Supporting information

Indium/Gallium Maltolate effects on human breast carcinoma cells: *in vitro* investigation on cytotoxicity and synergism with Mitoxantrone.

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Table S1. Representative viability percent of both MDA-MB-231 and NIH-3T3 cell types treated with GaMal or InMal (5 μM and 150 μM) or MTX (10 or 200 $ngmL^{-1}$) for 24 and 144 h, respectively. Data are presented as control percent (untreated cells) set as 100 %. The mean values ± SEM ($n = 3$, $p < 0.05$). of results from three experiments are also reported.

Metal complexes or drug	Concentration	Viability percent MDA-MB-231		Viability percent NIH-3T3	
		24 h	144 h	24 h	144 h
GaMal	5 μM	127 ± 3	114 ± 1	118 ± 2	71 ± 2
	150 μM	86 ±1	8 ± 3	56 ± 2	28 ± 1
InMal	5 μM	110 ± 4	104 ± 1	93 ± 1	84 ± 1
	150 μM	100 ± 2	5 ± 1	76 ± 1	18± 2
MTX	10 ng/mL	91 ± 3	68 ± 3	64 ± 8%	27 ± 3
	200 ng/mL	91 ± 2	41 ± 1	72 ± 3%	23 ± 4

Table S2. Representative viability percent of both MDA-MB-231 and NIH-3T3 cell types treated with two concentrations (5 μM or 150 μM) of GaMal or InMal in the co-presence of MTX (10 or 200 $ngmL^{-1}$) for 24 h and 144 h, respectively. Data are presented as control percent (untreated cells) set as 100 %. The mean values ± SEM ($n = 3$, $p < 0.05$) of results from three experiments are also reported.

Metal complexes	Concentration	Co-incubation with drug	Viability percent MDA-MB-231		Viability percent NIH3T3	
			24 h	144 h	24 h	144 h
GaMal	5 μM	+ MTX 10 ng/mL	95 ± 7	95 ± 1	103 ± 12	42 ± 6
	150 μM		87 ± 6	40 ± 2	85 ± 4	33 ± 6
InMal	5 μM	+ MTX 10 ng/mL	124 ± 2	95 ± 5	80 ± 1	34 ± 3
	150 μM		75 ± 5	8 ± 1	69 ± 6	16 ± 6
GaMal	5 μM	+ MTX 200 ng/mL	85 ± 1	43 ± 2	103 ± 12	33 ± 5
	150 μM		83 ± 2	25 ± 2	85 ± 4	38 ± 3
InMal	5 μM	+ MTX 200 ng/mL	80 ± 2	42 ± 2	80 ± 6	27 ± 4
	150 μM		65 ± 3	12 ± 3	65 ± 4	25 ± 3

Table S3. Representative viability percent of both MDA-MB-231 and NIH-3T3 cell types pretreated with two concentrations (5 μM or 150 μM) of GaMal or InMal for 24 h, followed by medium removal and supplementation with MTX (10 $ngmL^{-1}$) for 24 h and 144 h respectively. Data are presented as control percent (untreated cells) set as 100 %. The mean values ± SEM ($n = 3$, $p < 0.05$) from three experiments are also reported.

Metal complexes pretreatment for 24 h	**Concentration**	**Culture medium removal and replacement with**	**Viability percent MDA-MB-231**		**Viability percent NIH-3T3**	
			24 h	**144 h**	**24 h**	**144 h**
GaMal	5 μM	Fresh medium	46 ± 1	85 ± 5	81 ± 1	109 ± 4
	150 μM		41 ± 3	76 ± 4	82 ± 1	75 ± 2
	5 μM	Addition of MTX 10 ng/mL	93 ± 1	120 ± 2	42 ± 4	38 ± 2
	150 μM		46 ± 6	44± 6	36 ± 2	33 ± 3
InMal	5 μM	Fresh medium	77 ± 3	100 ± 2	69 ± 1	88 ± 3
	150 μM		72 ± 1	60 ± 5	77 ± 4	87± 7
	5 μM	Addition of MTX 10 ng/mL	82 ± 1	81 ± 3	70 ± 2	57 ± 2
	150 μM		87 ± 1	33 ± 1	62 ± 1	54± 3

Table S4. Representative viability percent of both MDA-MB-231 and NIH-3T3 cell types pretreated with MTX (10 $ngmL^{-1}$) for 24 h, followed by culture medium removal and replacement with two concentrations (5 μM and 150 μM) of GaMal or InMal for 24 and 144 h, respectively. Data are presented as control percent (untreated cells) set as 100 %. The mean values ± SEM (n = *3*, $p < 0.05$) from three experiments are also reported.

