COMPARISON OF RESPONSIVENESS OF PORCINE ISOLATED CORONARY ARTERIES CULTURED AND PERFUSED IN KREBS-HENSELEIT SOLUTION AND AQIX® RS-I SOLUTION

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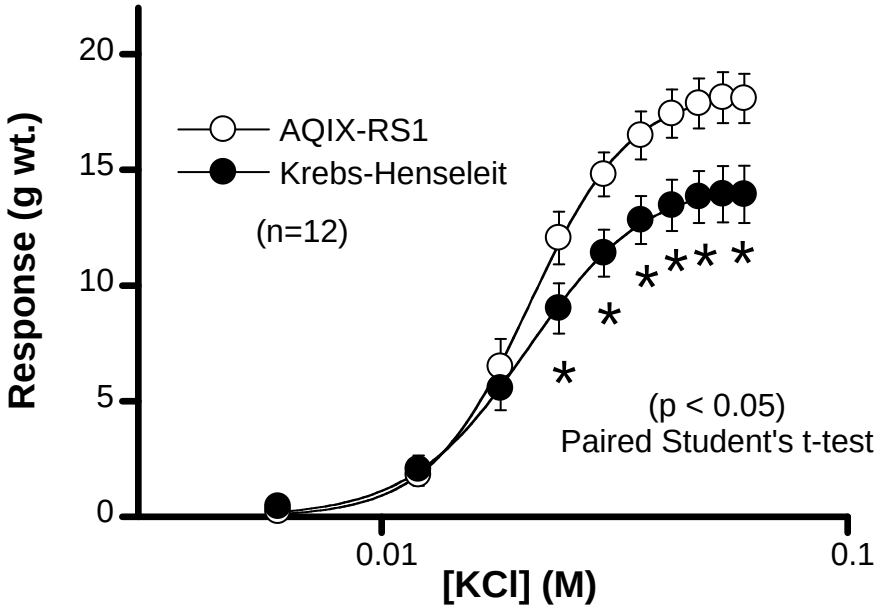
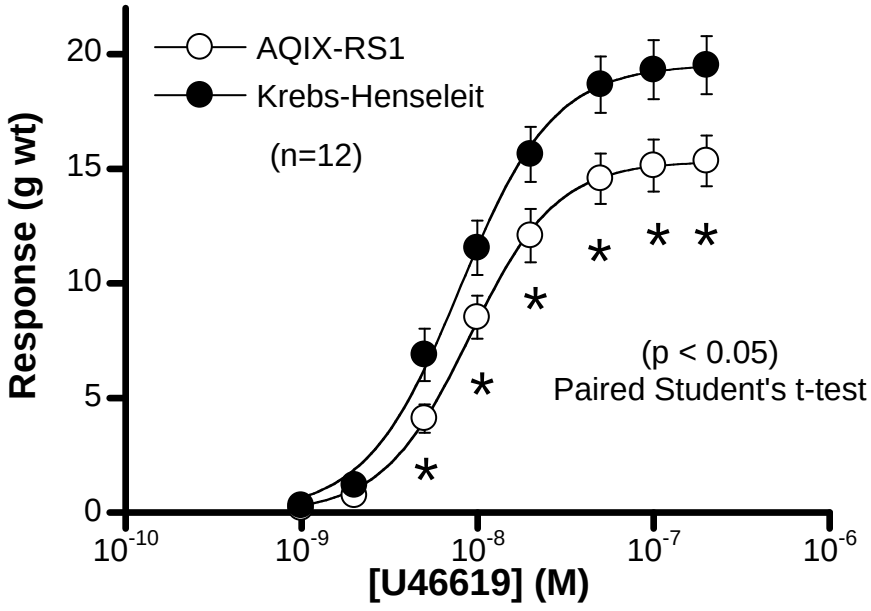
PHASE I Part I

Comparison of vasoconstrictor responses to KCl and U46619 in segments of the porcine isolated coronary artery stored overnight at 4^{o}C either AQIX RS-1 or Krebs-Henseleit solution

Porcine isolated coronary artery





KCl contractions - larger in AQIX RS-1 (?)

