Supporting Information

Drug release kinetics of DOX-loaded graphene-based nanocarriers for ovarian and breast cancer therapeutics

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List of supporting information tables and figures

Table S1. Table displaying the title, first author, journal, publication year and DOI for the seventeen publications analysed.

Paper No.	Title	First author	Journal	Publication Year	Digital Object Identifier (DOI)
1	Hyaluronic acid and Arg-Gly-Asp peptide modified Graphene oxide with dual receptor-targeting function for cancer therapy	Yufeng Guo	Journal of Biomaterials Applications	2017	doi.org/10.1177/0885328217712110
2	Mixed surfactant modified graphene oxide nanocarriers for DOX delivery to cisplatin-resistant human ovarian carcinoma cells	Qian Zhang	RSC Advances	2016	doi.org/10.1039/C6RA17609G
3	Smart pH-Responsive Nanocarriers Based on Nano-Graphene Oxide for Combined Chemo- and Photothermal Therapy Overcoming Drug Resistance	Liangzhu Feng	Advanced Healthcare Materials	2014	doi.org/10.1002/adhm.201300549
4	Hypericin-functionalised graphene oxide for enhanced mitochondria-targeting and synergistic anticancer effect	Chao Han	Acta Biomaterialia	2018	doi.org/10.1016/j.actbio.2018.07.018
5	Fe_3O_4@PEG-coated dendrimer modified graphene oxide nanocomposite as a pH-sensitive drug carrier for targeted delivery of doxorubicin	Soheyla Karimi	Journal of Alloys and Compounds	2021	doi.org/10.1016/j.jallcom.2021.160426
6	Chelating ZnO-dopamine on the surface of graphene oxide and its application as pH-responsive and antibacterial nanohybrid delivery agent for doxorubicin	Nastaran Alipour	Materials Science and Engineering: C	2020	doi.org/10.1016/j.msec.2019.110459
7	Development of a graphene oxide-poly lactide nanocomposite as a Smart Drug Delivery System	Aliyeh Ghamkhari	International Journal of Biological Macromolecules	2021	doi.org/10.1016/j.ijbiomac.2020.12.084
8	Folic acid-grafted bovine serum albumin decorated graphene oxide: An efficient drug carrier for targeted cancer therapy	Naxin Ma	Journal of Colloid and Interface Science	2017	doi.org/10.1016/j.jcis.2016.11.097
9	Self-Assembled Graphene-Dextran Nanohybrid for Killing Drug-Resistant Cancer Cells	Rong Jin	ACS Applied Materials & Interfaces	2013	doi.org/10.1021/am401523y

Table S1 continued

10	High-Efficiency Loading and Controlled Release of Doxorubicin Hydrochloride on Graphene Oxide	Xiaoying Yang	The Journal of Physical Chemistry C	2008	doi.org/10.1021/jp806751k
11	Remote Controlled drug release from multi-functional Fe_3O_4/GO/Chitosan microspheres fabricated by an electrospray method	Sheng Li	Colloids and Surfaces B: Biointerfaces	2017	doi.org/10.1016/j.colsurfb.2016.12.029
12	Engineering of a novel pluronic F127/graphene nanohybrid for pH responsive drug delivery	Haiqing Hu	Journal of Biomedical Materials Research	2011	doi.org/10.1002/jbm.a.33252
13	Sonochemically synthesized blue fluorescent functionalized graphene oxide as a drug delivery system	Hamed Hashemi	Ultrasonics Sonochemistry	2018	doi.org/10.1016/j.ultsonch.2017.11.010
14	A de novo theranostic nanomedicine composed of PEGylated graphene oxide and gold nanoparticles for cancer therapy	Hadi Samadian	Journal of Materials Research	2020	doi.org/10.1557/jmr.2020.3
15	Graphene oxide used as a carrier for Adriamycin can reverse drug resistance in breast cancer cells	Jing Wu	Nanotechnology	2012	DOI:10.1088/0957-4484/23/35/355101
16	A tumor-targeting near-infrared laser-triggered drug delivery system based on GO@Ag nanoparticles for chemo- and photothermal therapy and X-ray	Jinjin Shi	Biomaterials	2014	doi.org/10.1016/j.biomaterials.2014.03.042
17	Folic acid-functionalized graphene oxide nanosheets via plasma etching as a platform to combine NIR anticancer phototherapy and targeted drug delivery	Nicolò Mauro	Materials Science and Engineering: C	2020	doi.org/10.1016/j.msec.2019.110201

Table S2. Table displaying the nanocarrier characteristics of each of the seventeen publications analysed

No.	Composition of Nanocarrier	Method of fabrication	Therapeutic Application	Size of particles (nm)	Size of nanostructure (nm)		Ratio of components	Shape/ Morphology	Zeta Potential (mV)	Ref.
					Size/thickness /height of GO (nm)	Size/thickness /height of functionalised graphene (nm)				
1	GO modified with hyaluronic acid and Arg-gly-asp peptide (GO-HA-RGD)	GO synthesised by modified Hummer's method was then functionalised with HA through the EDC-mediated amidation reaction, followed by RGD through a Michael-type addition reaction	Cancer	70 – 490	Height = 1.2	Height = 13	43.19 wt% (GO) 49.34 wt% (HA) 7.47 wt% (RGD)	Almost circular with a course surface	NR	43
2	GO functionalised with hydroxymethyl cellulose and polyanionic cellulose (GO-PAC/HEC)	GO synthesised via a modified Hummer method and then stirred with PAC and HEC.	Cancer	30-200	Height = 1.592	Height = ≥3.084 (GO-PAC/HEC)	47.1 wt% (GO) 52.9 wt% (PAC/HEC)	Mottlings and floccules on surface when functionalised	~ -10 to -30 dependent on GO:DOX ratio	63
3	Nanoscale GO conjugated with PEG and poly(allylamine hydrochloride) which is then modified with 2,3-dimethyl maleic anhydride (NGO-PEG-DA) or succinic acid (NGO-PEG-SA)	GO prepared using modified Hummers method, then functionalised through coating with PEG and PAH. The PAH is then modified with either DA or SA in alkaline conditions.	Cancer	NR	NR	~70	~25.3% PEG content (other components NR)	NR	NGO-PEG-SA = -37.1 ± 1.05 NGO-PEG-DA = -34.4 ± 0.19	64

NR = Not Recorded, NA = Not Applicable, No. = publication/paper number, Ref. = Reference

Table S2 continued.

4	Functionalised GO modified with mitochondria-targeting hypericin (GO-PEG-SS-HY)	GO-PEG fabricated by carbodiimide catalysed amide formation and further functionalization with SS and HY followed sequential covalent conjugation reaction methods.	Cancer	NR	Height = 1	Width = 200, height = 8	NR	NR	NR	65
5	GO functionalised with triazine dendrimer and modified with Fe_3O_4 functionalised by polyethylene glycol (GO-TD-Fe_3O_4@PEG)	GO synthesised by a modified Hummer's method. GO-DT then fabricated by the divergent method and Fe_3O_4 nanoparticles were then attached to its surface.	Cancer	Fe_3O_4 NPs = 30	Thickness = 41	Thickness = 144.21	NR	Spherical, rough surface, regular spherical Fe_3O_4@PEG nanoparticles dispersed on graphene surface	GO = -28.4, GO-TD-Fe_3O_4@PEG = -39	66
6	Chelating ZnO-dopamine on the surface of GO. (Zn-d-rGO)	ZnO nanoparticles covalently chelated with catechol end groups in dopamine through In situ modification and then conjugated to surface of GO	Cancer	Zn-d 3 average size = 23	Thickness = 41	Thickness = 28-38	NR	Curtain and planner structure of GO seen throughout nanocarrier Mesoporous structure	Zn-d 3 = + 17.9 Zn-d 3 r-GO = NR	67

NR = Not Recorded, NA = Not Applicable, No. = publication/paper number, Ref. = Reference

Table S2 continued.

7	GO/poly(2-hydroxyethylmethacrylate)-g-poly(lactide)-b-polyethyleneglycol-b-poly(2-hydroxyethylmethacrylate)-g-poly(lactide) (GO/(PHEMA-g-PLA)-b-PEG-b-(PHEMA-g-PLA)	Synthesised via reversible addition fragmentation chain reaction and ring open polymerisation	Cancer	Average diameter 51.13 ± 5	Size = 28.44	Size = 125	NR	Folded and wrinkled	-22.8	68
8	GO decorated with folic acid grafted bovine serum albumin (FA-BSA/GO)	Fabricated by the physical adsorption of FA-BSA on the graphene oxide	Cancer	NA	Height = 1.29 ± 0.52 Size = 114.9 ± 2.14	Height = 2.29 ± 0.32 Size = 73.7 ± 1.30	1:1 to 4:1 ratio of DOX:FA-BSA/GO	Lamellar structure with no appreciable aggregation	~-19 to -20 at pH 7.4	69
9	GO functionalised with dextran and hematin (NGO-HDex)	NGO synthesised through a modified Hummers method and the composite was then fabricated by the one pot reduction of NGO in the presence of hematin-dextran conjugate	Cancer	NA	Size = 178	Size = 220-240 Thickness = 3.6-4.3	HDex wt% 42-78	NR	NGO = -28.7 NGO-HDex = -23.0 to -11.7 (depending on ratio of NGO-HDex)	70
10	Graphene Oxide (GO)	Fabricated by a modified Hummer's method	Drug delivery	NA	Height = 0.8-1.0	Height = 0.8-1.0	NA	Rough Surface compared to pristine graphene	NR	71

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Table S2 continued.

11	Fe_3O_4 nanoparticles and GO nanosheets incorporated into chitosan microspheres (Fe_3O_4/GO/Chitosan)	GO prepared by Marcano's method. Nanohybrid fabricated by stirring of Fe_3O_4 and GO in chitosan solution	Drug delivery	NR	NR	NR	Multiple conditions	Compact surface and spherical morphology	NR	72
12	Graphene nanosheet functionalised with Pluronic F127 (PF127/GN)	Simultaneous reduction of GO and functionalization with PF127	Cancer	NA	Average thickness = 0.876 Size = 80	Average thickness = 9.646	Graphene = 15 wt%	NR	NR	73
13	GO modified with 1-(10-bromoanthracene-9-yl)-1H-imidazole-4,5-dicarboxylic acid (GO-A-Im)	An ultrasound assisted copper catalysed cross coupling reaction used to synthesise A-Im. GO synthesised using modified Hummer's method then functionalised with A-Im	Cancer	NA	Size = 50	Size = 75	NR	Small round pieces distributed on GO flakes	NR	74
14	A PEG and FA conjugated GO decorated with gold nanoparticles (GO-PEG-FA/GNP)	GO was synthesised through oxidising graphite powder and then functionalised with PEG and FA. GNPs were synthesised through a citrate mediated reduction and decorated onto the functionalised GO	Cancer	GNPs = 8±2	Hydrodynamic diameter = 735	Hydrodynamic diameter = 128	Content of GNPs ~ 8 wt%	Crumpled, wrinkled porous structure of GO, GNPs had uniform spherical structure	NR	75

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Table S2 continued.

15	Graphene oxide (GO)	GO processed by sonication to obtain small-size graphene nanosheets	Cancer	NA	Size = 100, thickness = 0.8-1.5	Thickness ~ 2 nm	NA	Single or double layered graphene structure	NR	76
16	GO decorated with Ag nanoparticles and functionalised with DSPE-PEG2000-NGR (GO@Ag-DOX-NGR)	Ag nanoparticles deposited onto GO through a hydrothermal reaction.	Cancer	Ag NPs= 5-15	NR	NR	NR	Ag nanoparticle s deposited on GO sheets	-29.1 ± 1.9	77
17	Folic acid-functionalised PEGylated GO (GO-PEG-Fol)	A nano-GO sheet was fabricated through non-equilibrium plasma etching of GO and then functionalised through amide coupling and cycloaddition.	Cancer	NA	Width = 30-40 Thickness = 1	Size = 35, Thickness = 1.25	NR	Unilamellar GO sheets, roughness from PEG chains	-28 (GO-PEG-Fol/Doxo = -5)	78

NR = Not Recorded, NA = Not Applicable, No. = publication/paper number, Ref. = Reference

Table S3. Table displaying the payload characteristics and drug loading information, including both the drug loading capacity and drug loading/encapsulation efficiency, for the seventeen publications.

	Payload Characteristics			Drug Loading		
No.	Type of Payload	Loading Method	Payload	Drug loading capacity (%)	Drug loading/encapsulation efficiency (%)	Ref.
1	Small molecule	π-π stacking and hydrogen bonding	DOX	NR	72.90	43
2	Small molecule	π-π stacking and hydrogen bonding	DOX	216% (1:4 GO:DOX) 152% (1:2 GO:DOX) 49% (1:05 GO:DOX)	54% (1:4 GO:DOX) 76% (1:2 GO:DOX) 98% (1:0.5 GO:DOX)	63
3	Small molecule	π-π stacking and hydrogen bonding	DOX	NR	~50	64
4	Small molecule	π-π stacking and hydrogen bonding	DOX	80	NR	65
5	Small molecule	π-π stacking and hydrogen bonding and hydrophobic interactions	DOX	9.26	92.6	66
6	Small molecule	π-π stacking and hydrogen bonding	DOX	Zn-d 3-rGO = 39.9% GO = 39.6 %	Zn-d 3-rGO = 99.7 % GO = 99.3%	67
7	Small molecule	π-π stacking and hydrogen bonding	DOX	NR	82 ± 1.12	68
8	Small molecule	π-π stacking and hydrogen bonding	DOX	30.43	NR	69
9	Small molecule	π-π stacking and hydrogen bonding	DOX	Maximum = 346 %	96.5 %	70
10	Small molecule	π-π stacking and hydrogen bonding	DOX	NR	91	71
11	Small molecule	π-π stacking and hydrogen bonding	DOX	Maximum = 18.69 ± 5.6	Maximum = 80.9 ± 8.1	72
12	Small molecule	π-π stacking and hydrogen bonding	DOX	289	NR	73
13	Small molecule	π-π stacking and hydrogen bonding	DOX	NR	91	74

NR = Not Recorded, NA = Not Applicable, No. = publication/paper number, Ref. = Reference

Table S3 continued.

