Stimuli-free programmable drug release for combination chemotherapy

Supporting information

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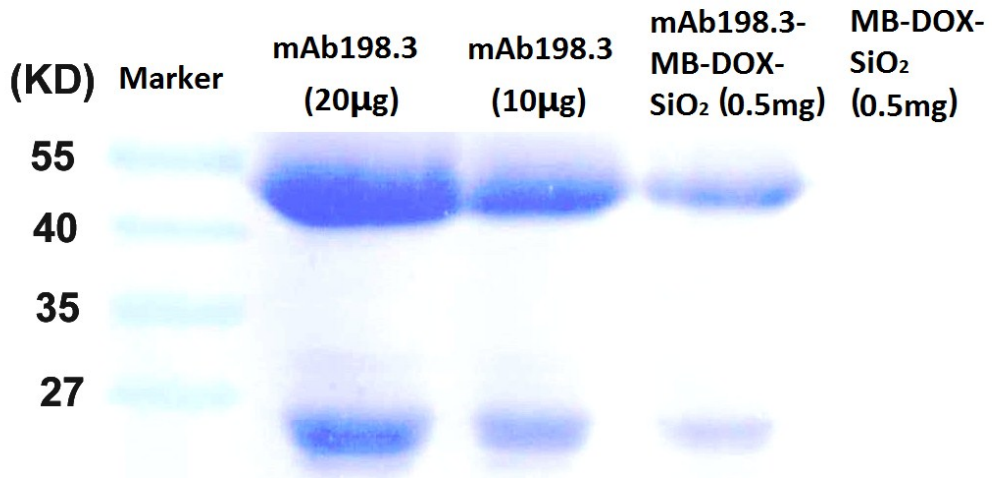

Figure SI1 The binding mAb198.3 to SiO_2-Dox/MB was determined by SDS-PAGE. 0.5mg of mAb198.3-SiO_2-Dox/MB (containing about 7.5μg mAb198.3) and SiO_2-Dox/MB were compared with free mAb198.3 groups. Gradient concentration (10μg

and 20μg) was chosen as positive controls. MAb198.3 migrated at 50 KD (heavy chain) and 25KD (light chain) on SDS-PAGE gel.