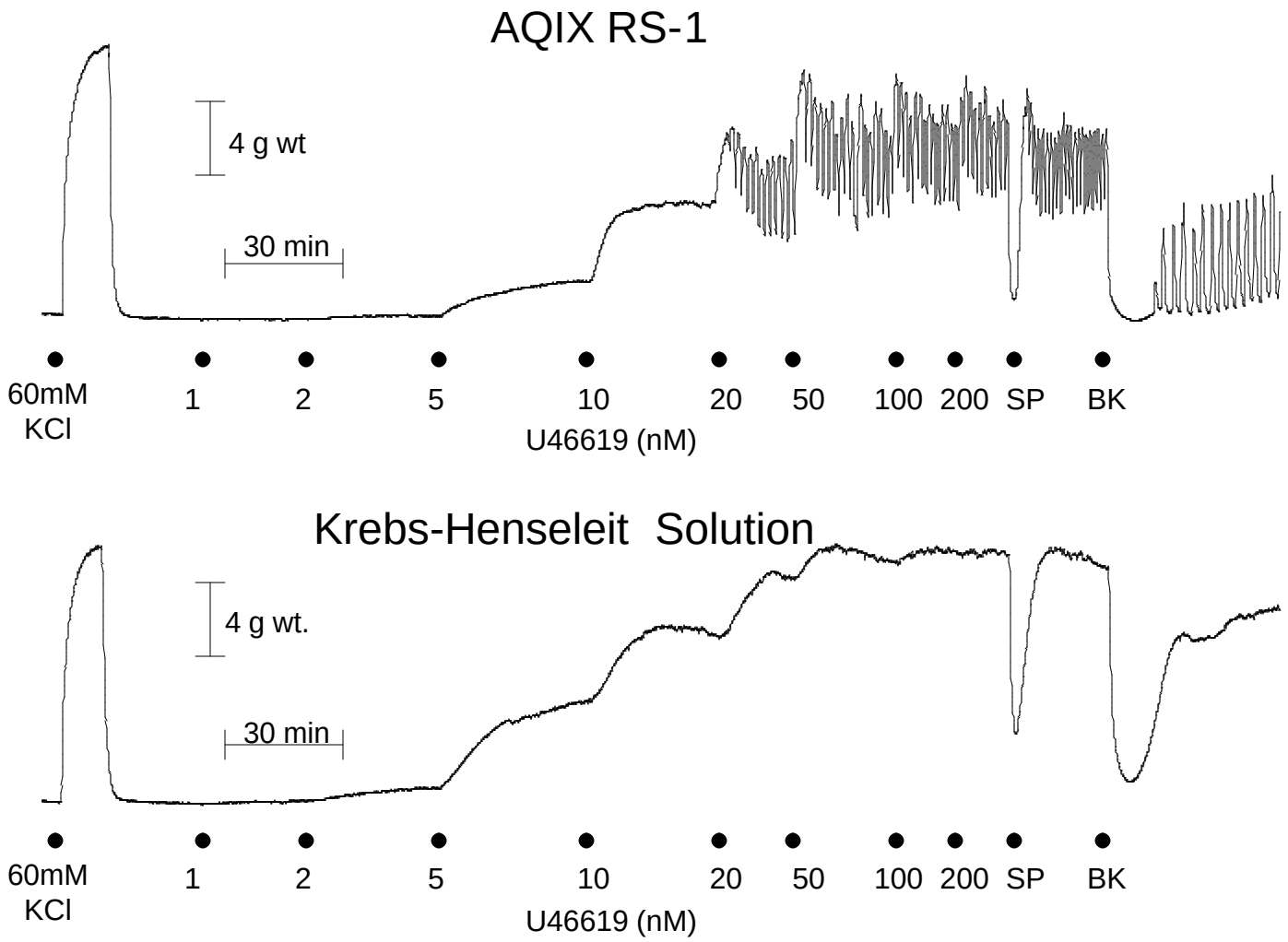
No difference in time course of contractions

U46619 contractions smaller in AQIX RS-1 -

Associated with the development of oscillatory contractions in 4 of 12 preparations.

