Table SI. Multitarget anticancer activities of Tan IIA and its derivatives in breast cancer models: Concentration context and translational interpretation.

Mechanism category	Compound/form	Key molecules/pathways	Antitumor effects	Study models	Dose/concentration	Translational interpretation	(Ref.)
ER signaling	ATA; HTA as intracellular metabolite	ERα ↓, polyubiquitinated ERα ↑, ESR1 ↓, GREB1 ↓, ERβ unchanged	Preferentially inhibits ER-positive breast cancer cell growth through ERα downregulation and reduced ER-responsive transcription	MCF-7, T-47D, MDA-MB-231; IMR-90 and C2C12 comparator cells	IC50 1.40 μM in T-47D, 1.48 μM in MCF-7 and 7.98 μM in MDA-MB-231 cells; 6 μM for mechanism assays	ER-positive, low-micromolar *in vitro* evidence; HTA binding is docking-supported and *in vivo* breast cancer validation remains needed	(21)
Endocrine combination therapy and ER imaging	Tan IIA formulation/sulfotanshinone IIA sodium + fulvestrant	FUL-associated ERα ↓; 18F-FES uptake ↓	FUL + Tan IIA delayed ZR-75-1 xenograft growth and enabled early PET/CT response monitoring; Tan IIA alone was not significantly effective	ZR-75-1 ER-positive xenografts in female Balb/c nude mice	Tan IIA 30 mg/kg i.v. every other day + FUL 250 mg/kg s.c. weekly for 21 days	Combination evidence from a single ER-positive xenograft model; Tan IIA's mechanistic contribution remains unclear	(37)
ER-associated nanodelivery	Tan-NH_2; Tan-Dox-MSN	ER-associated uptake; Dox delivery; energy-dependent endocytosis	Improves tumor targeting and Dox delivery, suppresses MCF-7 xenograft growth, and inhibits T47D migration/invasion *in vitro* while reducing Dox-related toxicity indicators	MCF-7, T47D, MCF-10A cells; MCF-7 xenograft-bearing female BALB/c nude mice	Tan-NH_2 1-50 μg/ml *in vitro*; Tan-NH_2 1-5 μg/ml for migration/invasion; Dox 2 mg/kg *in vivo*	Formulation-dependent evidence; ER expression in normal tissues and nanocarrier safety remain key translational concerns	(22)
ER-independent proliferation/apoptosis regulation	Native Tan IIA	p53 ↓, Bcl-2 ↓; cerbB-2 unchanged	Inhibits proliferation and induces apoptosis in ER-positive and ER-negative breast cancer models	MCF-7 and MDA-MB-231 cells; female nude mouse xenografts	0.0625-1.0 μg/ml *in vitro*; IC50 0.25 μg/ml; 30 mg/kg s.c. *in vivo*	*In vivo*-supported but broad antiproliferative/apoptotic evidence; PK/tumor exposure remains unclear	(38)
Dox chemosensitization and resistance attenuation	Native Tan IIA + Dox	PTEN ↑, p-AKT ↓, P-gp ↓, BCRP ↓, MRP1 ↓	Enhances Dox accumulation/apoptosis, suppresses xenograft growth and reduces Dox-related toxicity	MCF-7 and MCF-7/Dox cells; MCF-7 xenograft-bearing nude mice	Tan IIA 20 μg/ml + Dox 2 μg/ml *in vitro*; Tan IIA 10 mg/kg + Dox 5 mg/kg i.p. *in vivo*	Resistant-cell evidence is *in vitro*; *in vivo* validation used MCF-7 xenografts and high Tan IIA exposure requires PK confirmation	(42)
Dox chemosensitization via β-catenin nuclear translocation	Native Tan IIA + Dox	Nuclear β-catenin ↓, c-Myc ↓, E-cadherin ↑, MMP-2/9 ↓	Enhances Dox sensitivity and inhibits proliferation/migration *in vitro*	MCF-7, MCF-7/Dox cells	Tan IIA 20 μg/ml + Dox 2 μg/ml; WAY-262611 rescue assay	High-concentration *in vitro* evidence; no *in vivo* validation in this study	(43)
