

Appendix 1 - Pre-clinical studies using current haemostatics<sup>1-31</sup>

Lead Author	Year	Model	Subject Number (N)	Intervention	Test Agents	Survival (%)	Initial haemostasis achieved	Re-bleeding
Englehart <sup>1</sup>	2008	Swine 30 secs free-bleeding then 5 mins dressing application; resuscitation immediately mins post-compression; observed for 30 mins	30	Femoral vessel transection	Traumastat (N=10) HCG (N=10) SG (N=10)	90% 70% 90%	90% 20% 50%	-
Kozen <sup>2</sup>	2008	Swine 180 secs free-bleeding then 5 mins dressing application; resuscitation 8 mins post-injury; observed for 180 mins	32	Femoral vessel transection	SG (N=12) Cx (N=12) HCG (N=12) QuikClot granules (N=12)	50% 100% 67% 92%	-	83% 0% 33% 8%
Arnaud <sup>3</sup>	2009	Swine 120 secs free-bleeding then 5 mins dressing compression (with a standard dressing placed over the top) plus 175mmHg pressure; observed for 180 mins	88	Full femoral vessel transection	X-Sponge (N=8) WS (N=8) Celox granules (N=8) Quikclot ACS+ (granular) (N=8) InstaClot (N=8) HCG (N=8) BloodStop (N=8) Chitoflex (N=8) FP-21 (N=8) Alpha Bandage (N=8) SG (N=8)	84.4%   60%  50%   37%	-	25% 25% 30% 50% 0% 75% 70% 70% 80% 25% 45%
Arnaud <sup>4</sup>	2009	Swine 120 secs free-bleeding then 5 mins dressing compression (with a standard dressing placed over the top) plus 175mmHg pressure; observed for 180 mins	69	Femoral artery - 4mm hole	WS (N=8) Celox granules (N=8) X-Sponge (N=8) Quikclot ACS+ (granular) (N=8) InstaClot (N=8) Alpha Bandage (N=8) Chitoflex (N=8) FP-21 (N=8) HCG (N=8) BloodStop (N=8) SG (N=8)	87% 87% 75% 60% 50% 50% 25% 25% 25% 25% 10%	-	62.5% 50% 87.5% 75% 75% 100% 75% 100% 100% 100% 87.5%

Lead Author	Year	Model	Subject Number (N)	Intervention	Test Agents	Survival (%)	Initial haemostasis achieved	Re-bleeding
Kheirabadi <sup>5</sup>	2009	Swine 45 secs free-bleeding then haemostatic application and resuscitation; observed for 180 mins	46	Femoral artery - 6mm arteriotomy	Quikclot granules (N=6) HCG (N=10) Celox granules (N=10) SuperQuickRelief (N=10) WS (N=10)	17% 10% 60% 70% 100%	0% 60% 70% 90% 60%	-
Kheirabadi <sup>6</sup>	2009	Swine 45 secs free-bleeding then dressing application and resuscitation; observed for 180 mins	38	Femoral artery - 6mm arteriotomy	HCG (N=6) Celox (N=6) TraumaStat (N=10) SG (N=6) QCG (N=10)	0% 0% 20% 33% 80%	0% 0% 10% 17% 30%	-
Clay <sup>7</sup>	2010	Swine 45 secs free-bleeding then 6 mins dressing application; resuscitation 15 mins post-injury; observed for 120 mins	30	Femoral artery 6mm arteriotomy	SG (N=6) ACS+ (N=6) HCG (N=6) Celox granules (N=6) WS (N=6)	0% 50% 67% 83% 100%	-	-
Burgert <sup>8</sup>	2010	Swine 60 secs free-bleeding then 5 mins dressing application; resuscitation immediately mins post-compression; after 30 mins, dressings removed and blood pressure increased by resus fluid	15	Femoral vessel transection	Cx (N=5) TDX (N=5) PD (N=4)	-	100% 100% 20%	137.6 ± 41.8 113.2 ± 41.2 59.7 ± 14.5  Rebleeding MAP pressures (mmHg)
Gegel <sup>9</sup>	2010	Swine 60 secs free-bleeding then 5 mins dressing application; resuscitation immediately mins post-compression; after 30 mins, dressings removed and blood pressure increased by resus fluid	20	Femoral vessel transection	BleedArrest (N=5) TDX (N=5) Cx (N=5) PD (N=5)	-	100% 100% 100% unknown	-