14	Small molecule	π-π stacking and hydrogen bonding	DOX	GO-PEG-FA-SH = 67 GO-PEG-FA/GNPs = 76	GO-PEG-FA-SH = 72 GO-PEG-FA/GNPs = 84	75
15	Small molecule	π-π stacking and hydrogen bonding	ADR (DOX)	NR	93.6	76
16	Small molecule	Ester bond linkage	DOX	NR	82	77
17	Small molecule	π-π stacking, hydrogen bonding and hydrophobic interactions	DOX	33.3	98.65	78

NR = Not Recorded, NA = Not Applicable, No. = publication/paper number, Ref. = Reference

Table S4. A table displaying the experimental conditions under which the drug release was recorded, including the temperature and pH. The maximum cumulative release and the timeframe of the measurement was recorded. Information on the biological assays undertaken by each publication is also recorded.

	Drug Release Conditions				Maximum Cumulative Drug Release				Biological Assays			
No.	**Stimulation method**	**pH**	**Temp-erature (°C)**	**Nanocarrier**	**Cumulative release (%)**	**Condition**	**Time (hr)**	**Comments**	**Pre-clinical study**	**Model (cell line or animal)**	**Suggested mechanism of cellular uptake**	**Ref.**
1	pH response	5.5, 7.4	37	GO-HA-RGD/DOX	30.2	pH 5.0	72	Sustained release	*In vitro*	SKOV-3 and HOSEpiC	Uptake facilitated by the synergistic behaviour of CD44-HA and integrin-RGD mediated endocytosis	43
					7.6	pH 7.4						
2	pH response	5.0, 7.4	37	GO-PAC/HEC/DOX	80	pH 5.0	35	Fast release up to 12 hours (~69% DOX release)	*In vitro*	SKOV3 and SKOV3/DDP	NPs attach to cytomembrane and enter cells through endocytosis	63
					20	pH 7.4						
3	pH response	5.0, 6.8, 7.4	37	NGO-PEG-DA/DOX	31.4	pH 5.0	24	More rapid release from NGO-PEG-DA/DOX due to the electrostatic repulsion between DOX and DA which is positively charged under acidic pH	*In vitro*	MCF-7/WT, MCF-7/ADR	pH dependent cellular uptake	64
					13.7	PH 6.8						
					~6	pH 7.4						
				NGO-PEG-SA/DOX	23	pH 5.0						
					10.2	PH 6.8						
					5.4	pH 7.4						

NR = Not Recorded, NA = Not Applicable, No. = publication/paper number, Ref. = Reference

Table S4 continued.

4	pH response	5.5, 7.4	37	GO-PEG-SS-HY/DOX	29	pH 5.5	48	Most rapid release between 4 and 24 hours at pH 5.5	*In vitro/ In vivo*	MCF-10A, MDA-MB-231, MCF-7, BALC/c nude mice,	Endocytosis	65
					11	pH 7.4						
5	pH response	5.0, 6.8, 7.4	37	GO-TD-Fe3O4@PEG/DOX	97.3	pH 5.0	72	Sustained release	*In vitro*	MCF-10A, MCF-7	Endocytosis or diffusion	66
					69.5	PH 6.8						
					66.1	pH 7.4						
6	pH response	5.4, 7.4	37	Zn-d3-rGO/DOX	78	pH 5.4	312	Long time frame to measure release	*In vitro*	T47D, MCF-10A	NR	67
					52	pH 7.4						
7	pH response	5.4, 7.4	37	GO/(PHEMA-g-PLA)-b-PEG-b-(PHEMA-g-PLA/DOX	41.2	pH 5.4	72	Rapid release for 10 hours then more sustained to 72 hours	*In vitro*	4T1	Energy dependent endocytosis	68
					24.7	pH 7.4						
8	pH response	5.0, 7.4	37	FA-BSA/GO/DOX	70	pH 5.0	192	Rapid release before 12 hours then more sustained release after	*In vitro*	MCF-7, A549	FA receptor mediated endocytosis	69
					57	pH 7.4						
9	pH response	5.5, 7.4	37	NGO-HDex/DOX	27.3	pH 5.5	144	Controlled and sustained drug release profile over 144 hours	*In vitro*	MCF-7/ADR	Not elucidated to	70
					20.6	pH 7.4						

NR = Not Recorded, NA = Not Applicable, No. = publication/paper number, Ref. = Reference

Table S4 continued.

10	pH response	2.0, 7.0, 10.0	NR	GO/DOX	71	PH 2.0	30	Stronger hydrogen bonding under basic than acidic conditions – but both have partial dissociation of hydrogen bonding compared to neutral pH	NA	NA	NA	71
					11	PH 7.0						
					25	PH 10.0						
11	NIR and Ultrasound	7.4	37	Fe3O4/GO/Chitosan/DOX	37	Normal	1	With each pulse of NIR or ultrasound there is a burst release and therefore the release rate jumps	NA	NA	NA	72
					46	NIR						
					44	Ultrasound						
12	pH response	5.0, 7.0, 9.0	37	PF127/GN/DOX	56	pH 5.0	90	Higher DOX release under acidic conditions compared to basic is due to the higher solubility of DOX under acidic conditions Rapid release up to 20 hours then more sustained till maximum	*In vitro*	MCF-7	Not elucidated to	73
					15	PH 7.0						
					25	PH 9.0						

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Table S4 continued.

13	pH response	3.0, 5.4, 7.4	NR	GO-A-Im/DOX	73	PH 3.4	75	Rapid DOX release after 5 hours and then more continued sustained release to follow. Due to the different types of interactions	*In vitro /In vivo*	T47D, BALB/c mice injected with 4T1 murine cells	NR	74
					70	PH 5.4						
					33	PH 7.4						
14	pH response	4.0, 7.4	37	GO-PEG-FA-SH/DOX	38.5	PH 4.0	295	The DOX-loaded GO-PEG-FA/GNPs have higher cumulative release values	*In vitro*	MCF-7	NR	75
					21.9	PH 7.4						
				GO-PEG-FA/GNPs/DOX	42.8	PH 4.0						
					31.3	PH 7.4						
15	pH response	5.0, 7.2, 9.0	37±0.2	GO/ADR	16.1	PH 5.0	46	Acidic and basic conditions both had more rapid DOX release than neutral conditions	*In vitro*	MCF-7, MCF-7/ADR	Both endocytosis-dependent and independent manners (passive diffusion)	76
					5.3	PH 7.2						
					7.4	PH 9.0						
16	NIR light	NA	NA	GO@Ag/DOX	45.6	NIR	24	When NIR was present chemical bonding was broken and more DOX released; more also accumulated in the nucleus	*In vitro/ In vivo*	MCF-7, tumour-bearing mice	Endocytosis	77
					12.0	No NIR						

NR = Not Recorded, NA = Not Applicable, No. = publication/paper number, Ref. = Reference

Table S4 continued.

17	pH response	5.5, 7.4	37	GO-PEG-Fol/DOX	~22	PH 5.5	48	Nanocarrier released the drug in a time-dependent manner without the burst effect that is seen with free DOX	*In vitro*	MCF-7, MDA-MB-231, HDFa	Folate-mediated endocytosis	78
					~11	PH 7.4						

Table S5. This table displays the numerical results of the statistical analysis. The R^2 value, Sy.x value, gradient, and *P* value are recorded for each of the four kinetic models, for each nanohybrid under the different conditions recorded by the publications. The results are given to 4 decimal places.

No.	Nano carrier and Release Condition	Zero Order Model				First Order Model				Higuchi Model				Weibull Model			
		R^2	Sy.x	K_0	*P* value	R^2	Sy.x	K_1	*P* value	R^2	Sy.x	K_H	*P* value	R^2	Sy.x	β	*P* value
1	GO-HA-RGD (pH 5.5)	0.8597	4.0460	0.3754	0.0003	0.8746	0.0206	-0.0020	0.0002	0.9422	2.5970	4.1900	<0.0001	0.9611	0.1463	0.6868	<0.0001
	GO-HA-RGD (pH 7.4)	0.7367	1.3790	0.0866	0.0031	0.7390	0.0063	-0.0004	0.0030	0.8464	1.0530	0.9913	0.0004	0.8996	0.2068	0.5885	<0.0001
2	GO-PAC/HEC (pH 5.0)	0.6516	14.0100	1.4560	0.0085	0.7768	0.1097	-0.0155	0.0017	0.8431	9.4020	11.2100	0.0005	0.9694	0.1317	0.4790	<0.0001
	GO-PAC/HEC (pH 7.4)	0.6231	4.2050	0.4109	0.0114	0.6409	0.0214	-0.0022	0.0095	0.8261	2.8560	3.1950	0.0007	0.9502	0.1122	0.3106	<0.0001
3	NGO-PEG-DA (pH 5.0)	0.7288	5.6380	1.0000	0.0145	0.7710	0.0273	-0.0054	0.0093	0.8783	3.7760	6.2000	0.0018	0.8823	0.3178	0.5784	0.0017
	NGO-PEG-DA (pH 6.8)	0.9860	0.5752	0.4491	0.0007	0.9869	0.0026	-0.0021	0.0006	0.9609	0.9626	2.6140	0.0033	0.9720	0.1224	0.4757	0.0020
	NGO-PEG-DA (pH 7.4)	0.3289	0.7194	0.0521	0.2341	0.3297	0.0033	-0.0002	0.2333	0.4790	0.6339	0.3750	0.1276	0.6881	0.1123	0.1420	0.0823
	NGO-PEG-SA (pH 5.0)	0.8149	2.7040	0.5874	0.0137	0.8389	0.0129	-0.0030	0.0103	0.9244	1.7280	3.7480	0.0022	0.9273	0.1383	0.3774	0.0020
	NGO-PEG-SA (pH 6.8)	0.9118	0.8705	0.2898	0.0030	0.9177	0.0039	-0.0014	0.0026	0.9498	0.6563	1.7660	0.0010	0.9488	0.1248	0.4064	0.0010
	NGO-PEG-SA (pH 7.4)	0.4873	0.6833	0.0690	0.1230	0.4875	0.0031	-0.0003	0.1229	0.6830	0.5373	0.4885	0.0426	0.8610	0.0789	0.1489	0.0076

NR = Not Recorded, NA = Not Applicable, No. = publication/paper number, Ref. = Reference

Table S5 continued.

4	GO-PEG-SS-HY (pH 5.5)	0.7834	5.5160	0.5572	0.0035	0.8080	0.0270	-0.0029	0.0024	0.9150	3.4550	4.8180	0.0002	0.9451	0.2685	0.7420	<0.0001
	GO-PEG-SS-HY (pH 7.4)	0.8061	1.7590	0.1905	0.0025	0.8158	0.0079	-0.0009	0.0021	0.9304	1.0540	1.6370	0.0010	0.9309	0.2553	0.6243	0.0001
5	GO-TD-Fe_3O_4-PEG (pH 5.0)	0.8382	12.7700	0.9711	0.0104	0.9618	0.1224	-0.0205	0.0006	0.9327	8.2350	10.8800	0.0017	0.9817	0.1460	0.8623	0.0001
	GO-TD-Fe_3O_4-PEG (pH 6.8)	0.8707	7.7460	0.6708	0.0066	0.9491	0.0402	-0.0058	0.0010	0.9539	4.6270	7.4400	0.0008	0.9762	0.1146	0.5875	0.0002
	GO-TD-Fe_3O_4-PEG (pH 7.4)	0.8600	8.2610	0.6827	0.0077	0.9315	0.0448	-0.0055	0.0018	0.9453	5.1630	7.6100	0.0011	0.9708	0.1378	0.6413	0.0003
6	Zn-d-3 rGO (pH 5.4)	0.9085	8.3930	0.2445	<0.0001	0.9652	0.0424	-0.0021	<0.0001	0.9846	3.4440	4.5410	<0.0001	0.9870	0.1310	0.6047	<0.0001
	Zn-d-3 rGO (pH 7.4)	0.8866	6.8670	0.1775	<0.0001	0.9137	0.0401	-0.0012	<0.0001	0.9689	3.5960	3.3110	<0.0001	0.9749	0.1507	0.4893	<0.0001
	GO (pH 5.4)	0.5447	9.1330	0.0923	0.0011	0.5871	0.0543	-0.0006	0.0005	0.7012	7.3990	1.8680	<0.0001	0.7854	0.2941	0.2983	<0.0001
	GO (pH 7.4)	0.4561	7.9940	0.0676	0.0041	0.4868	0.0445	-0.4007	0.0027	0.6016	6.8420	1.3860	0.0004	0.6859	0.3441	0.2699	<0.0001
7	GO/(PHEMA-g-PLA)-b-PEG-b-(PHEMA-g-PLA) (pH 5.4)	0.8553	4.2930	0.3590	0.0029	0.8972	0.0215	-0.0022	0.0012	0.9515	2.4850	3.5180	0.0002	0.9830	0.0752	0.2862	<0.0001
	GO/(PHEMA-g-PLA)-b-PEG-b-(PHEMA-g-PLA) (pH 7.4)	0.5818	4.6230	0.1877	0.0461	0.6073	0.0233	-0.0010	0.0389	0.7737	3.4010	2.0090	0.0090	0.9155	0.1507	0.2485	0.0007

NR = Not Recorded, NA = Not Applicable, No. = publication/paper number, Ref. = Reference

Table S5 continued.

