Supporting Table 1. Reported solubility values of PTX in aqueous media

Medium	PTX solubility (μg/mL)	References
Deionized water	0.3	[1]
Deionized water	0.7	[2]
Deionized water	1.0	[3]
Deionized water	6	[4]
Deionized water	30	[5]
Phosphate buffered saline (PBS, pH 7.4)	0.3	[6]
PBS	0.95	[3]
PBS	3	[7]
PBS	6-10	[8]
PBS with 0.05% Tween 80	3	[9]
PBS with 0.1% Tween 80	2.7	[6]
PBS with 0.1% Tween 80	6.32	[9]
PBS with 0.15% Tween 80	6.8	[9]
PBS with 0.2% Tween 80	8.75	[9]
PBS with 1% Tween 80	13.8	[6]
PBS with 1% Tween 80	37	[9]
PBS with 2% Tween 80	20	[10]
PBS with 2% Tween 80	70	[9]
PBS with 3% Tween 80	115	[9]
Calf serum	171	[7]

Supporting Table 2. PTX release kinetics studies performed in PBS

Ref	PTX Formulation	Sampling methods	Total PTX used for the study	Release medium[1]	Initial PTX concentration in release medium	Conclusion
[11]	Thermo-sensitive polymeric micelles	Dialysis (MWCO: 1kDa): entire medium exchange	1 mg/mL as PMs, eq. to 39 μg/mL PTX (with 3.9% drug loading) in a dialysis bag	PBS 50 mL	39 μg/mL in a dialysis bag	61% release over 7d.
[12]	Thermo-sensitive polymeric micelles (PM)	Dialysis[2] (membrane MWCO: 10 kDa): Entire medium exchange at timed intervals	5 mg as PM, eq. to >225 μg PTX (with >4.5% drug loading) in 5 mL in a dialysis bag	PBS 50 mL	• 45 μg/mL in a dialysis bag • 4.1 μg/mL in the system[3]	<30% of PTX release in 3d and ~35% release in 6d.
[8]	Cholesterol-modified O-carboxymethyl chitosan (CCMC) NPs	Dialysis (membrane MWCO: 12–14 kDa): 0.5 mL sampling and replacement at timed intervals	Not specified ("PTX/PBS maintained at ≤4 μg/mL.")	PBS 50 mL	≤4 μg/mL in the system	32% release in 12h and 59.3% in 84h.
[13]	Thermo-responsive and reduction-sensitive polymeric micelles	Dialysis (MWCO 3.5kDa): medium change not specified.	1 mg/mL as PMs, eq. to 98 μg/mL PTX (with 9.8% drug loading) in PBS 1.5 mL in a dialysis bag (total PTX: 147 μg)	PBS 500 mL	• 98 μg/mL in a dialysis bag • 0.29 μg/mL in the system	Sustained drug release profile, with no obvious burst (23% by 8h and 62% by 24 h with no further release).
[14]	Chitosan-quercetin (CQ) micelles	Dialysis (MWCO: 14kDa): Entire medium exchange at timed intervals	200 μg PTX eq. in 1 mL in a dialysis bag	PBS 100 mL	• 200 μg/mL in a dialysis bag • 2 μg/mL in the system	Zero-order release up to 32.92% in 48h.

[15]	HGC (hydrophobically modified glycol chitosan) NPs	Dialysis (MWCO: 12–14 kDa): entire medium exchange at timed intervals	0.1 mg as HGC NPs, eq. to 10 μg PTX (with 10% drug loading) in 50 μL in a dialysis tube	PBS 30 mL	• 200 μg/mL in a dialysis tube • 0.33 μg/mL in the system	50% release in 1d, followed by a sustained release to 80% by 10d.
[6]	Polymeric NPs	• Dialysis (MWCO: 10kDa) • Franz diffusion cell method separated by a dialysis membrane (MWCO: 10kDa) Partial medium sampling and replacement at timed intervals	• Dialysis: 250 μg/mL PTX 1 mL in a dialysis cassette (total PTX: 250 μg) • Franz diffusion cell: 20 μg/mL PTX in 0.5 mL donor compartment (total PTX: 10 μg)	• Dialysis: PBS 200 mL • Franz diffusion cell: PBS 5 mL as a receptor compartment	• Dialysis: 250 μg/mL in a dialysis bag; 1.24 μg/mL in the system • Franz cell: 20 μg/mL in the donor; 1.8 μg/mL in the system	Near zero-order release over 72h • Dialysis: 5.9%, 12.1%, 19.4% over 6, 12, and 24h. • Franz diffusion cell: 6.0, 12.9, 18.8% over 6, 12, and 24h.
[6]	Polymeric NPs in HPMC gel	Franz diffusion cell method separated by a dialysis membrane (MWCO: 10kDa): Partial medium sampling and replacement at timed intervals	10 μg PTX in a donor compartment	PBS 5 mL as a receptor compartment	2 μg/mL in the system	Near zero-order release up to 22% over 48h.
[3]	Liposomes	Dialysis (MWCO: 10 kDa): partial sampling of release medium at timed intervals	Unspecified amount of liposomes in 2 mL in a dialysis cassette	PBS 400 mL	N/A	5.3% release over 120h.

