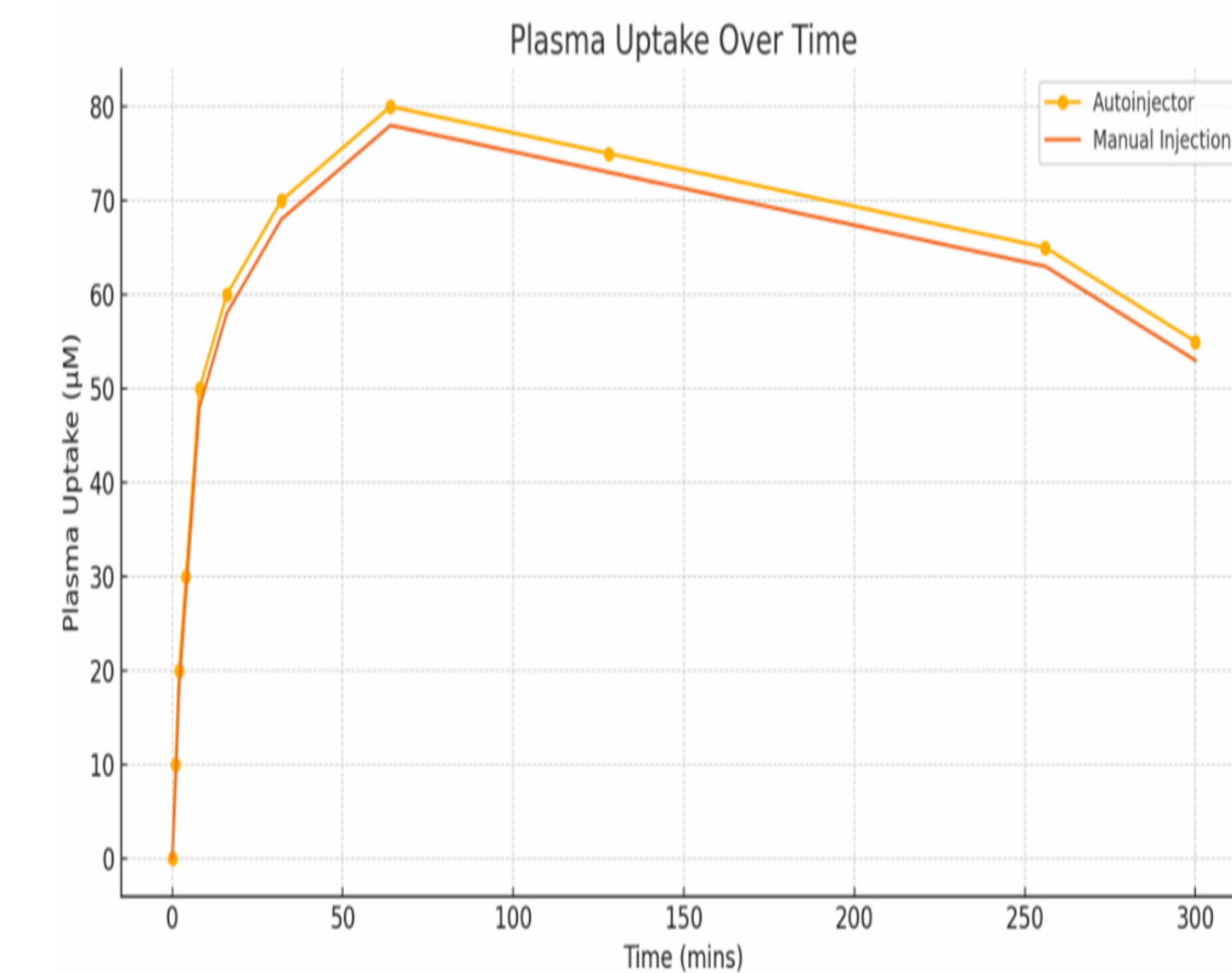


Figure 9: Plasma Uptake (µM)

Physiological Parameter : Over Time - Comparison between Autoinjector and Manual Injection

Conclusion

The Proprietary Auto-injectors performed satisfactorily in all 6 pigs, quickly dissolving powder and delivering the dose in seconds. When loaded with a precalculated dose, the dual injectors enable quick administration of sulfanegen antidotes by first responders or victims themselves in emergencies, following cyanide exposure. The study showed automatic delivery system and sulfanegen formulation as reliable and feasible, promising potential for timely cyanide antidote administration in emergencies and mass exposures. This efficient treatment could save lives before victims succumb to exposure

References

1. Brenner M, et al. Appl. Pharmacol. 248(3), 269–276 (2010).
2. Patterson SE, et al. J Med Chem. 2013; 56:1346–1349.