8	FA-BSA/GO (pH 5.0)	0.7846	4.9480	0.1434	<0.0001	0.8607	0.0388	-0.0015	<0.0001	0.9091	3.2150	2.4120	<0.0001	0.9772	0.0462	0.2224	<0.0001
	FA-BSA/GO (pH 7.4)	0.9032	3.0740	0.1414	<0.0001	0.9427	0.0181	-0.0011	<0.0001	0.9747	1.5700	2.3110	<0.001	0.9754	0.0505	0.2333	<0.0001
9	NGO-HDex (pH 5.5)	0.9624	1.4320	0.1591	<0.0001	0.9755	0.0060	-0.0008	<0.0001	0.9975	0.3679	2.5960	<0.0001	0.9982	0.0491	0.7256	<0.0001
	NGO-HDex (pH 7.4)	0.9914	0.4737	0.1115	<0.0001	0.9942	0.0020	-0.0006	<0.0001	0.9909	0.4850	1.7830	<0.0001	0.9892	0.0456	0.5493	<0.0001
10	GO (pH 2)	0.8323	9.4940	1.9300	0.0006	0.9360	0.0475	-0.0166	<0.0001	0.9322	6.0360	13.8200	<0.001	0.9123	0.2907	0.8191	<0.0001
	GO (pH 7)	0.5794	2.5280	0.2707	0.0172	0.5928	0.0114	-0.0013	0.0152	0.7161	2.0770	2.0330	0.0040	0.6499	0.9266	1.0960	0.0087
	GO (pH 10)	0.6437	4.3820	0.5377	0.0093	0.6752	0.0214	-0.0028	0.0066	0.7846	3.4080	4.0100	0.0015	0.7796	0.3244	0.5299	0.0016
11	Fe_3O_4/GO/Chitosan (Normal Release)	0.9845	1.6310	37.3500	<0.0001	0.9958	0.0048	-0.2097	<0.0001	0.9990	0.1024	53.5100	<0.0001	0.9877	0.0970	1.1750	<0.0001
	Fe_3O_4/GO/Chitosan (NIR assist)	0.9429	3.4260	47.2600	<0.0001	0.9643	0.0165	-0.2903	<0.0001	0.9690	2.5240	66.8100	<0.0001	0.9337	0.1954	1.1330	<0.0001
	Fe_3O_4/GO/Chitosan (Ultrasound assist)	0.9221	3.5230	41.1900	<0.0001	0.9464	0.0177	-0.2521	<0.0001	0.9538	2.7130	58.2800	<0.0001	0.9096	0.1949	0.9507	<0.0001
12	PF127/GN (pH 5)	0.6961	10.4000	0.5477	0.0002	0.7494	0.0653	-0.0039	<0.0001	0.8444	7.4430	6.2500	<0.0001	0.8964	0.2533	0.5527	<0.0001
	PF127/GN (pH 7)	0.5976	4.1360	0.1530	0.0087	0.6186	0.0200	-0.0008	0.0070	0.7643	3.1650	1.7720	0.0009	0.7734	0.3306	0.3658	0.0008
	PF127/GN (pH 9)	0.6758	5.2130	0.2492	0.0006	0.7080	0.0254	-0.0013	0.0003	0.8405	3.6560	2.7340	<0.0001	0.8397	0.3609	0.4695	<0.0001

NR = Not Recorded, NA = Not Applicable, No. = publication/paper number, Ref. = Reference

Table S5 continued.

13	GO-A-Im (pH 3.4)	0.5645	9.0460	0.4400	0.0012	0.6732	0.0794	-0.0049	0.0002	0.7116	7.3610	5.6740	<0.0001	0.8374	0.1681	0.4707	<0.0001
	GO-A-Im (pH 5.4)	0.6178	9.2160	0.5384	0.0009	0.7175	0.0737	-0.0540	0.0001	0.7600	7.3040	6.5920	<0.0001	0.8626	0.1750	0.5450	<0.0001
	GO-A-Im (pH 7.4)	0.5040	2.9850	0.1293	0.0031	0.5113	0.0175	-0.0008	0.0027	0.6534	2.4930	1.6770	0.0003	0.8166	0.0849	0.2225	<0.0001
14	GO-PEG-FA-SH (pH 4)	0.9831	1.1960	0.0803	0.0001	0.9920	0.0050	-0.0005	<0.0001	0.9983	0.3840	1.8550	<0.0001	0.9911	0.0390	0.4280	<0.0001
	GO-PEG-FA-SH (pH 7.4)	0.9473	1.1310	0.0422	0.0011	0.9542	0.0055	-0.0002	0.0008	0.9902	0.4867	0.9882	<0.0001	0.9958	0.0221	0.3456	<0.0001
	GO-PEG-FA/GNPs (pH 4)	0.9906	0.9999	0.0902	<0.0001	0.9975	0.0032	-0.0006	<0.0001	0.9970	0.5597	2.0720	<0.0001	0.9872	0.0481	0.4389	<0.0001
	GO-PEG-FA/GNPs (pH 7.4)	0.9899	0.6842	0.0595	<0.0001	0.9943	0.0029	-0.0003	<0.0001	0.9948	0.4917	1.3610	<0.0001	0.9786	0.0507	0.3533	0.0002
15	GO (pH 5)	0.9360	1.1380	0.2956	<0.0001	0.9440	0.0051	-0.0014	<0.0001	0.9887	0.4206	2.4880	<0.0001	0.9976	0.0268	0.5345	<0.0001
	GO (pH 7.2)	0.7671	0.6603	0.0814	0.0004	0.7705	0.0030	-0.0004	0.0004	0.9034	0.4253	0.7291	<0.0001	0.9491	0.1001	0.4237	<0.0001
	GO (pH 9)	0.8733	0.5736	0.1074	<0.0001	0.8778	0.0026	-0.0005	<0.0001	0.9597	0.3233	0.9985	<0.0001	0.9742	0.0576	0.4435	<0.0001
16	GO@Ag (NIR laser)	0.9674	3.0990	1.7810	0.0164	0.9868	0.0123	-0.0112	0.0066	0.9931	1.4220	13.2600	0.0034	0.9885	0.0835	1.0540	0.0058
	GO@Ag (No NIR laser)	0.9909	0.4810	0.5285	0.0046	0.9912	0.0022	-0.0025	0.0044	0.9831	0.6552	3.8630	0.0085	0.9943	0.0624	1.1190	0.0028
17	GO-PEG-Fol (pH 5.5)	0.8911	1.8630	0.2953	0.0014	0.9003	0.0091	-0.0015	0.0011	0.9735	0.9193	2.4720	<0.0001	0.9933	0.0347	0.3185	<0.0001
	GO-PEG-Fol (pH 7.4)	0.9944	0.1602	0.1160	<0.0001	0.9947	0.0007	-0.0005	<0.0001	0.9636	0.4091	0.9255	0.0005	0.9220	0.0853	0.2171	0.0023

NR = Not Recorded, NA = Not Applicable, No. = publication/paper number, Ref. = Reference

Figure S1-S17. The linear regression graphs of the zero-order, first-order, Higuchi, and Weibull models for each of the seventeen publications analysed. The equation of the linear regression is displayed as well as the R^2 value for each model under each condition.

Figure S1. Linear regression graphs created using results from Paper 1.[43]

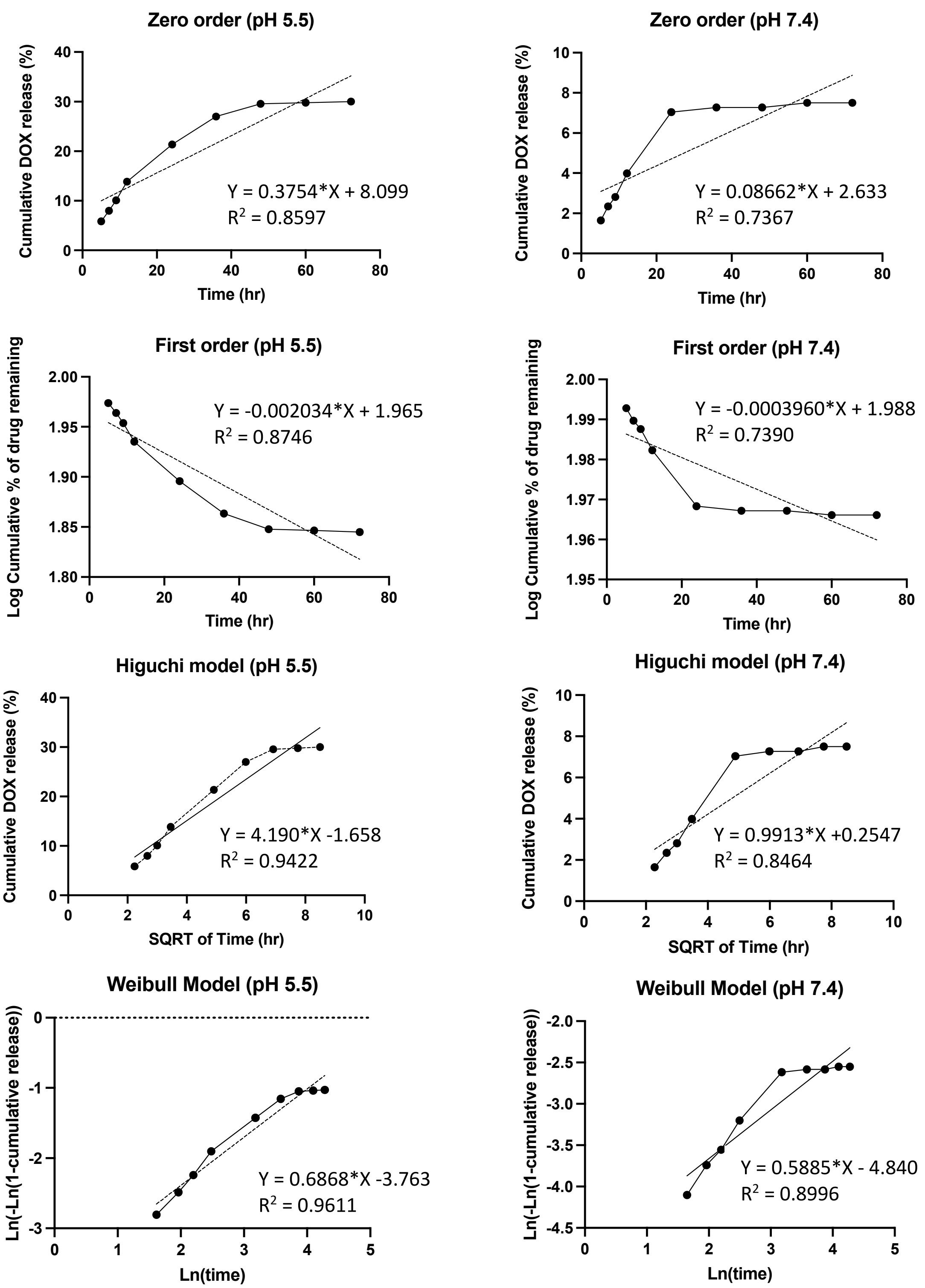


Figure S2. Linear regression graphs created using results from Paper 2.[63]