[16]	Polymeric NPs	Centrifugation[4] (11,500 rpm for 15 min): Entire medium exchange at timed intervals	1 mg as NPs, eq. to 52 µg PTX (PLA-TPGS NPs with 5.2% drug loading) and 55 µg PTX (PLGA NPs with 5.5% drug loading)	PBS 2 mL	26 µg/mL (PLA-TPGS NPs) or 27.5 µg/mL (PLGA NPs)	>20% in 6h, followed by sustained release up to 80% over 18d (PLA-TPGS NPs); ~20% release in 6h, followed by sustained release up to 60% over 18d (PLGA NPs).
[17]	Polymeric NPs	Centrifugation: Entire medium exchange at timed intervals	Not specified	PBS 20 mL	N/A	20% release in 1h, followed by sustained release over 80h.
[18]	Chitosan–lipid implants	Partial medium exchange (2 mL out of 5 mL) at timed intervals	10-15 mg film, eq. to 1-1.5 mg PTX (with 10% drug loading)	• 0.01 M PBS • 0.01 M PBS containing 2 mg/mL of lysozyme • Human ascites fluid 5 mL each	200-300 µg/mL in the system	Near zero-order release over 84d: • Total 9.4% release in PBS • Total 62% release in lysozyme/PB • Total 69% release in ascites fluid.
[19]	PLGA/Polycaprolactone (PCL) layered stents	Entire medium exchange at timed intervals	Not specified	PBS 3 mL	N/A	Three stage release (initial burst, diffusion-controlled release, and degradation-controlled release): release rate depending on the number of layers and drug loading.

1. Release experiments were performed at 37°C under constant agitation.
2. Dialysis method: NP suspension is placed in a dialysis bag or cassette with a specified molecular weight cut-off (MWCO) and sealed. The dialysis bag is immersed in a release medium and continuously stirred. Partial or entire release medium is exchanged with an equal volume of fresh medium at timed intervals.
3. Initial PTX concentration in the system: Total amount of PTX / Volume of the total release medium in the beginning of experiment.
4. Centrifugation: NPs with a known amount are dispersed in a release medium and continuously agitated. At timed intervals, the NP suspension is centrifuged to separate the NP pellet and supernatant. The entire supernatant or a large fraction of the supernatant is exchanged with an equal volume of fresh medium. The NP pellet is resuspended and agitated till the next time point.

Supporting Table 3. PTX release kinetics studies performed in PBS with a dissolution aid