	AQIX RS-1 (n=12)		Krebs Henseleit Solution (n=12)	
	Max response (g wt)	pD_2	Max response (g wt)	pD_2
KCl	18.1±1.1*	20.9±1.6 (mM)	13.2±1.2	20.5±2.6 (mM)
U46619	15.5±1.1*	8.03±0.06	19.5±1.3	8.10±0.05

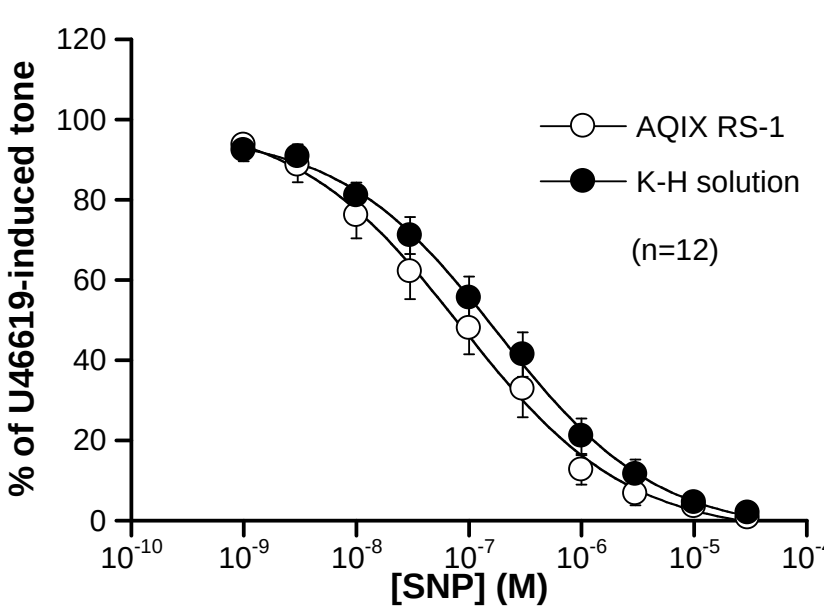
* - denotes a significant difference in response compared to Krebs-Henseleit solution

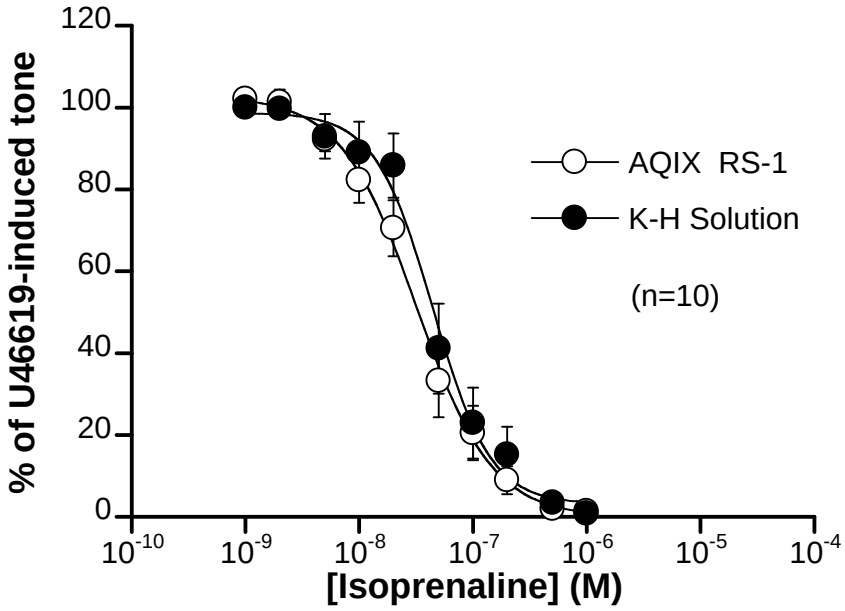

AQIX RS-1
4 g wt
30 min
60mM KCl
1
2
5
10
20
50
100
200
SP
BK
U46619 (nM)
Krebs-Henseleit Solution
4 g wt.
30 min
60mM KCl
1
2
5
10
20
50
100
200
SP
BK
U46619 (nM)