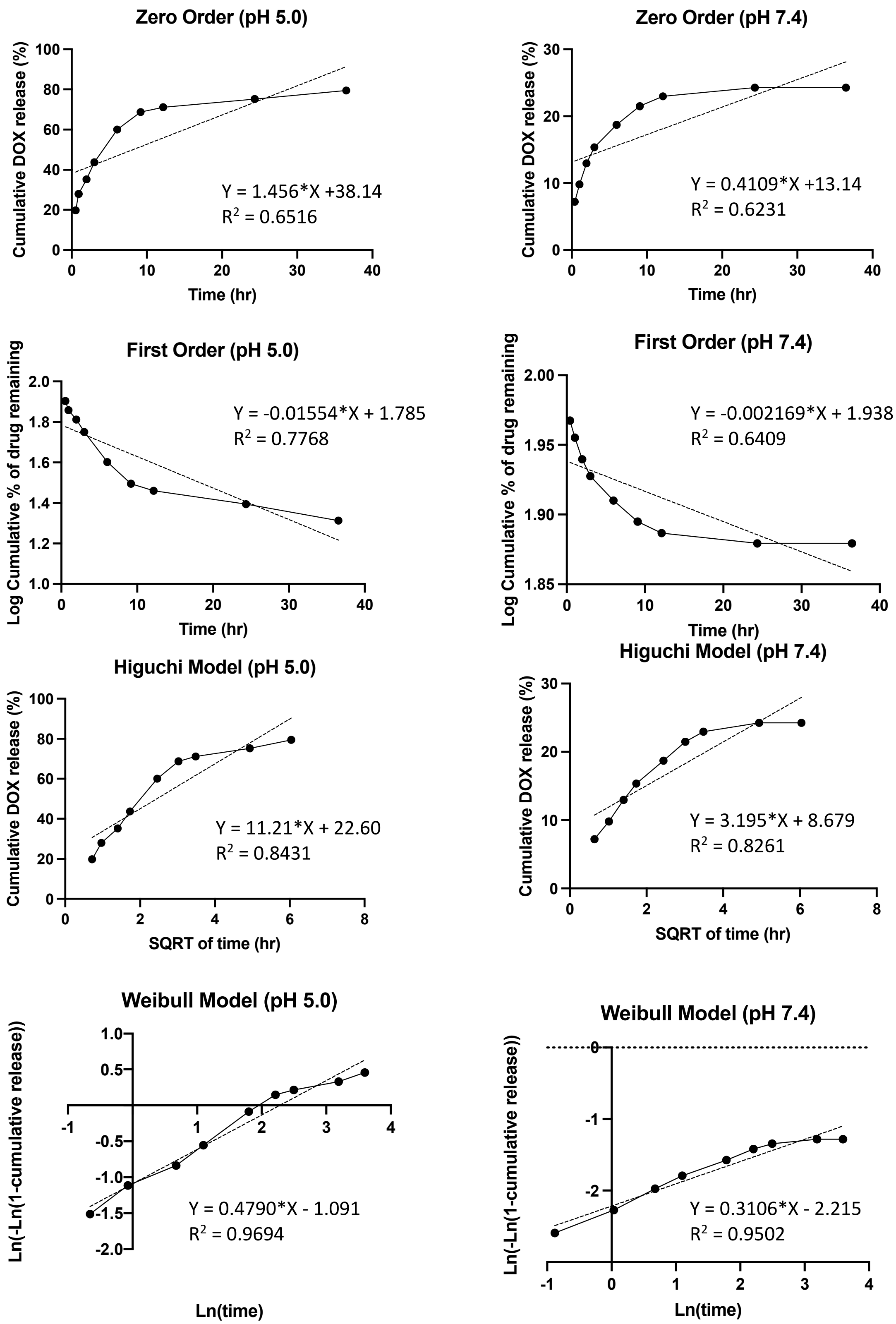
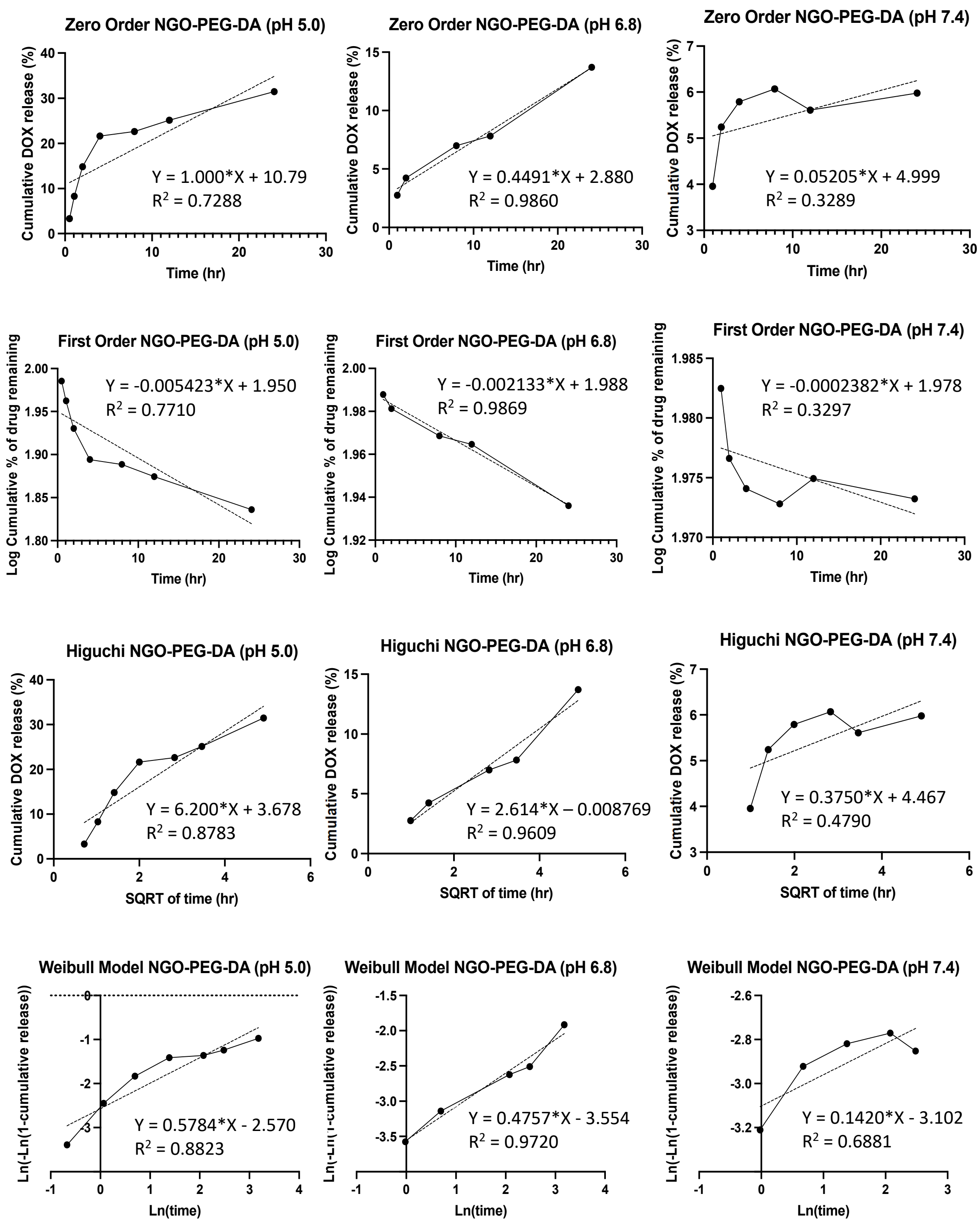
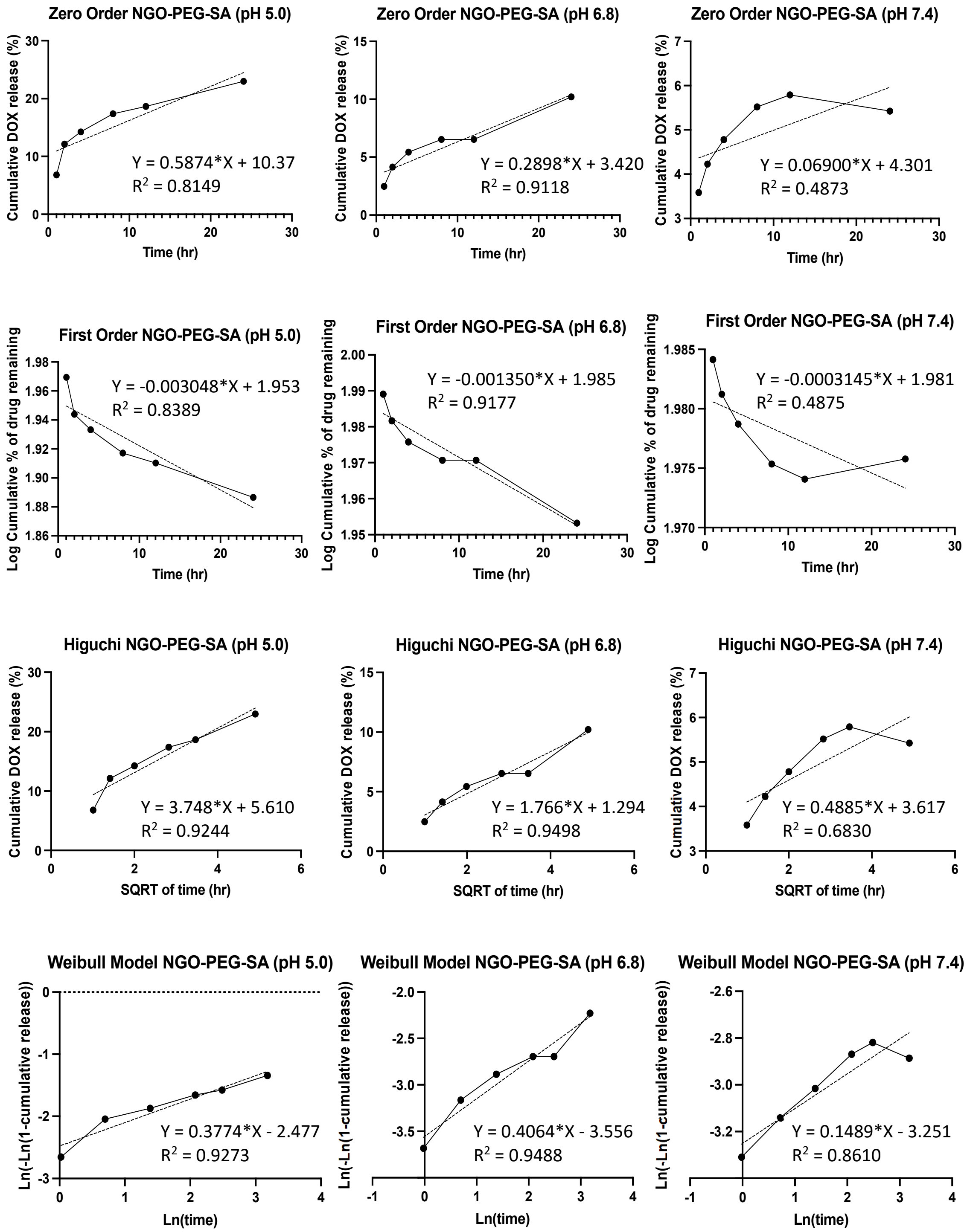


Figure S3. Linear regression graphs created using results from Paper 3.[64]





Zero Order NGO-PEG-SA (pH 5.0)
Y = 0.5874*X + 10.37
R^2 = 0.8149
Zero Order NGO-PEG-SA (pH 6.8)
Y = 0.2898*X + 3.420
R^2 = 0.9118
Zero Order NGO-PEG-SA (pH 7.4)
Y = 0.06900*X + 4.301
R^2 = 0.4873
Cumulative DOX release (%)
Time (hr)
First Order NGO-PEG-SA (pH 5.0)
Y = -0.003048*X + 1.953
R^2 = 0.8389
First Order NGO-PEG-SA (pH 6.8)
Y = -0.001350*X + 1.985
R^2 = 0.9177
First Order NGO-PEG-SA (pH 7.4)
Y = -0.0003145*X + 1.981
R^2 = 0.4875
Log Cumulative % of drug remaining
Time (hr)
Higuchi NGO-PEG-SA (pH 5.0)
Y = 3.748*X + 5.610
R^2 = 0.9244
Higuchi NGO-PEG-SA (pH 6.8)
Y = 1.766*X + 1.294
R^2 = 0.9498
Higuchi NGO-PEG-SA (pH 7.4)
Y = 0.4885*X + 3.617
R^2 = 0.6830
Cumulative DOX release (%)
SQRT of time (hr)
Weibull Model NGO-PEG-SA (pH 5.0)
Y = 0.3774*X - 2.477
R^2 = 0.9273
Weibull Model NGO-PEG-SA (pH 6.8)
Y = 0.4064*X - 3.556
R^2 = 0.9488
Weibull Model NGO-PEG-SA (pH 7.4)
Y = 0.1489*X - 3.251
R^2 = 0.8610
Ln(-Ln(1-cumulative release))
Ln(time)

Figure S4. Linear regression graphs created using results from Paper 4.[65]

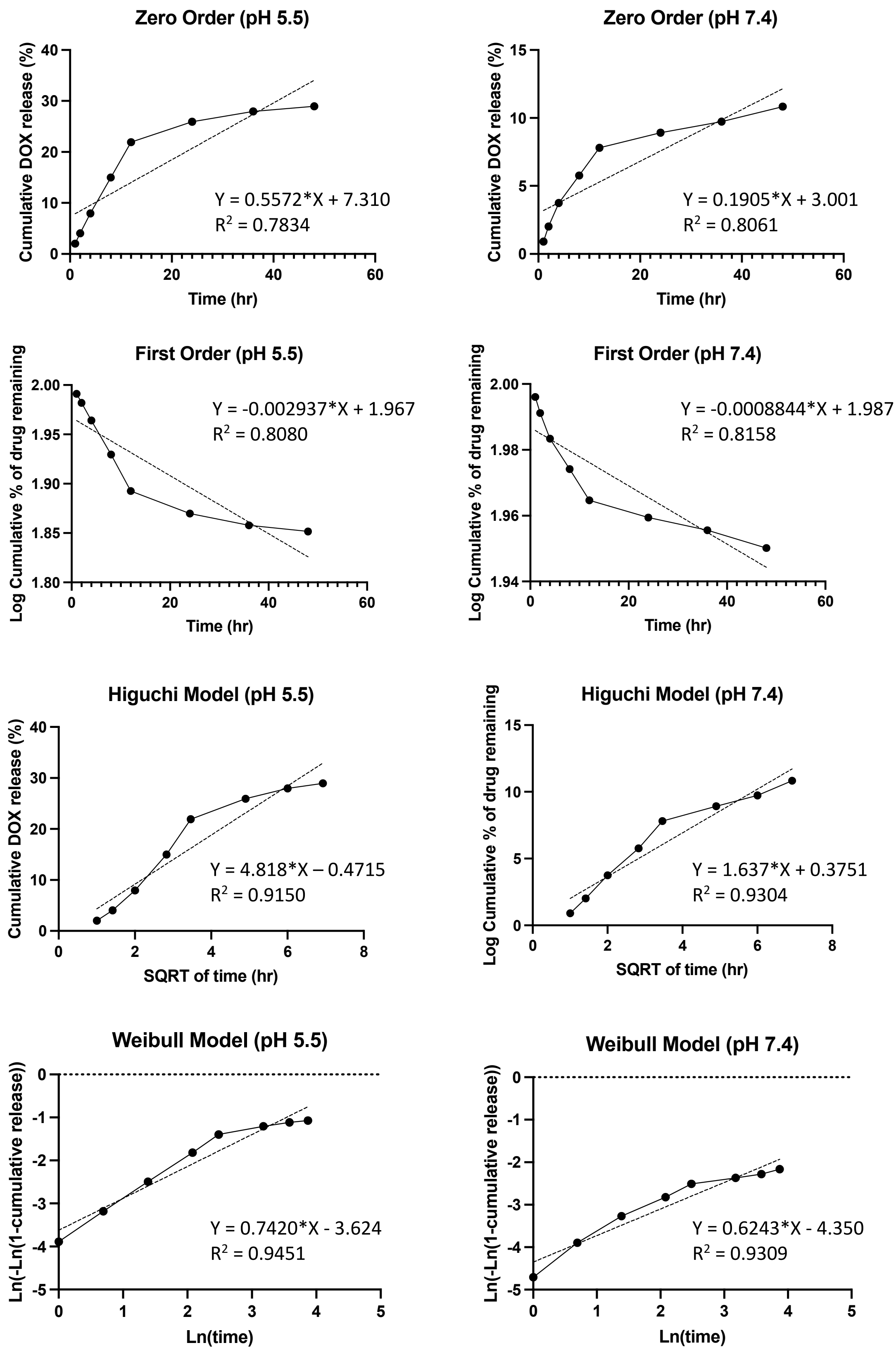


Figure S5. Linear regression graphs created using results from Paper 5.[66]