Taxol/paclitaxel	Native Tan IIA +	Tau ↓	Produces mainly	Taxol-resistant MCF-	Tan IIA 1-20 μM +	*In vitro*, model-specific	(44)

sensitization	Taxol/paclitaxel		additive cytotoxicity and partially attenuates Taxol resistance *in vitro*	7/Taxol cells	Taxol 5-100 μM; IC50: Tan IIA 8.4 μM, Taxol 23.7 μM	evidence; additive rather than consistently synergistic effect	
Tissue-context-dependent ERK1/2 regulation	Native Tan IIA + Dox	p-ERK1/2 ↓ in breast cancer cells but ↑ in AC16 myocardial cells; c-Myc/MMP-2/cleaved caspase-3 modulated accordingly	Enhances Dox antitumor effects and attenuates Dox-induced myocardial injury	MCF-7, MDA-MB-231, AC16 cells; 4T1 tumor-bearing mice	Dox 2 μg/ml + Tan IIA 0.02 mg/l in MCF-7, 0.6 mg/l in MDA-MB-231 and 0.02-5 mg/l in AC16 cells; *in vivo*: Dox 5 mg/kg + Tan IIA 10 mg/kg	Cell-type-specific ERK1/2 regulation; requires PK/tumor and cardiac exposure validation	(45)
ABC transporter-mediated resistance and BCSC-like phenotype	Native Tan IIA + Dox	P-gp ↓, BCRP ↓, MRP1 ↓, CD44+/CD24-/low phenotype ↓	Increases intracellular Dox accumulation, enhances apoptosis and reduces BCSC-like phenotype *in vitro*	MCF-7, MCF-7/Dox cells	Tan IIA 0.02 mg/l + Dox 2 μg/ml for 24 h	Low-concentration *in vitro* evidence; no *in vivo* validation or relapse-prevention data	(46)
Hypoxia-associated Dox chemoresistance and EMT	Native Tan IIA + Dox	HIF-1α ↓, E-cadherin ↑, vimentin ↓; TWIST implicated	Reverses hypoxia-induced Dox resistance and suppresses EMT-associated marker changes *in vitro*	MCF-7 and HCC1937 cells under DFO-induced hypoxia	DFO 100 μM; Tan IIA 10 μM + Dox 0.2 μg/ml	*In vitro* hypoxia-mimetic evidence; no *in vivo* or metastasis validation	(47)
Derivative-associated cytotoxicity and apoptosis	1-hydroxy-Tan IIA	DNA fragmentation; Bax/Bcl-2 ↑ and PARP cleavage in PC3 cells	Inhibits MCF-7 viability and induces apoptotic DNA fragmentation	MCF-7 cells; PC3 mechanistic comparator cells	IC50 21.81 ± 2.65 μg/ml in MCF-7; PI assay 25 μg/ml; PC3 WB 12.5 and 25 μg/ml	MCF-7 evidence is *in vitro* only; MDA-MB-231 was not analyzed and apoptosis-protein validation was mainly in PC3 cells	(19)
Apoptosis in MDA-MB-231 TNBC cells	Native Tan IIA	Bax ↑, Bcl-xL ↓, p21 ↑, caspase-8 ↑	Inhibits proliferation and induces sub-G1/apoptosis in a dose- and time-dependent manner	MDA-MB-231 cells	1-30 μg/ml for 24-72 h; IC50 34.14, 11.85 and 2.40 μg/ml at 24, 48 and 72 h; WB at 6 and 12 μg/ml	Single-cell-line *in vitro* evidence; exposure-time dependence and *in vivo* relevance require validation	(20)
Endoplasmic reticulum stress-mediated apoptosis	Native Tan IIA	Caspase-12 ↑, GADD153/CHOP ↑, cleaved caspase-3 ↑, Bax/Bcl-xL ratio ↑, p-p38/p-JNK ↑, p-ERK ↓	Induces endoplasmic reticulum stress-related apoptosis and sub-G1 accumulation *in vitro*	BT-20 cells	0.25-8 μg/ml; IC50 3.3, 1.87 and 0.67 μg/ml at 24, 48 and 72 h	Single-cell-line *in vitro* evidence; sustained exposure and *in vivo* relevance require validation	(50)
GPER/EGFR/ERK signaling	Native Tan IIA	GPER ↓, EGFR ↓, ERK1/2 ↓, c-Fos ↓, c-Jun ↓, cyclin A2/D1 ↓,	Inhibits proliferation/migration, induces apoptosis and	MDA-MB-231 cells; HEK293 comparator cells	1-100 μM for proliferation; 5, 10 and 50 μM for 48 h	Single-cell-line *in vitro* evidence; GPER involvement is	(51)