Lead Author	Year	Model	Subject Number (N)	Intervention	Test Agents	Survival (%)	Initial haemostasis achieved	Re-bleeding
Kranokpiraksa <sup>10</sup>	2010	Sheep Dressing applied immediately after removal of 8F catheter; compression for 5 mins; angiography then confirmed haemostasis, if not another 2.5 mins of pressure was applied; this was repeated every 2.5 mins	18	Femoral artery 8F catheter	PACD (N=9) HCG (N=9)	-	100% 100%	-
Devlin <sup>11</sup>	2011	Swine 30 secs free-bleeding then dressing application; resuscitation 10 mins post-injury; observed for 180 mins	48	Femoral vessel transection	ChitoFlex (N=9) Cx (N=9) Quikclot ACS+ (N=9) SG (N=9)	83% 75% 83% 83%	-	8% 25% 0% 17%
Littlejohn <sup>12</sup>	2011	Swine 45 secs free-bleeding then 5 mins dressing application; resuscitation 10 mins post-injury; observed for 180 mins	80	Femoral vessel transection	Cx (N=16) Chitoflex (N=16) QCG (N=16) SG (N=16) WS (N=16)	88% 81% 75% 81% 56%	100% 81% 94% 81% 69%	25% 56% 25% 31% 25%
Watters <sup>13</sup>	2011	Swine 30 secs free-bleeding then dressing application; resuscitation immediately post-compression; observed for 120 mins	24	Femoral artery 6mm arteriotomy	QCG (N=8) Cx (N=8) SG (N=8)	100% 100% 100%	-	88% 63% 63%
Köksal <sup>14</sup>	2011	Rat 30 secs free-bleeding then dressing application	48	Femoral artery 24G needle perforation	Compression (N=8) Hypothermia + Compression (N=8) Compression + Warfarin (N=8) Cx (N=8) Hypothermia + Cx (N=8) Hypothermia + Cx + Warfarin (N=8)	-	50% 75% 25% 100% 100% 100%	-

Lead Author	Year	Model	Subject Number (N)	Intervention	Test Agents	Survival (%)	Initial haemostasis achieved	Re-bleeding
Arnaud <sup>15</sup>	2011	Swine 1. Femoral vessel transection with 45 secs free-bleeding then 5 mins dressing application; resuscitation immediately mins post-compression; observed for 180 mins  2. Femoral arteriotomy with 120 secs free-bleeding then 5 mins dressing application; resuscitation immediately mins post-compression; observed for 180 mins	28	Femoral vessel transection or 4mm femoral arteriotomy	Femoral vessel model QCG (N=6) TraumaStat (N=6)  Femoral arteriotomy model QCG (N=8) TraumaStat (N=8)	100% 100%  88% 50%	-	0% 17%  63% 75%
Schwartz <sup>16</sup>	2011	Swine 45 secs free-bleeding then 3 mins dressing application; resuscitation immediately mins post-compression; observed for 180 mins	14	Femoral artery 6mm arteriotomy	HCG (N=7) QCG (N=7)	100% 100%	-	-
Hoggarth <sup>17</sup>	2011	Swine 45 secs free-bleeding then dressing application; resuscitation immediately mins post-injury; observed for 120 mins	20	Femoral artery 6mm arteriotomy	Cx Rapid (N=12) QCG (N=8)	100% 100%	83% 50%	0% 0%
Turingan <sup>18</sup>	2011	Swine 45 secs free-bleeding then 5 mins dressing application; resuscitation 15 mins post-injury; observed for 180 mins	27	Femoral artery 4mm arteriotomy	SilverLeaf (N=9) QCG (N=9) WS (N=9)	89% 78% 100%	-	22% 44% 22%
Floyd <sup>19</sup>	2012	Swine 30 secs free-bleeding then 3 mins dressing application; resuscitation was started post-application observed for 150 mins	20	Femoral artery 6mm arteriotomy	Salmon Thrombin-Fibrinogen (N=10) QCG (N=10)	90% 50%	90% 70%	