Drug pretreatment for 24 h	Concentration	Culture medium removal and replacement with	Viability percent MDA-MB-231		Viability percent NIH-3T3	
			24 h	144 h	24 h	144 h
MTX	10 ng/mL	Fresh medium	98 ± 4	45 ± 2	58 ± 1	17 ± 1
		Addition of 5 μM GaMal	55 ± 7	53 ± 1	97 ± 1	60 ± 1
		Addition of 150 μM GaMal	49 ± 9	34 ± 1	75 ± 2	53 ± 2
		Addition of 5 μM InMal	86 ± 1	82 ± 9	45 ± 3	13 ± 1
		Addition of 150 μM InMal	82 ± 2	6 ±1	40 ± 3	17 ± 5

Figure S1. a) ^{13}C-NMR and b) ^{1}H-NMR spectra of gallium maltolate in d6-DMSO. Signal at δ=40 ppm in a) is attributed to DMSO. Signals at δ = 2.5 ppm and 3.2 ppm in b) are attributed to DMSO and water respectively. For other signals attribution see the text.

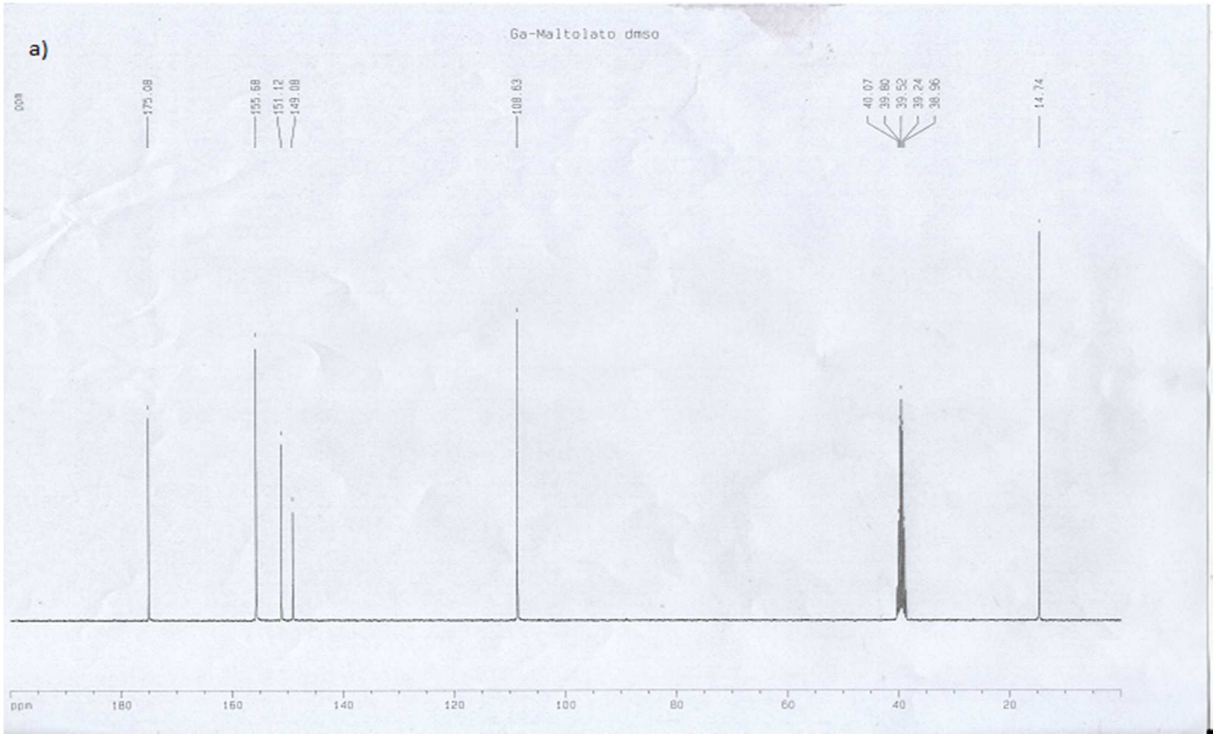
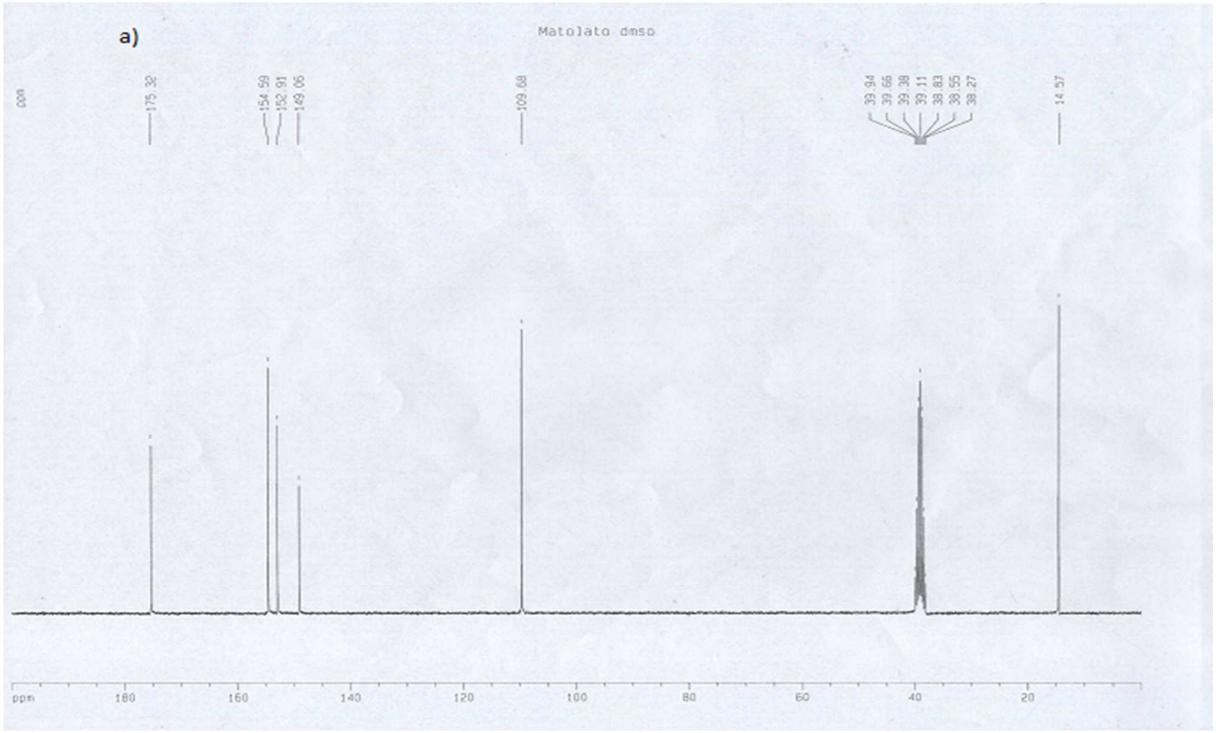