		CDK2/4/6 ↓, caspase-3 ↑	suppresses G1/S-associated proteins *in vitro*		validation assays; G15 + 10 μM rescue	docking/G15-supported and requires *in vivo* target validation	
Apoptosis and LC3-II/Erb-B2/NF-κB-associated signaling	Native Tan IIA	LC3-II ↓, Erb-B2 ↓, NF-κBp65 ↓, caspase-3 ↑	Suppresses MDA-MB-231 xenograft growth; 60 mg/kg significantly reduced tumor weight	MDA-MB-231 cells; female nude SCID mouse xenografts	IC50 11.85 μg/ml at 48 h; WB at 3, 10 and 25 μg/ml; oral 20 or 60 mg/kg every other day for 90 days	*In vivo*-supported but single-cell-line evidence; LC3-II change and high oral dosing require autophagy-flux and PK validation	(52)
TNBC apoptosis and network-predicted pathway modulation	Native Tan IIA	Bcl-2 ↓, p53 ↑, p-p53 ↑; predicted p53/PI3K-AKT/MAPK/mTOR pathways	Inhibits 4T1 proliferation/colony formation, induces apoptosis and suppresses tumor growth	4T1 cells; MCF-10A comparator cells; 4T1-bearing female BALB/c mice	10-80 μM for viability; IC50 49.78 μM at 48 h; 12.5, 25 and 50 μM for mechanism assays; *in vivo* 10 mg/kg	High-micromolar evidence; pathway/docking findings require biochemical and *in vivo* target-engagement validation	(53)
Proliferation/apoptosis and gene-expression modulation	Native Tan IIA	ADPRTL1 ↑, CDKN1A ↑, CYP1A1 ↑, MAP3K1 ↓, MMP7 ↓, CEACAM6 ↓; tumor caspase-3 ↑	Inhibits MCF-7 proliferation/colony formation and suppresses ER-negative breast IDC xenograft growth	MCF-7 cells; ER-negative breast IDC orthotopic xenografts in female nude mice	0.0625-1.0 μg/ml *in vitro*; IC50 0.25 μg/ml; 30 mg/kg s.c. three times/week for 10 weeks *in vivo*	*In vivo*-supported but model-mismatched evidence; microarray-derived targets require functional validation	(55)
Anti-invasion derivative activity	TA12, para-hydroxyphenyl-substituted Tan IIA imidazole derivative	ROS ↑, DNA damage/γH2AX ↑, p53 ↑, AKT ↓, p21 ↑, cyclin A ↓; FAK ↓, GSK3β ↑, MMP9 ↓; apoptosis markers modestly ↑	Inhibits MDA-MB-231 proliferation, migration, invasion and metastatic dissemination in zebrafish xenografts; induces ROS-mediated DNA damage and S-phase arrest	MDA-MB-231 cells; L02 cells as normal-cell comparator; MDA-MB-231 zebrafish xenograft model	IC50 13.2±3.9 μM in MDA-MB-231 and 49.1±7.4 μM in L02 cells; migration/invasion assays used 3 and 6 μM; DNA-damage assays used 10 and 20 μM; zebrafish xenograft exposure: 5 μM	Derivative-specific activity supported by MDA-MB-231 and zebrafish models; mammalian PK, systemic toxicity, tumor exposure and efficacy in mammalian metastasis models remain to be validated	(54)
BCSC-like properties and inflammatory signaling	Native Tan IIA	IL-6 ↓, STAT3/p-STAT3 ↓, nuclear NF-κB p65 ↓, cyclin D1 ↓	Inhibits MCF-7M proliferation, mammosphere formation and MCF-7M-initiated xenograft growth	MCF-7 and MCF-7M CSC-like cells; female Balb/c nude mouse xenografts	0.125-2.0 μg/ml; IC50 0.40 μg/ml in MCF-7M; *in vivo* 10-40 mg/kg i.p.	Low-concentration CSC-like evidence; relapse prevention and broader subtype validation remain needed	(57)