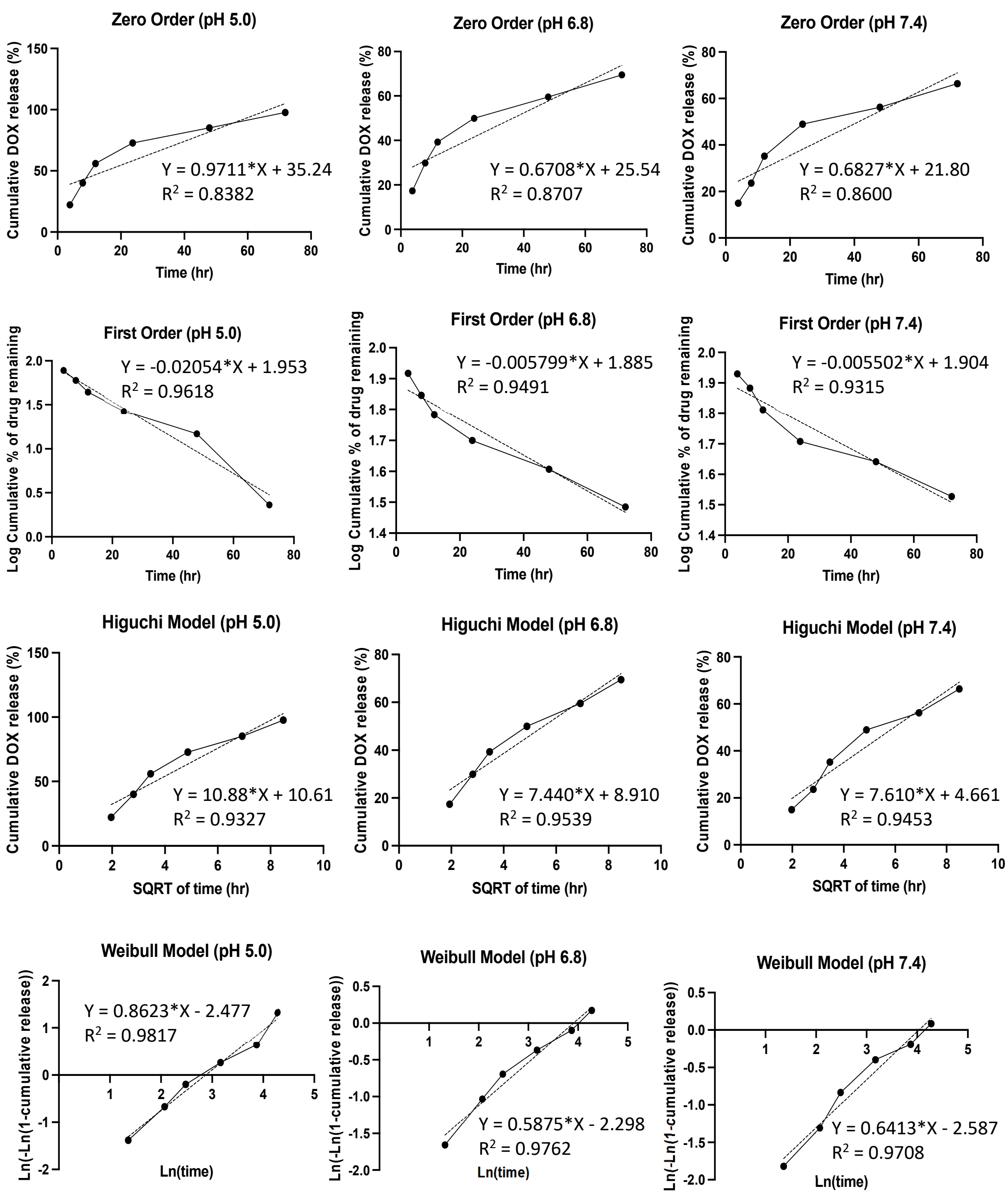
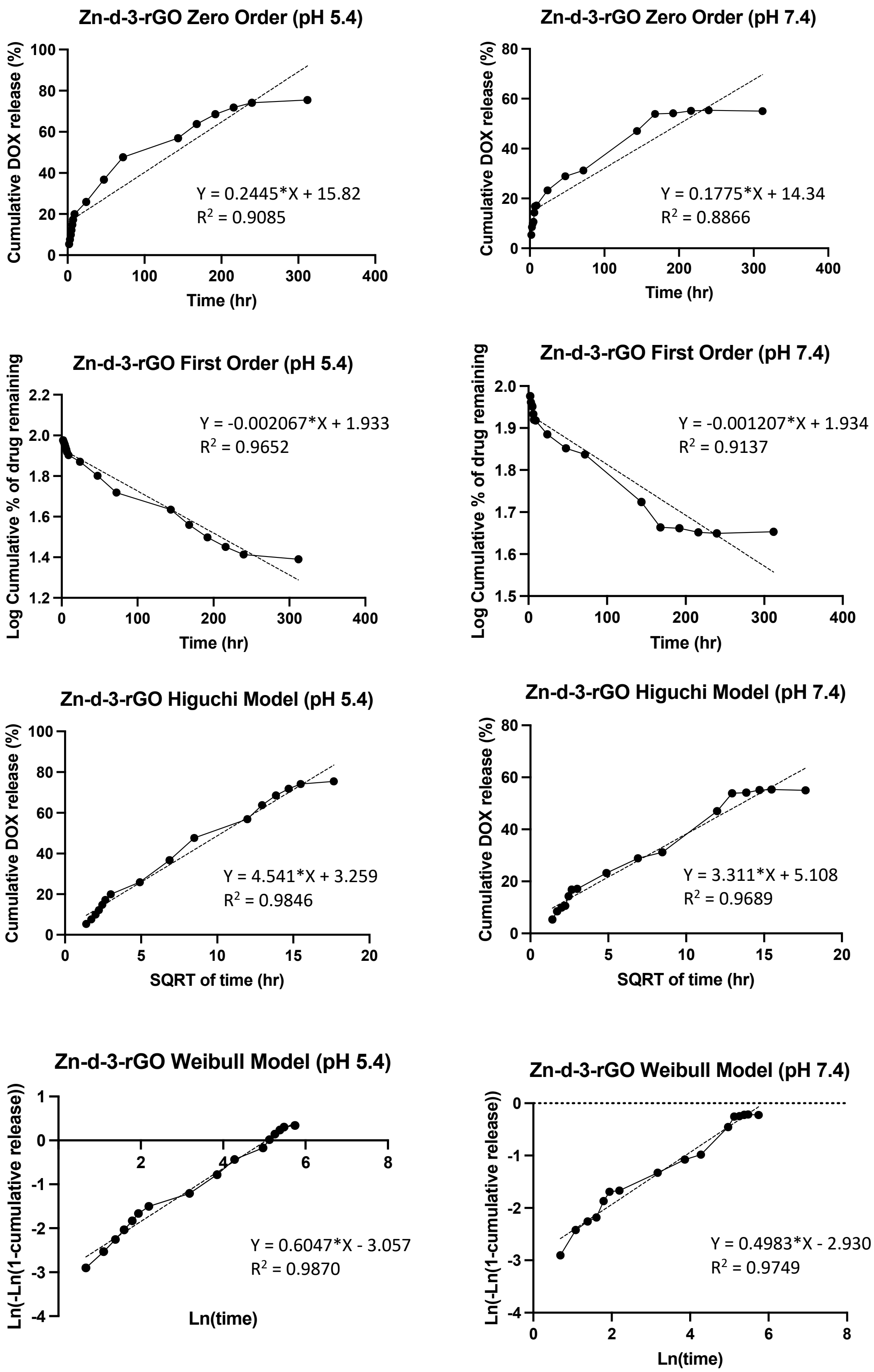
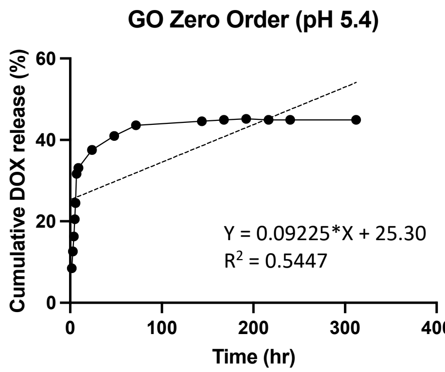
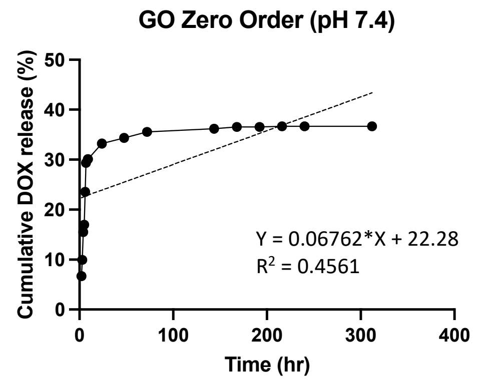
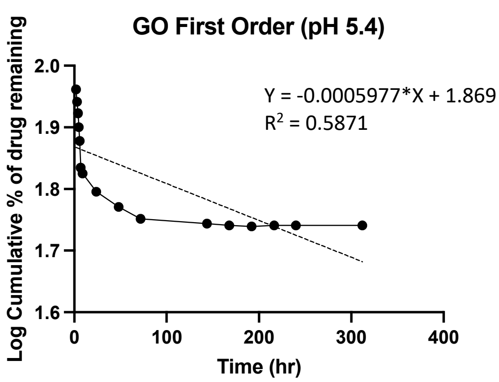


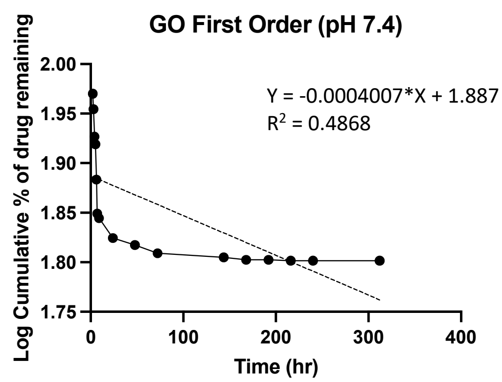
Figure S6. Linear regression graphs created using results from Paper 6.[67]

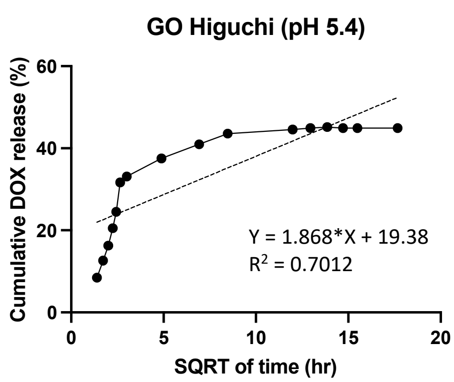


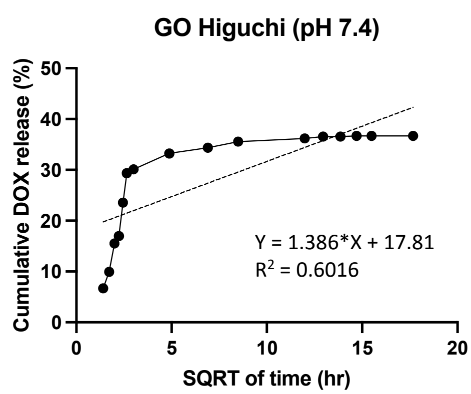

GO Zero Order (pH 5.4)
Cumulative DOX release (%)
Time (hr)
Y = 0.09225*X + 25.30
R2 = 0.5447

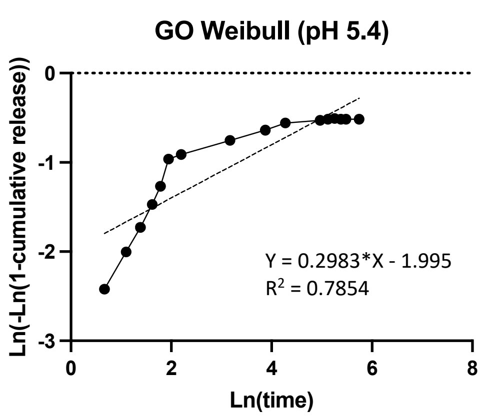

GO Zero Order (pH 7.4)
Cumulative DOX release (%)
Time (hr)
Y = 0.06762*X + 22.28
R2 = 0.4561


GO First Order (pH 5.4)
Log Cumulative % of drug remaining
Time (hr)
Y = -0.0005977*X + 1.869
R2 = 0.5871


GO First Order (pH 7.4)
Log Cumulative % of drug remaining
Time (hr)
Y = -0.0004007*X + 1.887
R2 = 0.4868


GO Higuchi (pH 5.4)
Cumulative DOX release (%)
SQRT of time (hr)
Y = 1.868*X + 19.38
R2 = 0.7012


GO Higuchi (pH 7.4)
Cumulative DOX release (%)
SQRT of time (hr)
Y = 1.386*X + 17.81
R2 = 0.6016


GO Weibull (pH 5.4)
Ln(-Ln(1-cumulative release))
Ln(time)
Y = 0.2983*X - 1.995
R2 = 0.7854

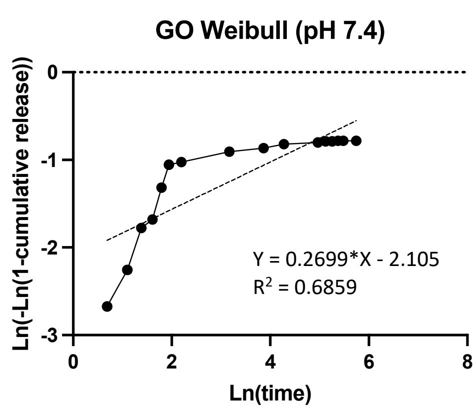

GO Weibull (pH 7.4)
Ln(-Ln(1-cumulative release))
Ln(time)
Y = 0.2699*X - 2.105
R2 = 0.6859

Figure S7. Linear regression graphs created using results from Paper 7.[68]