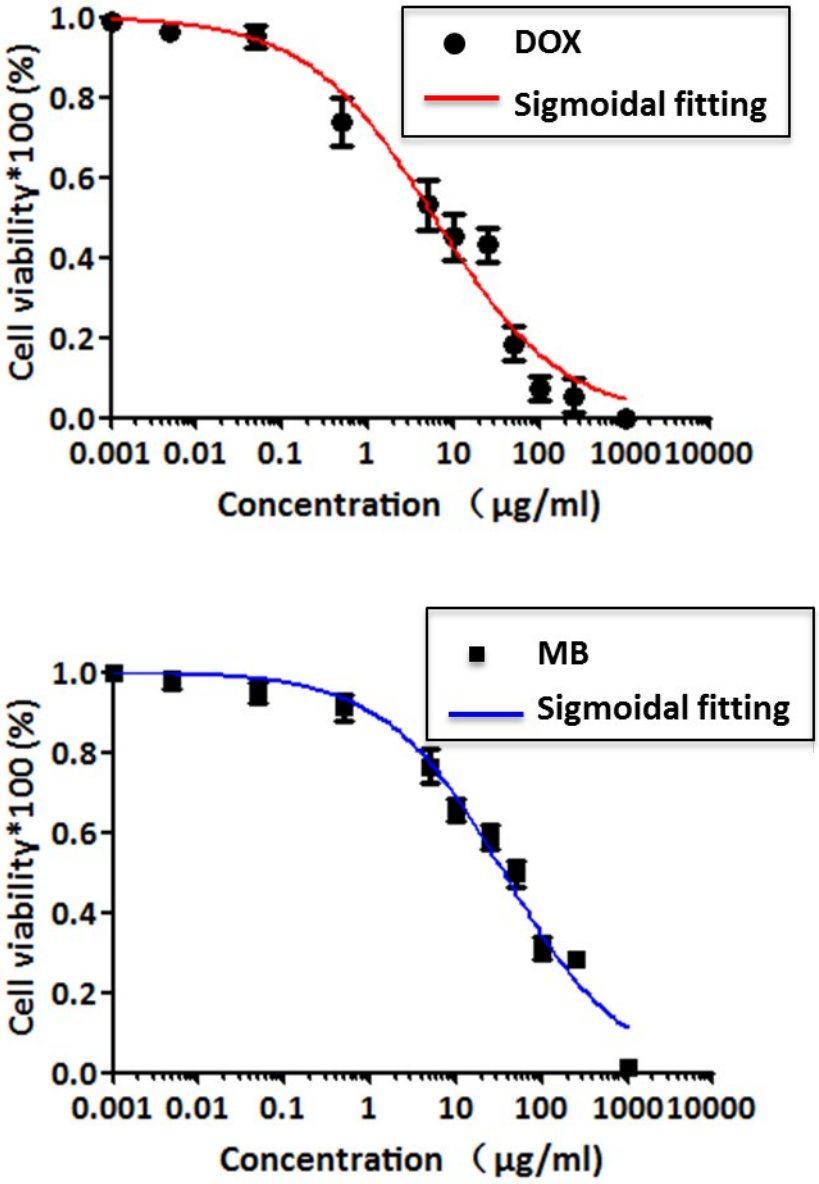

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Figure SI2 Cell viability of MB and DOX at different concentrations from 1ng/ml to 1mg/ml as determined by MTT assay.

A time lag between the the delivery of Dox and MB would lead to a sensitizing effect of MB to enhance the efficacy of Dox. Cell viability measured as a function of the time lag between Dox and MB shown that a best sensitizing effect was achieved when there was a 12hrs. lag betwee the administration of Dox and MB (Figure SI3).