PHASE I Part 2

Comparison of the effect of sodium nitroprusside, Isoprenaline and substance P against U466190-induced tone in segments of the porcine isolated coronary artery stored overnight at 4^{o}C either in AQIX-RS-1 or Krebs-Henseleit solution

Porcine isolated coronary artery





Sodium Nitroprusside		Isoprenaline	
AQIX RS-1	K-H Solution	AQIX RS-1	K-H Solution
7.18±0.21	6.87± 0.16	7.46±0.10	7.24±0.16

Trend towards an increase in sensitivity (pD_2) for both agonists in the presence of AQIX RS-1 but it did not attain statistical significance.

Percentage relaxation to substance P and bradykinin against U46619 -induced contractions of the porcine isolated coronary artery following overnight storage at 4^{o}C in either K-H solution or AQIX RS-1

	Substance P (10nM)	Bradykinin (0.1µM)
Krebs-Henseleit	72.4±1.9	96.9±1.5
AQIX RS-1	82.7±2.7	97.4±1.2

Observations in paired segments from 12 animals

Phase 1 Part 3

Comparison of vasoconstrictor responses to KCl and U46619, and endothelium-dependent relaxations to SP and bradykinin, in segments of the porcine isolated coronary artery stored overnight at 37^{o}C in either AQIX RS-1 or Krebs-Henseleit solution

Please note that due to the shortage of AQIX RS-1 (early July) the protocol was modified in two respects

i) The heart were collected in Krebs-Henseleit solution rather than AQIX RS-1

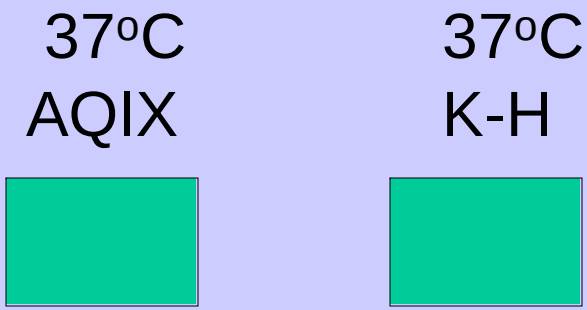
ii) **All** experiments were conducted in Krebs-Henseleit solution

Prepare 4 segments from each coronary of artery which are then stored at 37^{o}C in either:

2 ml of K-H solution (with Ficoll and antibiotics)
(Gas container before closure)

2ml of AQIX RS-1 (with Ficoll and antibiotics)
(Rinse segment in excess AQIX solution before placing in container and gas before closure)