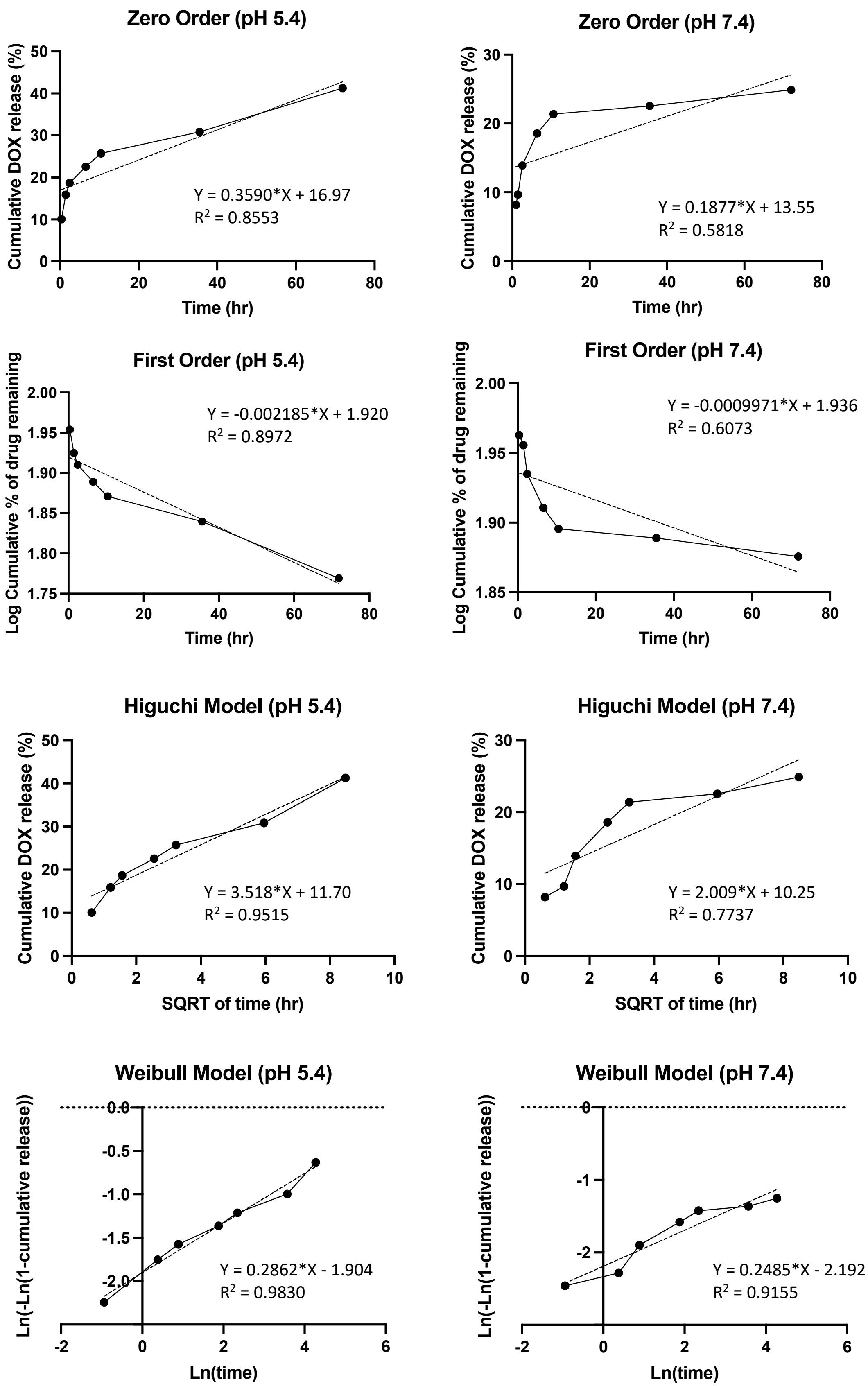


Figure S8. Linear regression graphs created using results from Paper 8.[69]

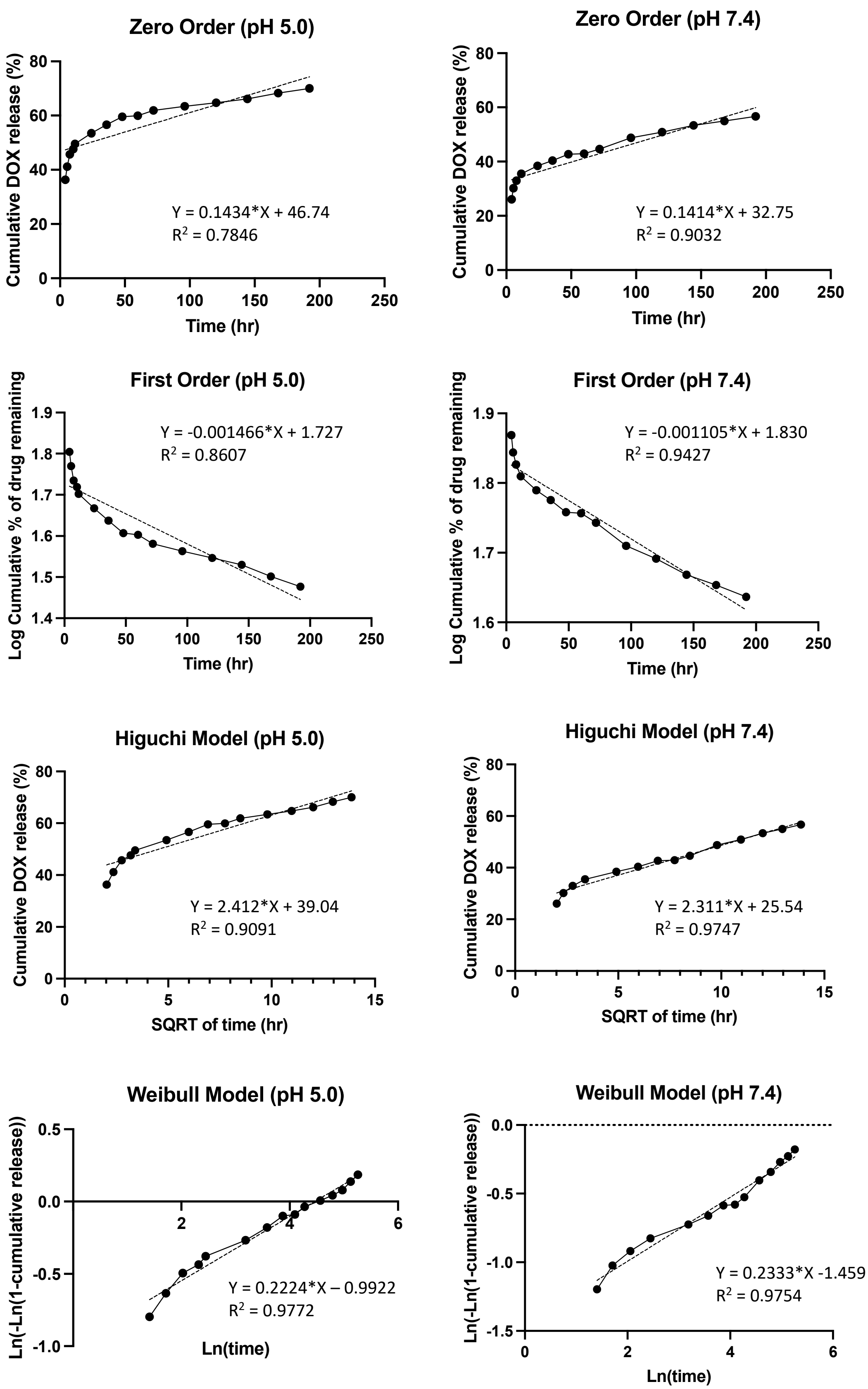


Figure S9. Linear regression graphs created using results from Paper 9.[70]

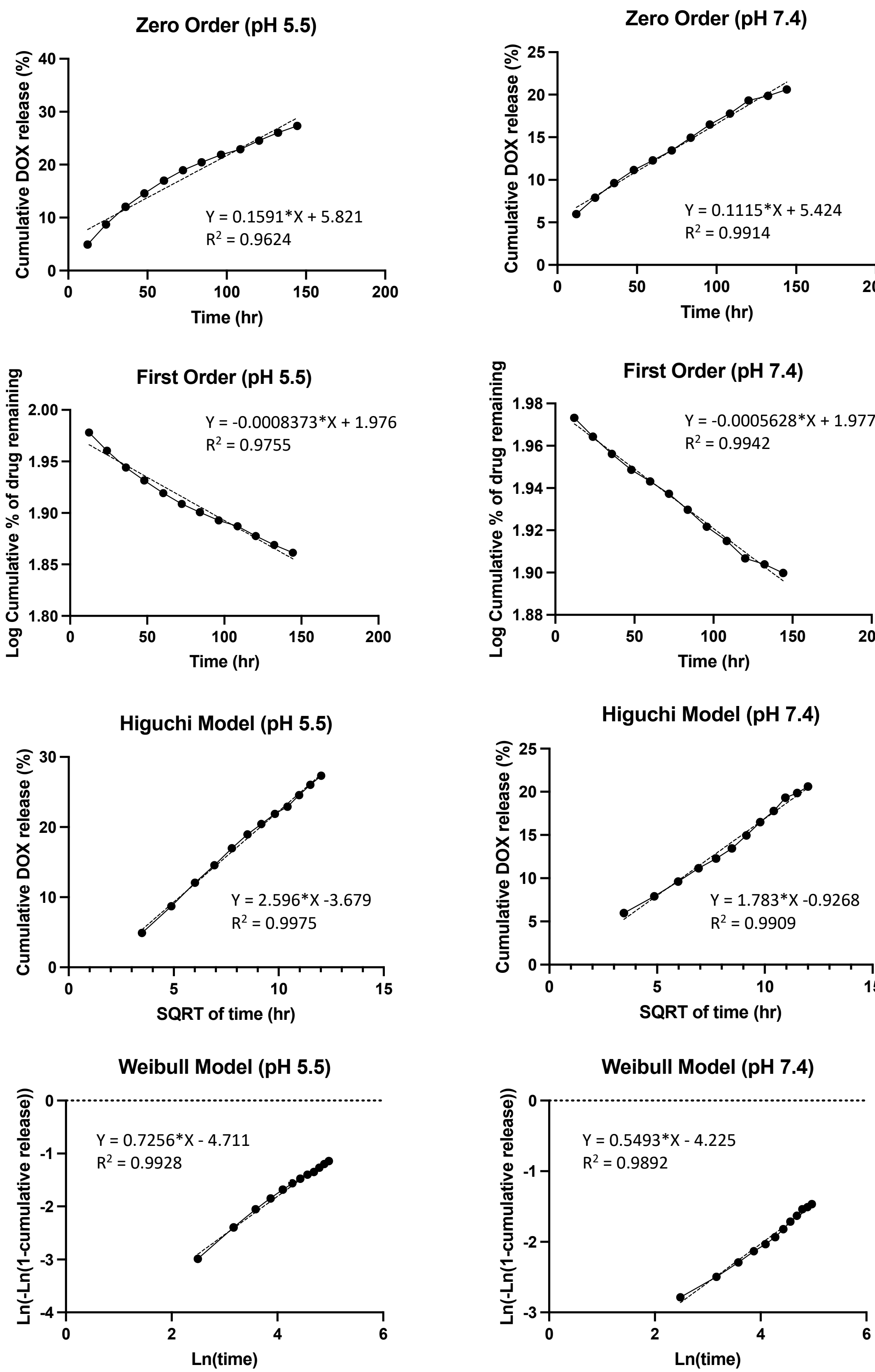


Figure S10. Linear regression graphs created using results from Paper 10.[71]

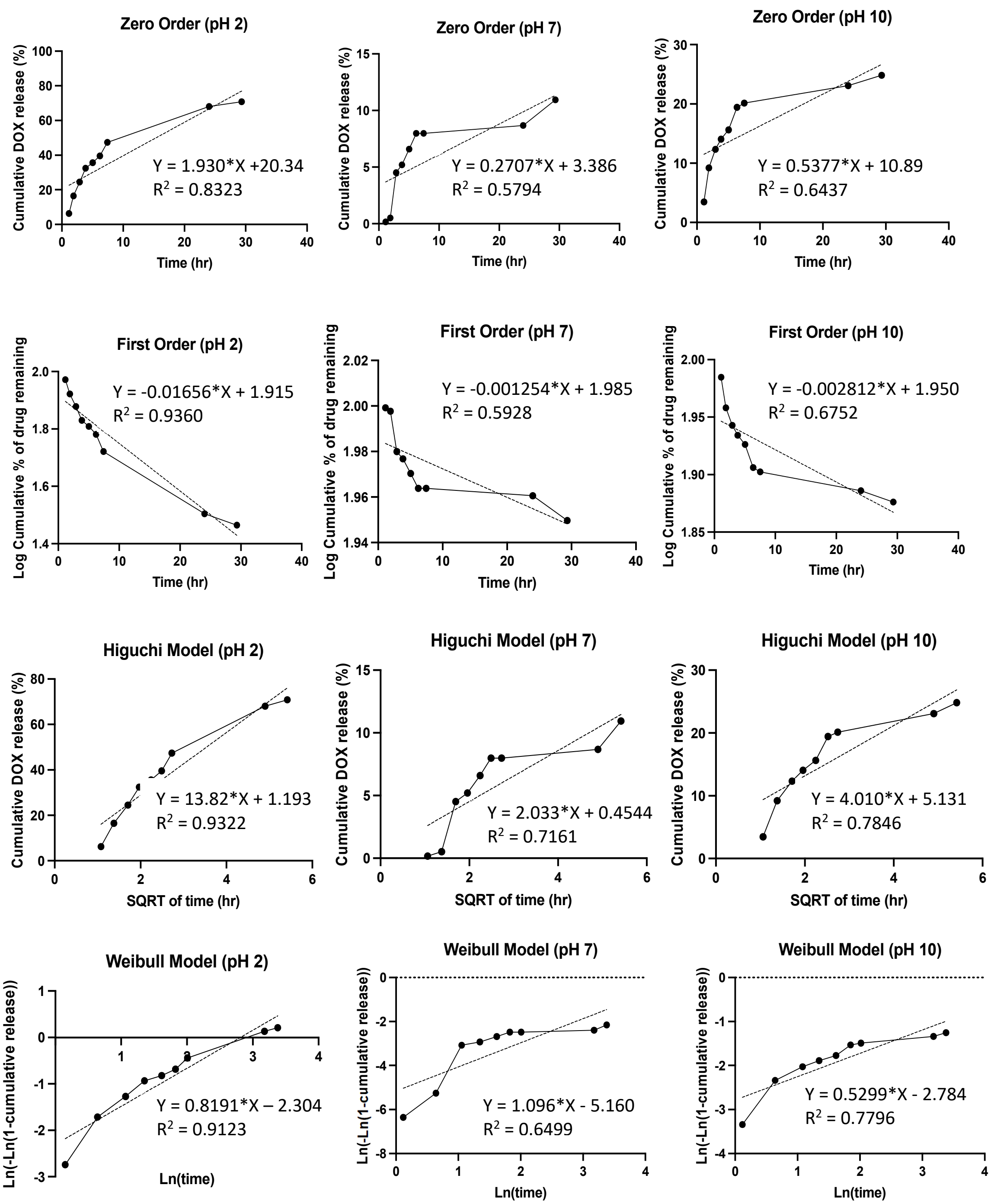


Figure S11. Linear regression graphs created using results from Paper 11.[72]