Ref	PTX Formulation	Sampling methods	Total PTX used for the study	Release medium	Initial PTX concentration in release medium	Conclusion
[20]	Liposomes	Dialysis (MWCO: 8-14 kDa): Partial replacement (0.5 mL out of 900 mL) at timed intervals.	Liposome suspension eq. to 1 mg/mL PTX 1 mL in a dialysis bag	0.1%Tween 80/PBS 900 mL	• 1 mg/mL in a dialysis bag • 1.1 µg/mL in the system	19.24% release in 2h and a total of 60.26% release in 24h
[9, 21]	PEGylated liposomes and PEGylated immune-liposomes	Dialysis (MWCO: 6-8 kDa): Partial (0.5mL out of 200 mL) sampling and replacement at timed intervals.	1.5 mg/mL PTX eq. in 0.1 mL in a dialysis tube (Total PTX: 150 µg)	0.1% Tween 80/PBS 200 mL	• 1.5 mg/mL in a dialysis bag • 0.75 µg/mL in the system	• PEGylated liposomes: 15% initial release in the first 2h and 33% in 24 h. • PEGylated immunoliposomes: 36% in 24h.
[22]	Superpara-magnetic iron oxide NPs	Dialysis (MWCO: 10 kDa): Partial (2 mL out of 10 mL) replacement of release medium at timed intervals.	60 mg NPs eq. to 10 mg PTX	1% Tween 80/PBS 20 mL	500 µg/mL in the system	27% release over the first 8h, 76% by 110h, and ~100% by 15d.
[23]	Hydrotropic oligomer-glycol chitosan (HO-GC) NPs	Dialysis (membrane (MWCO: 8 kDa): Entire medium exchange at timed intervals	1 mg as HO-GC NPs, eq. to 200 µg PTX (with 20% drug loading) in 1 mL PBS in a dialysis tube	PBS with 0.1 M sodium salicylate, volume unspecified	N/A	>60% release in 24h followed by sustained release up to >80% in 3d.
[24]	Pluronic/Span	Dialysis: 1 mL	Unspecified amount	0.1% Tween	N/A	30% release in 8h and

	40 NPs	exchange at timed intervals	of NPs dispersed in 1 mL PBS or fetal bovine serum in a dialysis bag	80/PBS 50 mL		<60% release (as suspended in FBS) or 70% (as suspended in PBS) in 48h.
[25]	Polymeric micelles stabilized with ionic complexation	Dialysis (membrane MWCO: 3.5 kDa): Partial (1 mL) sampling of release medium at timed intervals.	Not specified	0.1% Tween 80/PBS, volume not specified	N/A	45% release in 24h, followed by a sustained, slow release up to 65% over 2 weeks.
[26]	PLGA NPs and PLGA-chitosan NPs	Centrifugation (10,000 rpm for 10 min): Partial replacement (0.9 mL out of 1 mL) of release medium at timed intervals.	NPs eq. to 3 µg PTX	0.1% Tween 80/PBS 1 mL	3 µg/mL in the system	11~12% in 3h and a total release of 76~83% by 24h.
[27, 28]	PLGA NPs	Centrifugation (10,000 rpm for 10 min at 4°C): Partial replacement (0.8 mL out of 1 mL) of release medium at timed intervals.	NPs eq. to 3 or 8.75 µg PTX	PBS or 0.2% Tween 80/PBS 1 mL	3 or 8.25 µg/mL in the system	• In PBS: 20% release in 4h with no further release. • In 0.2% Tween 80/PBS: 60-70% of PTX release in 4h.
[29]	PEG-PLA NPs	Centrifugation (13,500 rpm for 10 min)	1 mg as NPs, eq. to 25.8 µg PTX (with 2.58% drug loading)	0.1% Tween 80/PBS 1 mL	25.8 µg/mL in the system	10% release in 1h and a total of 30% release in 24h.
[30]	PLA-Tween 80 copolymer NPs	Centrifugation (11,500 rpm for 20 min): Entire medium	1 mg as NPs, eq. to 60 µg PTX (with 6% drug loading)	0.1% Tween 80/PBS 2 mL	30 µg/mL in the system	23-26.1 % release in the first day and 52.1-62% release in 21d.

		change at timed intervals.				
[31]	PLGA microparticles	Centrifugation	50 µg PTX eq.	0.1% Tween 80/PBS 1 mL	50 µg/mL in the system	An initial burst release during the first 24h, followed by slower sustained release over 3 weeks and a third phase with a more accelerated release. 12-71% release over 28d according to the polymer composition, molecular weight, and particle size.
[32]	Polymeric NPs	Centrifugation (25,000 rpm for 15 min): entire medium change at timed intervals.	5 mg as NPs, eq. to 400-500 µg PTX (with 8-10% drug loading)	0.1% Tween 80/PBS 8 mL	50-62.5 µg/mL in the system	33.35-47.38% release in the first 5 h, followed by a sustained release up to 45-65% in 28d.
[33]	Chitosan NPs	Centrifugation (10,000g for 10 min)	10 mg as NPs, eq. to 3.54 mg PTX (with 35.4% drug loading)	0.1% Tween 80/PBS 10 mL	354 µg/mL in the system	59.4% release in 9 days and 72% in 22 days
[34]	PLGA NPs	Centrifugation: Partial (2mL out of 10 mL) sampling and replacement at timed intervals.	5 mg PTX eq.	0.3% Tween 80/PBS 10 mL	500 µg/mL in the system	A rapid initial release during the first 24 h, followed by a slower and continuous release: 53.5 – 93.3% release over 48h depending on drug/polymer ratio
[35]	Polyester Nanosponges	Centrifugation: Entire medium exchange at	4.8 mg PTX eq.	0.1% Tween 80/PBS 5	960 µg/mL in the system	An initial burst release followed by near zero-