BCSC-like stemness and adriamycin/doxorubicin sensitivity	Native Tan IIA	miR-125b ↓, STARD13 ↑, Oct3/4 ↓, ALDH1A1 ↓,	Reduces spheroid formation and tumor-initiating ability;	MCF-7, MDA-MB-231, MCF-7-Adr cells; female athymic	2.5-20 μM *in vitro*; 10 μM for rescue/adriamycin	Stemness-focused evidence; *in vivo* assay used *ex vivo* pretreatment	(58)

		CD24−/CD44+ ↓, Ki67 ↓, cleaved PARP ↑	enhances adriamycin sensitivity and attenuates MCF-7-Adr resistance *in vitro*	BALB/c nude mice	assays; cells pretreated with 10 μM for 72 h before implantation	rather than systemic dosing, and clinical chemoresistance relevance remains uncertain	
Ferroptosis induction via KDM1A/PIAS4/SLC7A11 axis	Native Tan IIA	KDM1A ↓, PIAS4 ↓, SLC7A11 SUMOylation/stability ↓, MDA/Fe^{2+}/LDH/lipid ROS ↑, GSH ↓	Promotes ferroptosis and suppresses proliferation, migration, invasion, xenograft growth and experimental lung metastasis	MCF-7 and T47D responsive cells; MDA-MB-231/BT549 comparator cells; BALB/c nude mouse models	25-200 μM *in vitro*; 50 μM for key mechanism assays; 10 mg/kg i.p. every two days *in vivo*	Detailed mechanistic evidence but high-micromolar exposure and subtype-specific responsiveness require PK/PD and broader validation	(61)
HER2-positive breast cancer suppression	ATA	HER2/EGFR ↓, p-Akt/p-Stat3/p-NF-κB ↓, cyclin D1/A and CDK2/4/6 ↓, p21 ↑, cleaved PARP ↑, Bax ↑, Bcl-2/Bcl-xL ↓, p-AMPK/p-ACC ↑, FASN/p-ACLY ↓, ROS/CHOP ↑, VEGFR2 ↓	Induces cell-cycle arrest/apoptosis, suppresses HER2/EGFR survival and metabolic signaling, inhibits MDA-MB-453 xenograft growth and reduces HUVEC angiogenic behavior *in vitro*	MDA-MB-453, SK-BR-3, BT-474; MCF-10A comparator cells; HUVECs; MDA-MB-453 xenografts in female BALB/c nude mice	1-20 μM *in vitro*; IC50 1.97, 9.17 and 6.79 μM in MDA-MB-453, SK-BR-3 and BT-474 cells; 35 mg/kg i.p. three times/week *in vivo*	ATA-specific HER2-overexpressing evidence; *in vitro* antiangiogenic data and HER2-low/therapy-resistant relevance require validation	(64)
G4 DNA stabilization and DNA-damage response	Compound 4, imidazole-modified Tan IIA derivative	c-myc/K-ras/VEGF/Bcl-2/Tel-26 G4 stabilization; γH2AX ↑; G-rich gene transcription ↓	Induces DNA damage and S-phase arrest; suppresses proliferation, migration, invasion, zebrafish dissemination and angiogenesis-related phenotypes	MDA-MB-231 cells; MCF-10A comparator cells; HUVECs; zebrafish xenograft/angiogenesis models	IC50 12.8 μM in MDA-MB-231 and 95.7 μM in MCF-10A; 2.5-20 μM across functional assays; zebrafish 5-20 μM	Derivative-specific zebrafish/*in vitro* evidence; mammalian PK, toxicity and metastasis validation remain needed	(67)

Translational interpretation reflects the degree to which the reported mechanism is supported by concentration range, model specificity, compound form and *in vivo* validation. Tan IIA, tanshinone IIA; ATA, acetyltanshinone IIA; HTA, hydroquinone tanshinone IIA; Dox, doxorubicin; BCSC, breast cancer stem cell; G4, G-quadruplex; PK/PD, pharmacokinetic/pharmacodynamic; ER, estrogen receptor.

Table SII. Quantitative comparison of representative Tan IIA derivatives and nanodelivery systems in breast cancer models.

Category	Compound/system	Structural or formulation feature	Main mechanism/action	Study models	IC50/effective range	Selectivity or formulation advantage	*In vivo* evidence	Key translational limitation	(Ref.)