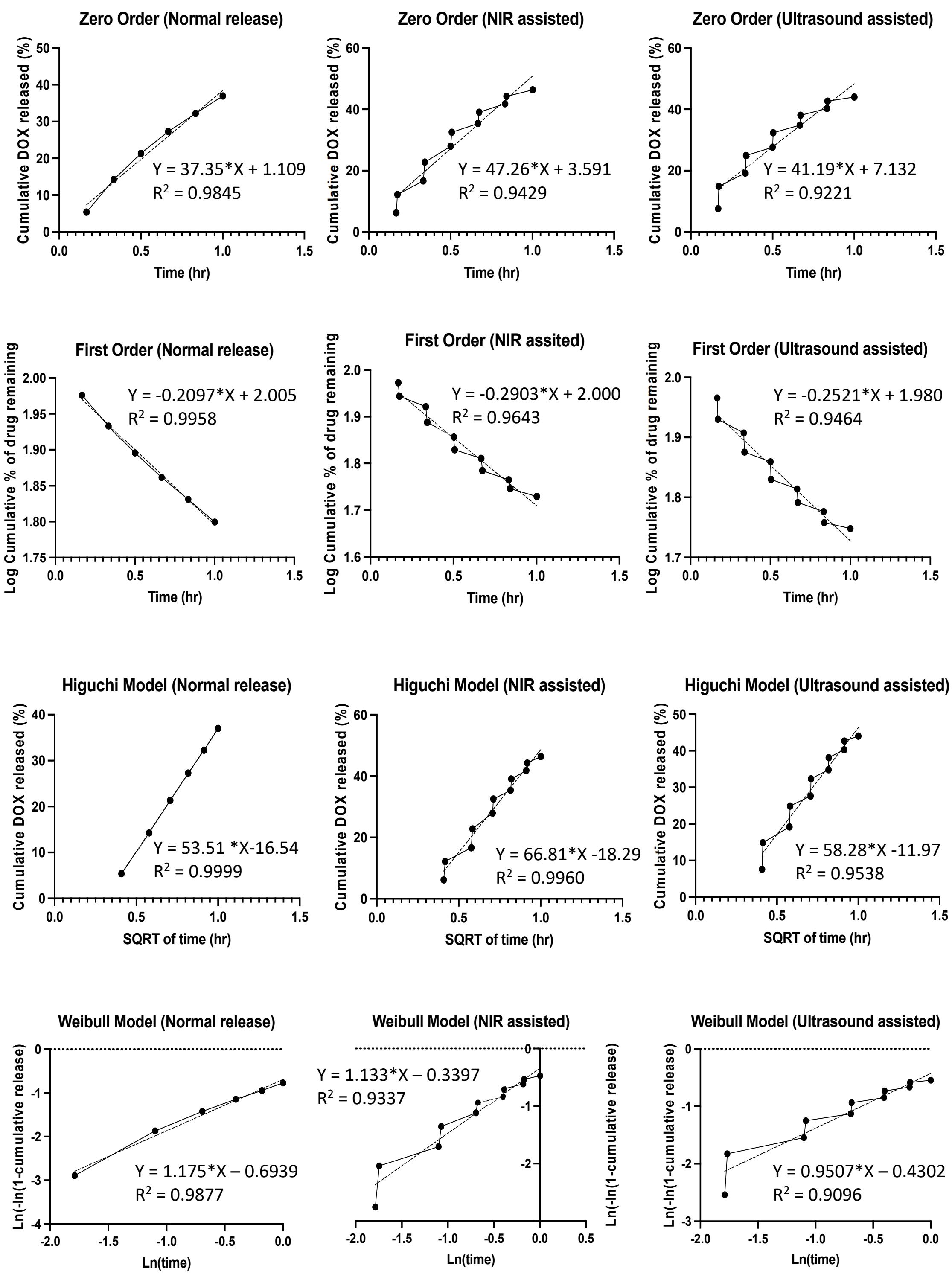


Figure S12. Linear regression graphs created using results from Paper 12.[73]

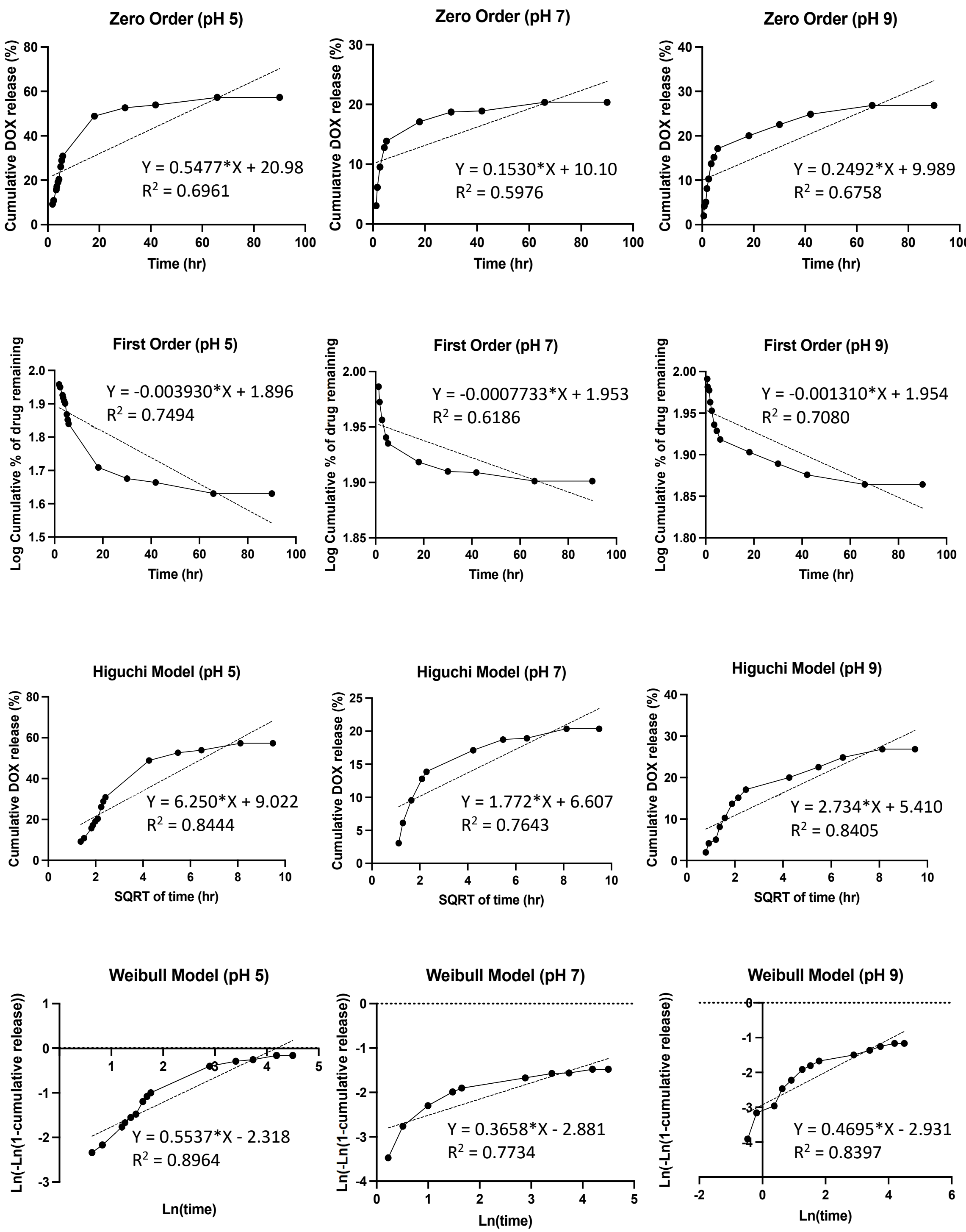


Figure S13. Linear regression graphs created using results from Paper 13.[74]

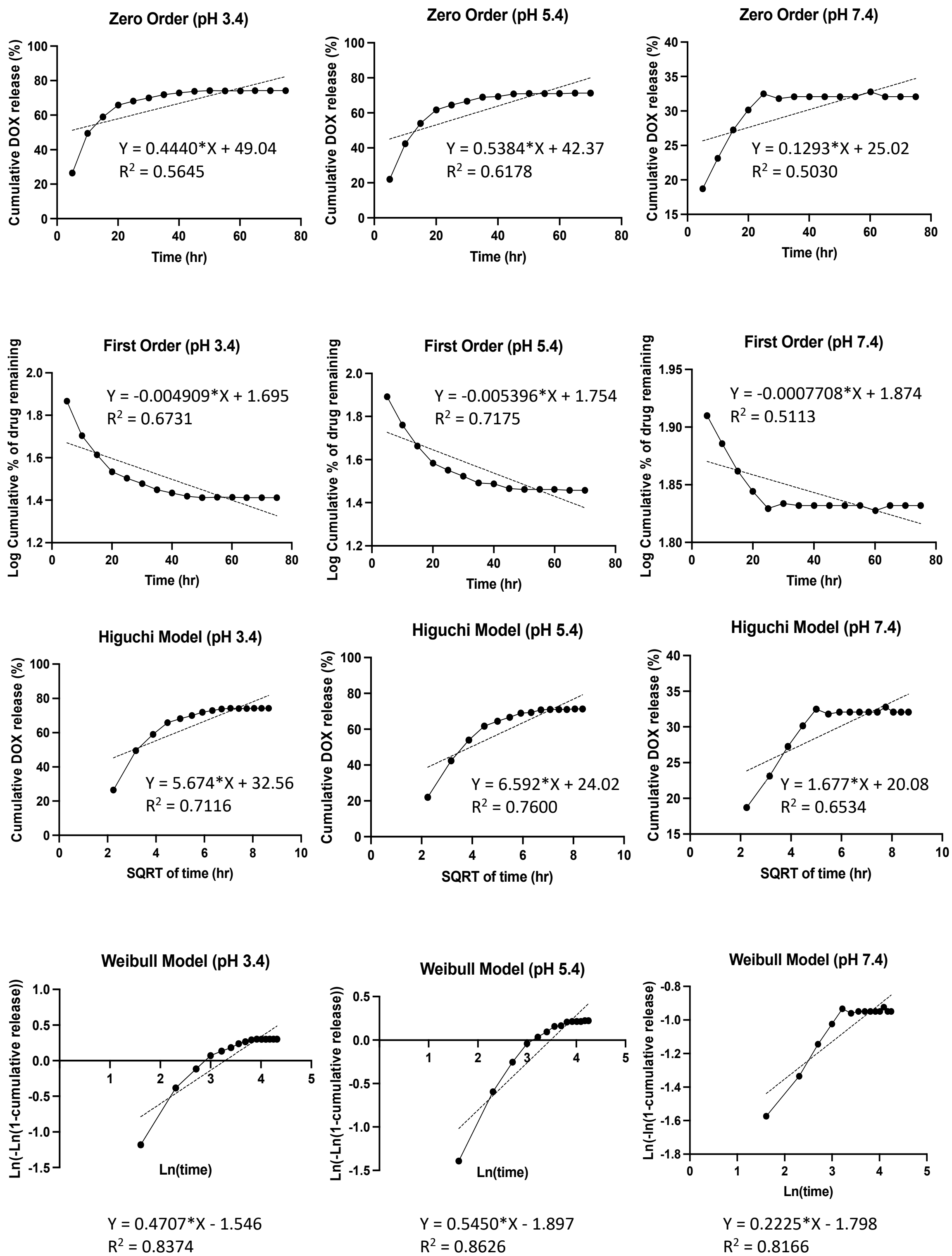
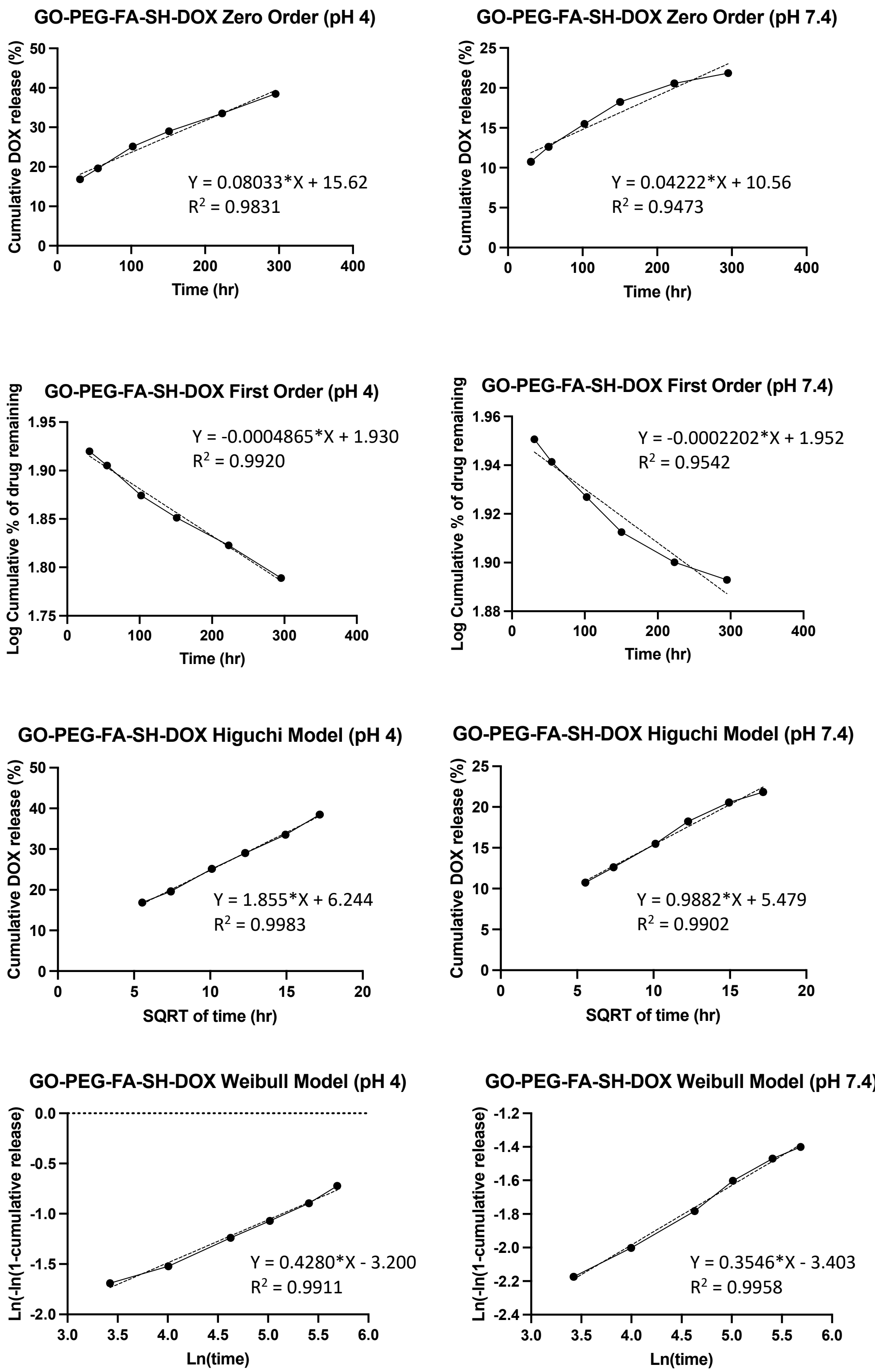
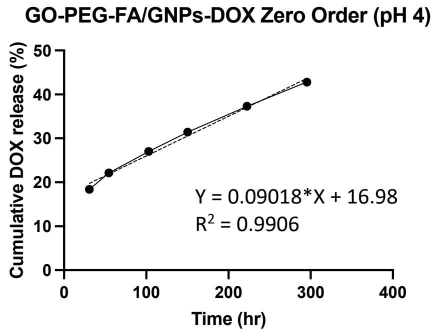
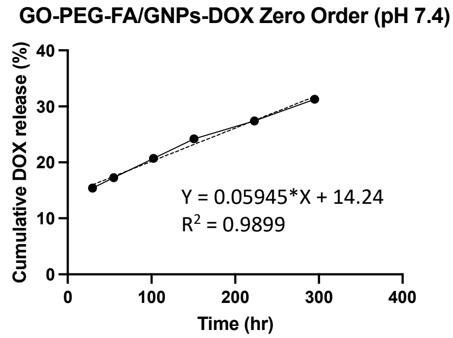
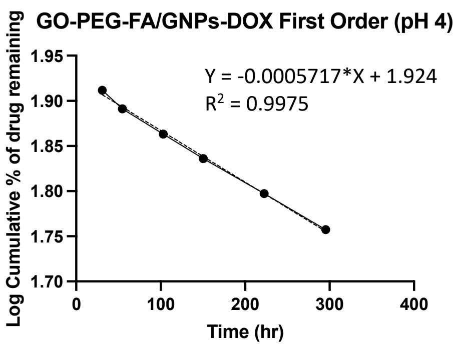