		timed intervals.		mL		order release: Release rate and total drug release varied with the crosslinking density of polymer network.
[36]	Eudragit S100-coated alginate microspheres	Centrifugation (1000g for 10 min)	Microparticles eq. to 2 mg PTX	0.02% Tween 80 with a varying pH 10 mL	1 mg/mL in the system	Initial burst release to varying degrees according to the polymer concentration and crosslinking density, followed by a sustained release.
[37]	Polyanhydride NPs	Partial medium exchange at timed intervals.	Not specified	0.1% Tween 80/PBS 20 mL	N/A	Zero-order release up to 89.73 or 97.17% over 90h, depending on drug loading.
[38]	Polymeric microparticles	Centrifugation (4,000 rpm for 2 min): Entire medium exchange at timed intervals.	Not specified	0.05% Tween 80/PBS, volume not specified	N/A	24% in 4d, followed by a slow release up to 30% in 2 weeks.
[39]	PLGA/PEG films	Partial replacement of medium at timed intervals.	30 μm thick x 1 cm^2 as polymer films, eq. to ~300 μg PTX (with 10% drug loading).	2% Tween 80/PBS 2 mL	150 μg/mL in the system	Initial burst release to varying degrees according to the amount of PEG additives, followed by a slow release.
[10]	PLGA/PEG films	Partial sampling	15 mm punchouts eq. to ~730 μg (with ~4 $\mu g/mm^2$ drug loading)	2% Tween 80/PBS 2 mL	365 μg/mL in the system	<20% release in 20 days with PLGA film containing ≤15% PEG.

[40]	Polymer films	Entire medium exchange at timed intervals	Not specified	10% ethanol/PBS 10 mL	N/A	60–85% burst release in 24h; 80-95% release by 5d.