Figure S2. a) ^{13}C-NMR and b) ^{1}H-NMR spectra of indium maltolate in d6-DMSO. Signal at δ=40 ppm in a) is attributed to DMSO. Signals at δ = 2.5 ppm and 3.2 ppm in b) are attributed to DMSO and water respectively. For other signals attribution see the text.



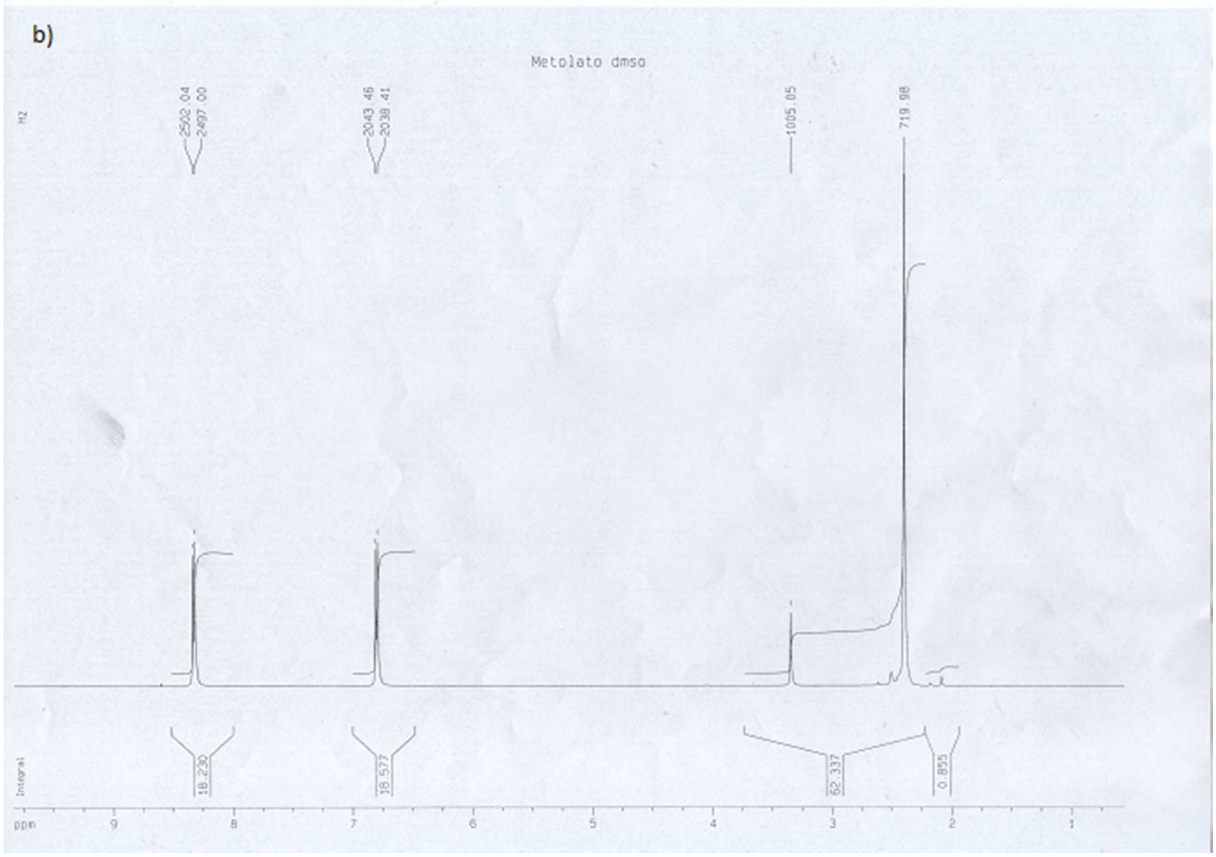


Figure S3. IR spectra of a) gallium maltolate b) indium maltolate and c) maltol.

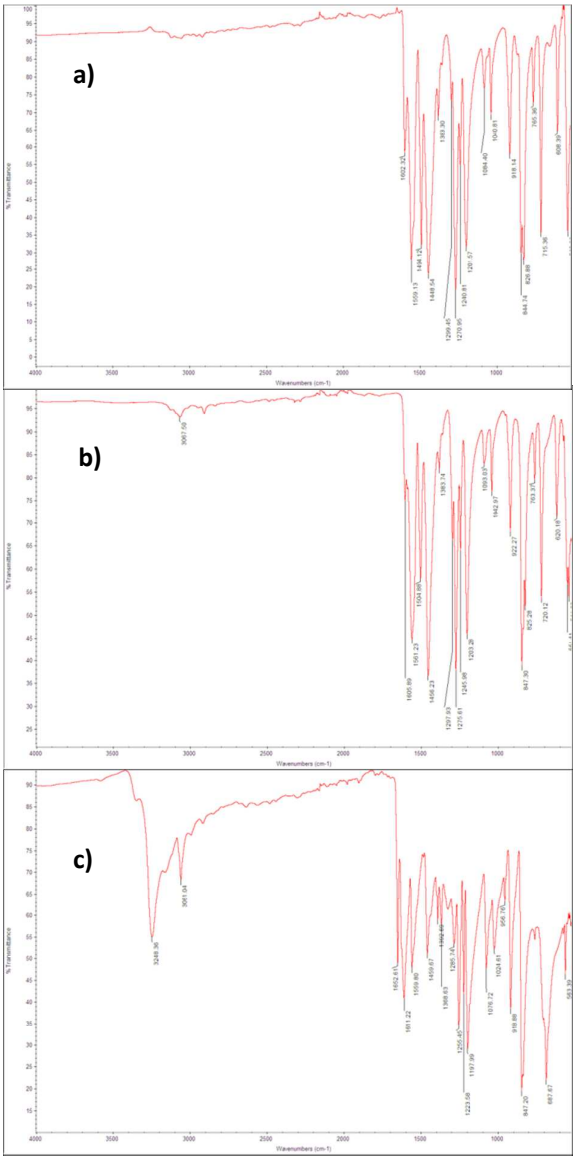


Figure S4. Representative viability percent of both MDA-MB-231 and NIH-3T3 cell types pretreated with MTX (10 $ngmL^{-1}$) for 24 h, followed by culture medium removal and replacement with two concentrations (5 μM or 150 μM) of GaMal or InMal for 24 and 144 h, respectively. The experiments were performed with (a, d) 100 μM, (b, e) 250 μM, (c, f) 500 μM iron (III) citrate. Data are presented as control percent (untreated cells) set as 100 %. The mean values ± SEM from three experiments are also reported ($n = 3$, $p < 0.05$).