Comparator	Native Tan IIA	Parent lipophilic diterpene quinone	Suppresses proliferation and induces apoptosis in ER-positive and ER-negative breast cancer models, associated with reduced p53 and Bcl-2 expression	MCF-7, MDA-MB-231 cells; female BALB/c nude mice	0.0625-1.0 μg/ml tested; IC50 ~0.25 μg/ml in both cell lines	Broad ER-positive and ER-negative activity; stronger than tamoxifen in the tested ER-positive model	30 mg/kg s.c., four times/week for 4 weeks inhibited MCF-7 and MDA-MB-231 xenograft growth	Poor solubility, low oral bioavailability and short half-life; breast tumor exposure and target coverage remain uncertain	(18, 38)
Compound	ATA	Acetylated Tan IIA derivative	Promotes ERα degradation via the ubiquitin-proteasome pathway, reduces ESR1 transcription and suppresses ER-responsive genes	MCF-7, T-47D, MDA-MB-231 cells	IC50 ~1.4-1.5 μM in ER-positive cells; 1.56-25 μM tested; 6 μM used for mechanistic studies	Preferential inhibition of ER-positive breast cancer cells under tested conditions; lower growth inhibition was observed in non-cancerous IMR-90 fibroblast and C2C12 muscle cells at 3.13 μM	NR for standalone ATA in ER-positive xenografts in the reviewed study	ERα degradation evidence is mainly based on ATA/HTA in ER-positive models; *in vivo* exposure and target engagement require validation	(21)
Compound/metabolite	HTA	Intracellular metabolic product of ATA identified by LC-MS	Computational docking suggests potential ERα binding; ATA/HTA-associated activity is linked to ERα degradation and suppression of ESR1 and GREB1 transcription	MCF-7 ER-positive breast cancer mechanistic model	NR as standalone IC50; HTA was detected after 10 μM ATA treatment for 2 h; 6 μM ATA was used for ERα/ESR1/GREB1 mechanistic studies	Mechanistically linked to ATA activity and predicted to show preferential ERα binding over other nuclear receptors in docking analysis	NR	HTA-specific cellular potency, direct biochemical ERα binding, independent PK profile and *in vivo* target engagement remain unvalidated	(21)
Compound	ATA in HER2-overexpressing models	Acetylated derivative with HER2/EGFR and metabolic pathway	Downregulates EGFR/HER2-AKT/STAT3/NF-κB signaling,	MDA-MB-453, SK-BR-3, BT-474, MCF-10A and HUVEC cells;	IC50: 1.97 μM in MDA-MB-453, 9.17 μM in SK-BR-3, 6.79 μM in	Higher IC50 in MCF-10A than in HER2-overexpressing	Suppressed MDA-MB-453 xenograft tumor growth without	ATA-specific evidence; anti-angiogenic and HER2-	(64)

		activity	activates AMPK, suppresses lipid/protein biosynthesis, and induces ROS/ER stress, cell-cycle arrest and apoptosis	MDA-MB-453 xenograft-bearing female BALB/c nude mice	BT-474, and 31.74 μM in MCF-10A cells; *in vivo*: 35 mg/kg i.p.	breast cancer cells; inhibited HUVEC angiogenic activity *in vitro*	obvious body-weight loss	low/ADC-resistance relevance require further validation	
Optimized derivative	Semisynthetic abietane analogues, including tanshinone and carnosol analogues	C18-functionalized ferruginol, ortho-quinone and catechol analogues	Inhibit proliferation and induce dose-dependent cell death with apoptosis-like morphology; precise mechanism remains undefined	SUM149, MDA-MB-231, T47D, MCF-7 cells	Active analogues showed IC50 values of ~1.3-18.7 μM after 72 h; TI vs. BJ cells ranged from 1 to 44	Stronger activity was observed in TNBC models for selected compounds	NR	No *in vivo* efficacy, PK, solubility or detailed mechanistic validation	(68)
Optimized derivative	Extended ferruginol, tanshinone and carnosol analogue library	Ferruginol-, tanshinone- and carnosol-related abietane scaffold modifications	Inhibit proliferation and colony formation; induce mitochondrial depolarization and apoptosis-like morphology in selected assays	SUM149, MDA-MB-231, MCF-7 cells	Active analogues showed IC50 values of ~1.3-13 μM; TI vs. BJ cells reached up to 43	Compounds 10 and 11 showed stronger activity in TNBC models	NR	*In vitro*/*in silico* evidence only; experimental PK, solubility, metabolic stability and *in vivo* efficacy remain unvalidated	(69)