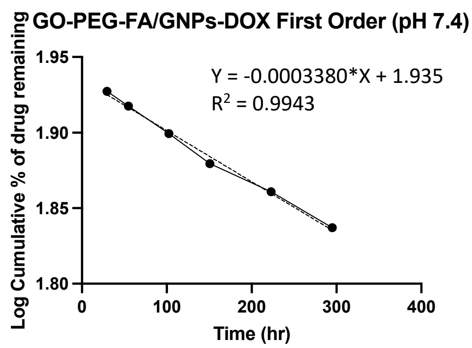
Figure S14. Linear regression graphs created using results from Paper 14.[75]

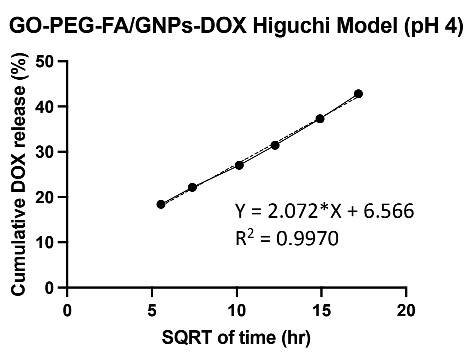


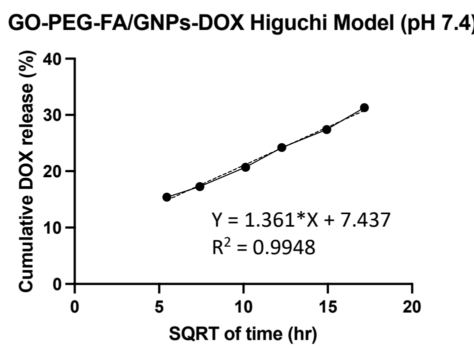

GO-PEG-FA/GNPs-DOX Zero Order (pH 4)
Cumulative DOX release (%)
Time (hr)
Y = 0.09018*X + 16.98
R2 = 0.9906

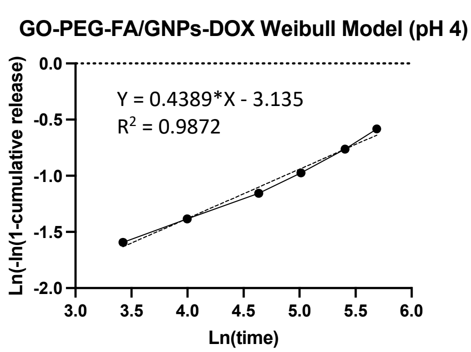

GO-PEG-FA/GNPs-DOX Zero Order (pH 7.4)
Cumulative DOX release (%)
Time (hr)
Y = 0.05945*X + 14.24
R2 = 0.9899


GO-PEG-FA/GNPs-DOX First Order (pH 4)
Log Cumulative % of drug remaining
Time (hr)
Y = -0.0005717*X + 1.924
R2 = 0.9975


GO-PEG-FA/GNPs-DOX First Order (pH 7.4)
Log Cumulative % of drug remaining
Time (hr)
Y = -0.0003380*X + 1.935
R2 = 0.9943


GO-PEG-FA/GNPs-DOX Higuchi Model (pH 4)
Cumulative DOX release (%)
SQRT of time (hr)
Y = 2.072*X + 6.566
R2 = 0.9970


GO-PEG-FA/GNPs-DOX Higuchi Model (pH 7.4)
Cumulative DOX release (%)
SQRT of time (hr)
Y = 1.361*X + 7.437
R2 = 0.9948


GO-PEG-FA/GNPs-DOX Weibull Model (pH 4)
Ln(-ln(1-cumulative release)
Ln(time)
Y = 0.4389*X - 3.135
R2 = 0.9872

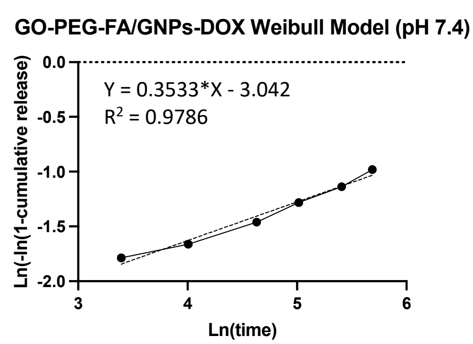

GO-PEG-FA/GNPs-DOX Weibull Model (pH 7.4)
Ln(-ln(1-cumulative release)
Ln(time)
Y = 0.3533*X - 3.042
R2 = 0.9786

Figure S15. Linear regression graphs created using results from Paper 15.[76]

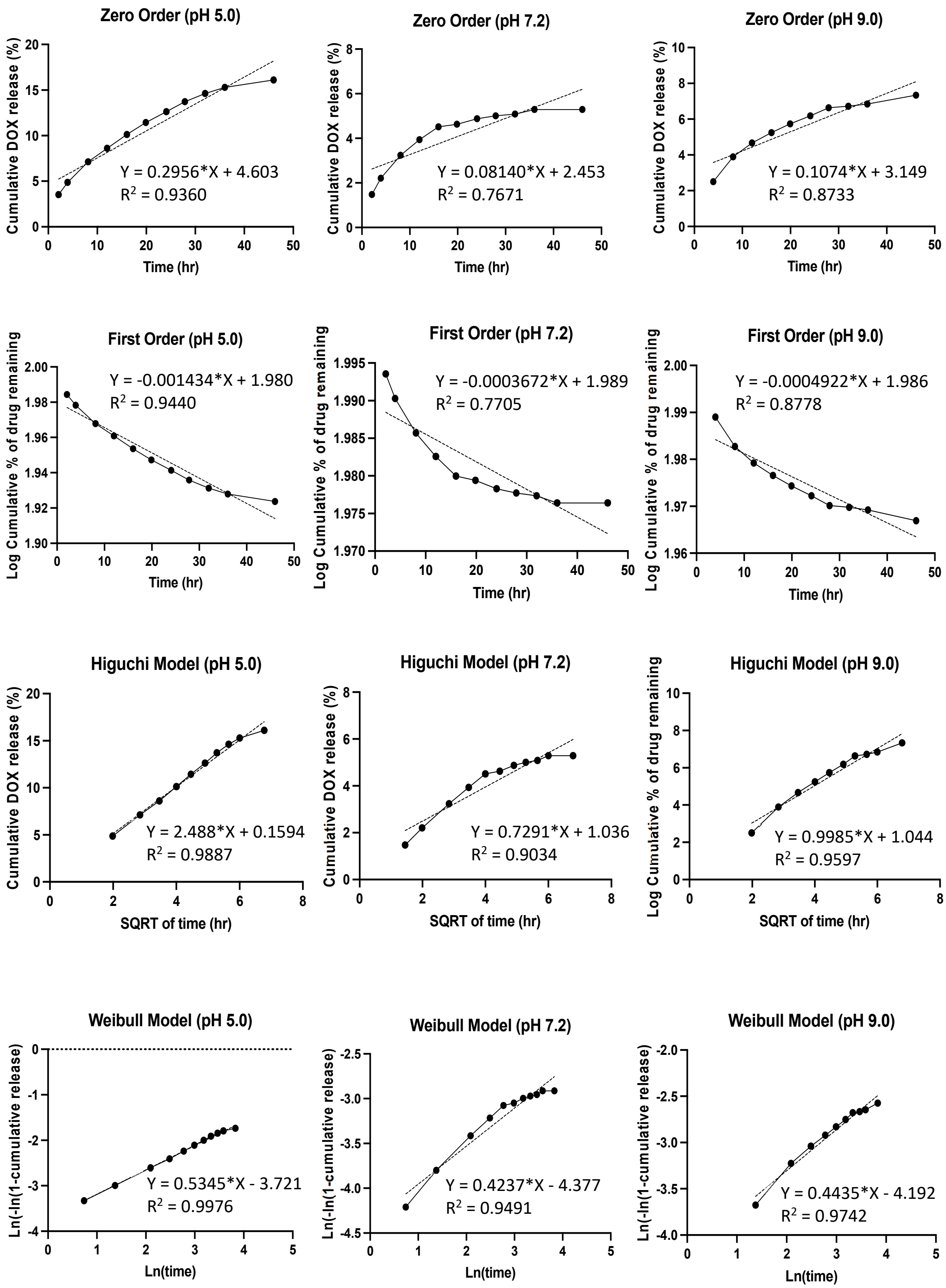


Figure S16. Linear regression graphs created using results from Paper 16.[77]

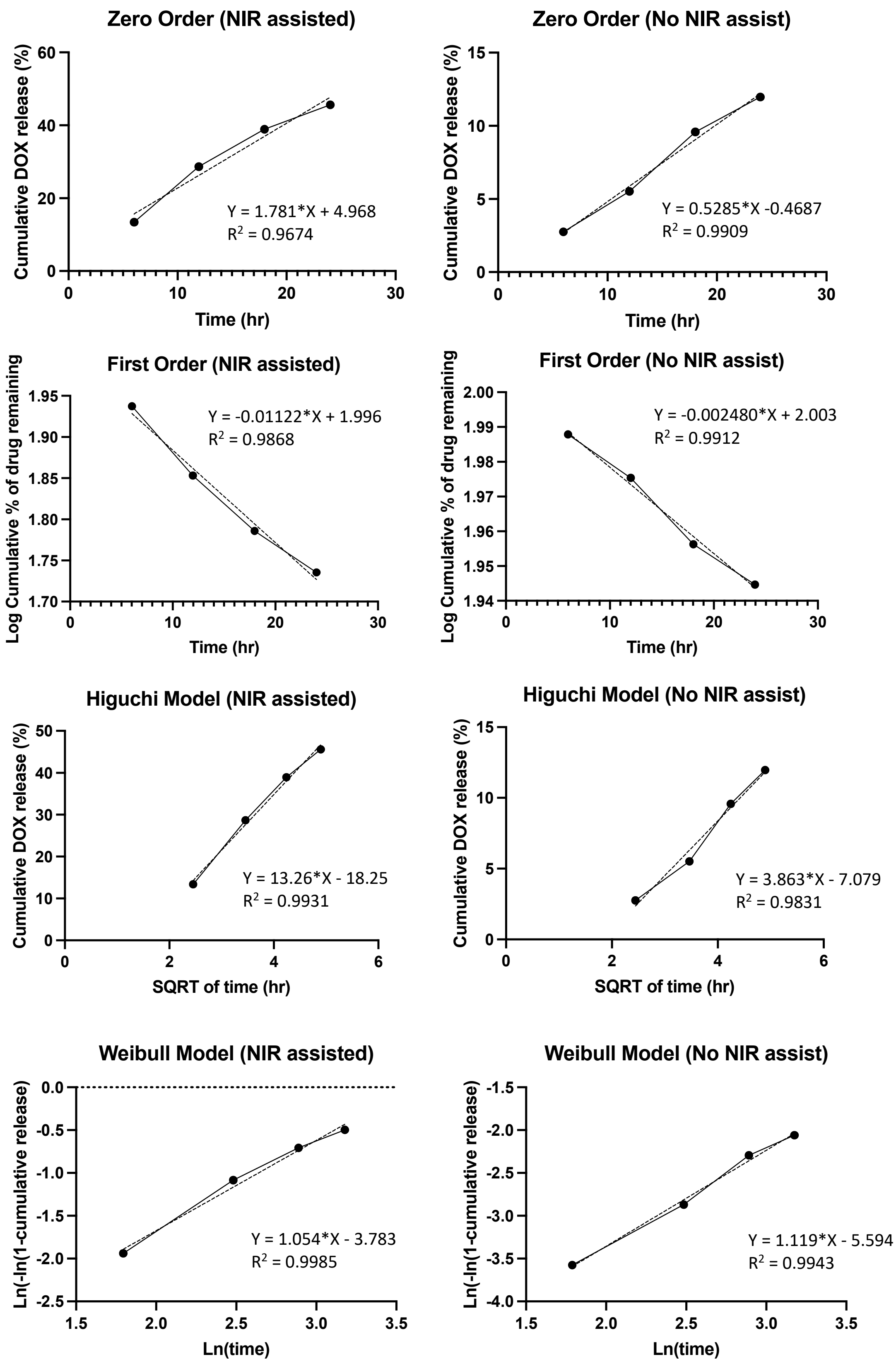


Figure S17. Linear regression graphs created using results from Paper 17.[78]