Overnight



EXPERIMENT

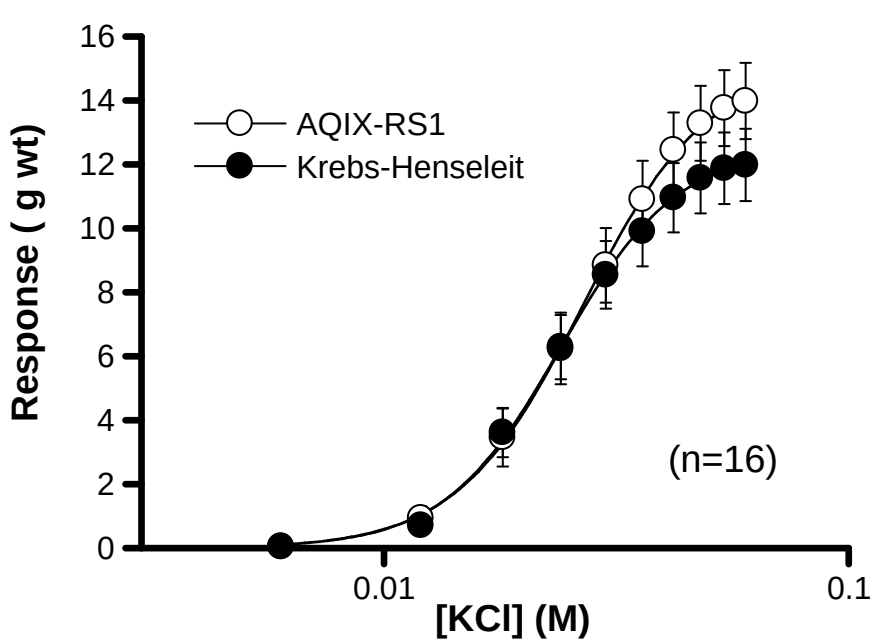
3 x 60mM KCl

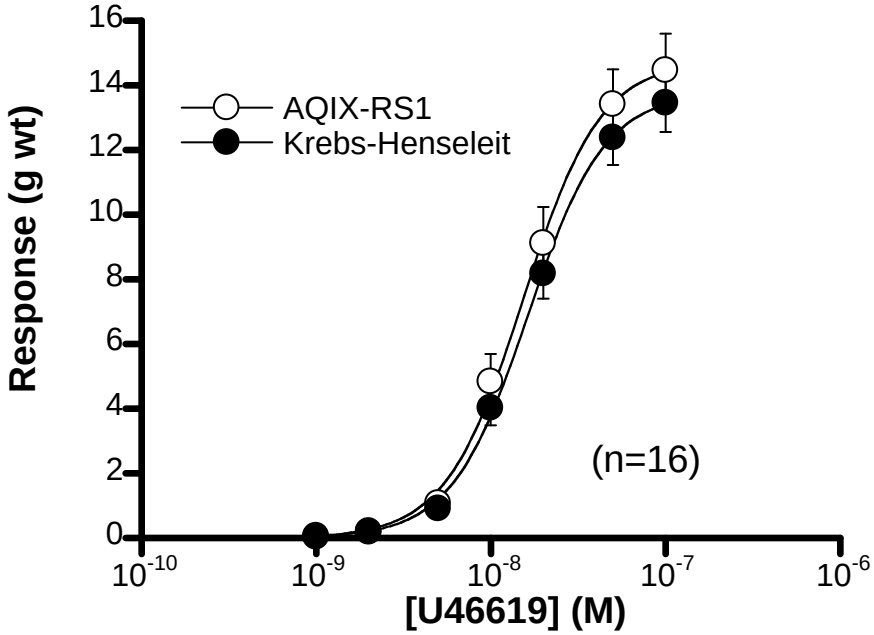
KCl CRC

U46619 CRC
10nM SP
0.1µM Bradykinin

Porcine Coronary Artery

Stored overnight in solution shown but experiment conducted in Krebs





	KCl (pD_2)	U46619 (pD_2)
AQIX RS-1	1.56±0.04	7.76±0.05
Krebs-Henseleit Soln.	1.61±0.02	7.70±0.05

No difference in responses to KCl and U46619

Porcine Coronary Artery

Stored overnight in solution shown but experiment conducted in Krebs

Percentage relaxation to substance P and bradykinin against U46619 -induced contractions of the porcine isolated coronary artery following overnight storage at 37^{o}C in either K-H solution or AQIX RS-1

	Substance P (10nM)	Bradykinin (0.1µM)
Krebs-Henseleit (n=16)	43.4±6.2	54.2±6.3
AQIX RS-1 (n=16)	46.8±5.7	61.1±6.5

Responses to both endothelium-dependent relaxants are reduced compared to tissues stored at 4^{o}C, but there is no difference between K-H solution and AQIX RS-1