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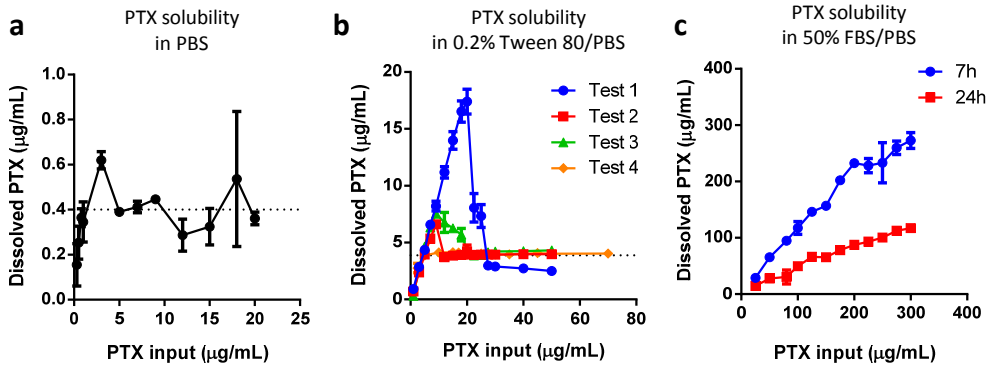
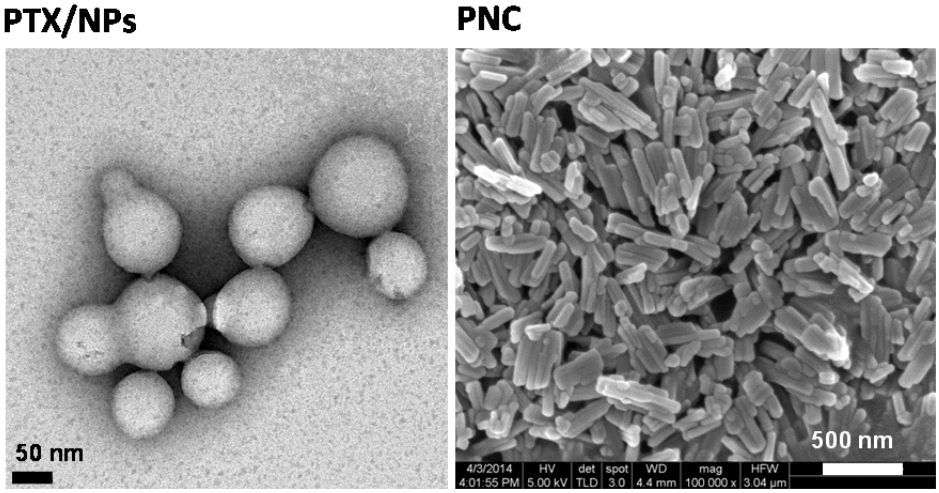
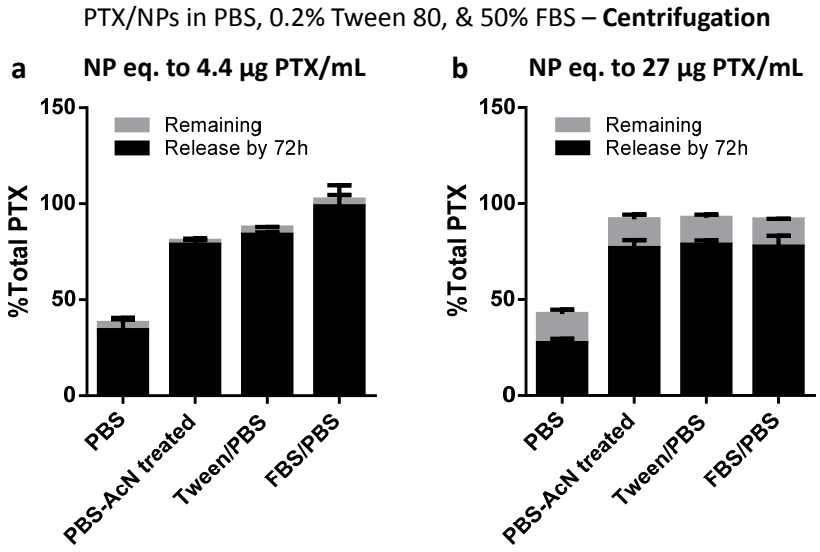
Supporting Figures



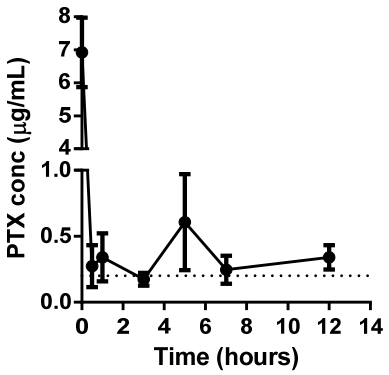
Supporting Fig. 1. Paclitaxel (PTX) solubility in (a) PBS, (b) 0.2% Tween 80/PBS, and (c) 50% FBS/PBS determined in an alternative way. PTX was added to each medium in the amount indicated in the x-axis as a 10 mg/mL stock solution in DMSO. After 24h (7 or 24h for 50% FBS/PBS) incubation at 37°C, solutions were centrifuged and filtered to remove precipitated PTX and analyzed with HPLC.



Supporting Fig. 2. Micrographs of PTX/NPs (taken with a FEI Tecnai T20 transmission electron microscope after negative staining with 1% phosphotungstic acid) and PNCs (taken with a FEI Nova NanoSEM^{TM} scanning electron microscope).



Supporting Fig. 3. Mass balance after release kinetics studies of PTX/NPs in media containing PBS, FBS, or Tween 80 (See Fig. 2).



Supporting Fig. 4. Kinetics of PTX precipitation in PBS. To determine how quickly PTX precipitated in PBS (pH 7.4) at 37°C, PTX solution in PBS at a concentration of 20 µg/mL was prepared by diluting PTX stock solution in 0.2% Tween 80/PBS with PBS, aliquoted by 1 mL, and incubated at 37°C with shaking. At predetermined time points, 3 aliquots were taken and centrifuged at 3,000 rpm for 5 min. The supernatants were additionally centrifuged at 10,000 rpm (20 min) and filtered with 0.45 µm PVDF syringe filters and analyzed with HPLC. Dotted line indicates PTX solubility in PBS (0.2 µg/mL).