Optimized derivative	TA12	Tan IIA-based imidazole analogue	Induces ROS-mediated DNA damage, γH2AX/p53 activation, AKT inhibition, S-phase arrest and FAK/GSK3β/MMP9-associated anti-invasive effects	MDA-MB-231 cells, L02 cells; zebrafish xenograft model	IC50: 13.2±3.9 μM in MDA-MB-231 and 49.1±7.4 μM in L02 cells; zebrafish exposure: 5 μM	Most potent analogue against MDA-MB-231 cells in the TA01-TA12 series; improved activity vs. native Tan IIA	Suppressed MDA-MB-231 xenograft proliferation and metastatic dissemination in zebrafish	Zebrafish and single-cell-line evidence; mammalian PK, toxicity and efficacy remain needed	(54)
Optimized derivative	Compound 4	Para-methylsulfinylphenyl-substituted Tan IIA imidazole derivative	Stabilizes multiple G4 DNAs, including MYC, KRAS, VEGF, BCL2 and Tel-26; induces DNA damage, γH2AX accumulation and S-phase arrest	MDA-MB-231, MCF-7, HeLa, HepG2, MCF-10A and HUVEC cells; zebrafish xenograft/angiogenesis models	IC50: 12.8±5.3 μM in MDA-MB-231 and 95.7±12.14 μM in MCF-10A cells; zebrafish assays used 5-20 μM	G4-selective binding over dsDNA; safe index 7.48 vs. MCF-10A cells	Suppressed MDA-MB-231 growth/metastasis and angiogenesis in zebrafish; inhibited HUVEC tube formation	Derivative-specific G4 mechanism; mammalian PK, toxicity and target engagement remain unvalidated	(67)

Delivery system	T/CM-L	Sequential-release liposomes co-loaded with STS and celastrol-loaded coix oil microemulsion	STS is released first to normalize tumor vessels and reduce TAFs, followed by celastrol/coix oil release for tumor cell killing	MCF-7 cells, L-02 cells; MCF-7 xenograft-bearing female BALB/c nude mice	IC50 in MCF-7 cells: 1.52±0.09 μM at 24 h and 0.64±0.04 μM at 48 h; *in vivo*: STS 5 mg/kg and celastrol 2 mg/kg once every two days	Sequential release improved tumor microenvironment modulation and reduced celastrol-related systemic toxicity	Tumor inhibition rate of 71.5%; increased tumor apoptosis and reduced Ki-67-positive proliferation	Complex multicomponent formulation; long-term safety, organ accumulation and manufacturability require further validation	(23)
Delivery system	Tan-Dox-MSN	Tan-NH_2-grafted mesoporous silica nanoparticles loaded with doxorubicin	Enhances ER-associated uptake and doxorubicin delivery through receptor-mediated endocytosis	MCF-7, T47D, MCF-10A cells; female BALB/c nude mice	*In vitro*: Dox-equivalent concentrations varied by assay; cellular uptake commonly assessed at Dox 5 μg/ml; *in vivo*: Dox 2 mg/kg	Improved tumor targeting, high Dox loading, enhanced tumor accumulation and reduced liver/cardiac toxicity indicators compared with free Dox formulations	Suppressed MCF-7 xenograft tumor growth in female BALB/c nude mice; Tan-NH_2/Tan-MSN inhibited T47D migration and invasion *in vitro*	ER expression in normal tissues and nanocarrier immunogenicity, organ accumulation and long-term tolerability require further evaluation	(22)
Delivery-related ligand	Tan-NH_2	Terminal amino-modified Tan IIA derivative used as an ER-associated targeting ligand	Serves as a phytoestrogen-derived targeting ligand; supports ER-associated nanoparticle uptake and shows anti-migration/anti-invasion activity in T47D cells	MCF-7, T-47D, MCF-10A cells	Cytotoxicity tested at 1-50 μg/ml; migration/invasion assays used 1, 2 and 5 μg/ml	Good biocompatibility toward MCF-10A cells within the tested range; supports construction of Tan-Dox-MSN and Tan-MSN systems	Evaluated *in vivo* as part of Tan-Dox-MSN/Tan-MSN formulations rather than as a standalone therapeutic agent	Tumor specificity may be limited by ER expression in normal tissues; endocrine-related safety requires evaluation	(22)

This table distinguishes cytotoxic potency from broader drug-likeness and translational feasibility. TAFs, tumor-associated fibroblasts. Tan IIA, tanshinone IIA; ATA, acetyltanshinone IIA; HTA, hydroquinone tanshinone IIA; STS, sodium tanshinone IIA sulfonate; CM, celastrol; MSN, mesoporous silica nanoparticles; Dox, doxorubicin; G4, G-quadruplex; ADC, antibody-drug conjugate; PK/PD, pharmacokinetic/pharmacodynamic; ER, estrogen receptor; NR, not reported in the cited breast cancer study or not sufficiently specified for direct quantitative comparison.