Lead Author	Year	Model	Subject Number (N)	Intervention	Test Agents	Survival (%)	Initial haemostasis achieved	Re-bleeding
Johnson <sup>20</sup>	2012	Swine 60 secs free-bleeding then 5 mins dressing application; resuscitation immediately mins post-compression; 5l crystalloid administered post-haemostasis to assess rebleeding volume	22	Femoral vessel transection	QCG (N=11) SG (N=11)	-	-	4818 209  Mean resus fluid required to trigger rebleeding (ml)
Causey <sup>21</sup>	2012	Swine 45 secs free-bleeding then 3 mins dressing application; resuscitation immediately mins post-compression; observed for 180 mins	17	Femoral artery 50% transection	QCG (N=9) SG (N=8)	-	100% 13%	-
Mueller <sup>22</sup>	2012	Swine 30 secs free-bleeding then 3 mins dressing application; resuscitation started post-injury; observed for 60 mins	16	Subclavian vessel transection	Cellulose Minisponges (N=8) QCG (N=8)	100% 37.5%	100% 25%	-
Rall <sup>23</sup>	2013	Swine 45 secs free-bleeding then 3 mins dressing application; resuscitation immediately mins post-compression; observed for 150 mins	50	Femoral artery 6mm arteriotomy	QCG (N=10) QCG XL (N=10) Cx Trauma (N=10) Cx (N=10) HCG (N=10)	60% 70% 50% 90% 70%	30% 80% 30% 70% 60%	-
Xie <sup>24</sup>	2013	Swine 45 secs free-bleeding then 3 mins dressing application; resuscitation immediately mins post-compression; observed for 180 mins	16	Femoral artery 6mm arteriotomy	QCG (N=8) HCG (N=8)	63% 88%	25% 63%	-
Kunio <sup>25</sup>	2013	Swine 60 secs free-bleeding then unpressurised dressing application; resuscitation immediately mins post-injury; observed for 120 mins	36	Femoral artery 6mm arteriotomy	Cx Rapid (N=12) QCG (N=12) SG (N=12)	100% 100% 100%	-	67% 75% 58%

Lead Author	Year	Model	Subject Number (N)	Intervention	Test Agents	Survival (%)	Initial haemostasis achieved	Re-bleeding
Satterly <sup>26</sup>	2013	Swine and Goat 5 secs free-bleeding then 2 mins dressing application; haemorrhaged blood measured at 2 and 4 mins	126	Femoral or axillary artery 50% transection	QCG (N=42) HCG (N=11) Cx (N=45) HemCon (N=28)	-	83% 69% 76% 53%	-
Johnson <sup>27</sup>	2014	Swine 60 secs free-bleeding then 5 mins dressing application; resuscitation immediately mins post-compression; 5l crystalloid administered post-haemostasis to assess rebleeding volume	26	Femoral vessel transection	QCG (N=13) PD (N=13)	-	84.6% 30.8%	-
Gegel <sup>28</sup>	2014	Swine 60 secs free-bleeding then 5 mins dressing application; resuscitation immediately mins post-injury; observed for 35 mins	22	Femoral vessel transection	QCG (N=11) SG (N=11)	-	-	-
Burnett <sup>29</sup>	2014	Swine 45 secs free-bleeding then 3 mins dressing application; resuscitation immediately mins post-injury; observed for 180 mins	28	Femoral artery 6mm arteriotomy	SG (N=7) Nanosan-Sorb (N=7) HCG (N=7) KeraStat (N=7)	28% 71% 45% 55%	-	-
Conley <sup>30</sup>	2015	Swine 30 secs free-bleeding then intervention by Navy Medics	24	Femoral artery 6mm arteriotomy	Cx (N=8) HCG (N=8) QCG (N=8)	average: 96% QCG = 86%	62.5% 62.5% 75%	50% 25% 25%
Bayir <sup>31</sup>	2016	Rat 10 secs free-bleeding then dressing application	38	Femoral artery 26G needle perforation	SG (N=12) Kaolin (N=13) Clinoptilolite (N=13)	42% 77% 100%	0% 54% 62%	100% 31% 8%

SG = standard gauze; QCG = Quikclot Combat Gauze; HCG = HemCon Chitogauze/Chitoflex/RTS; Cx = Celox; WS = Woundstat; TDX = TraumaDEX; PD = Standard pressure dressing; PACD = Percutaneous Arterial Closure Device

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