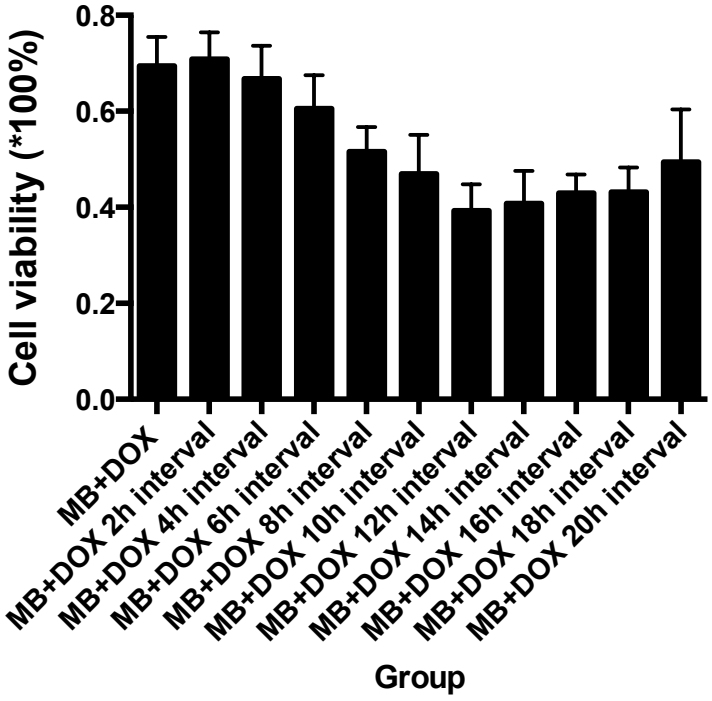
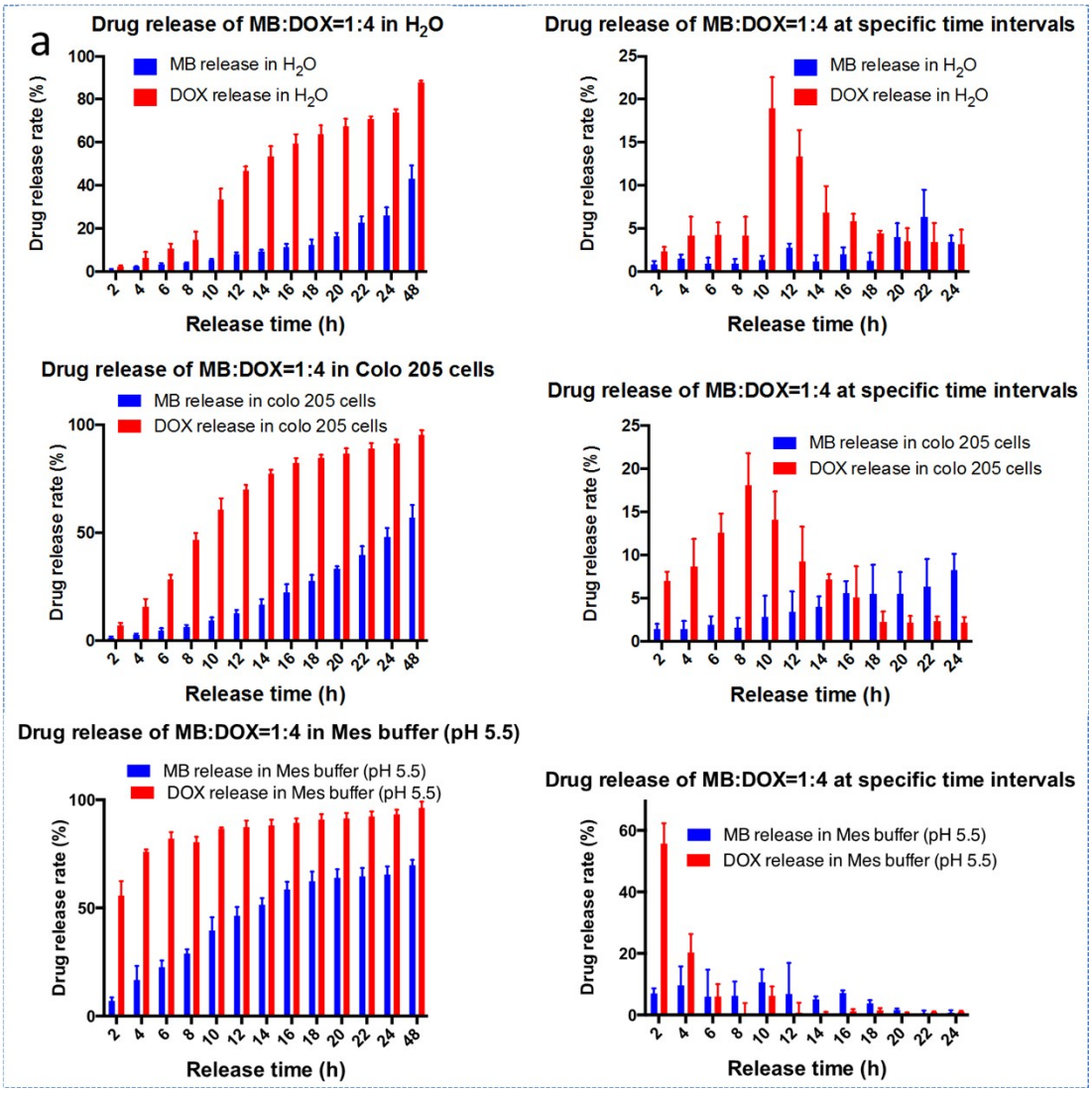
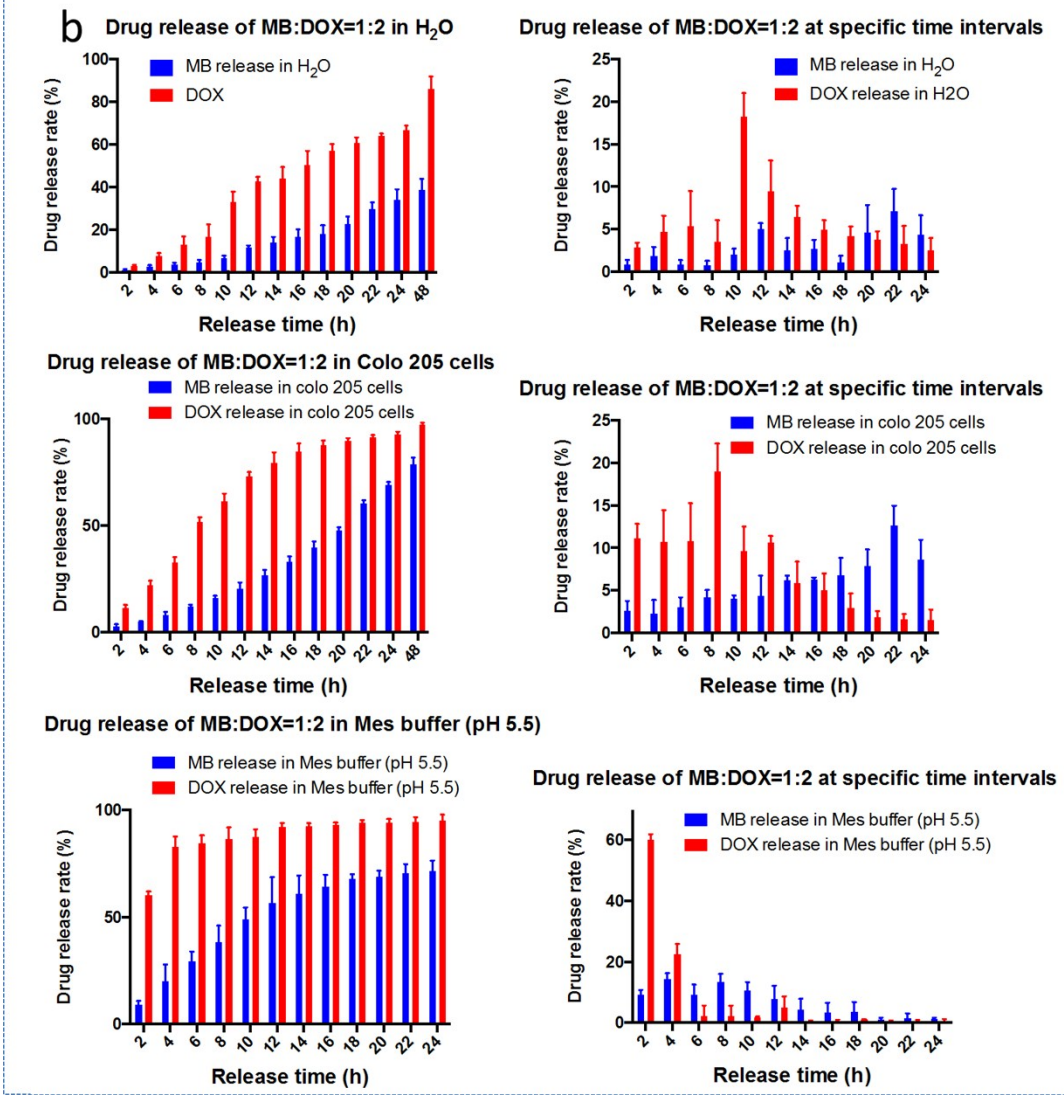


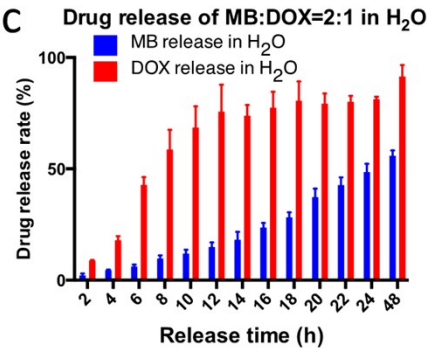
Figure SI3 Cell viability of sequential administration of DOX and MB (Dox first, followed by MB with specific interval between them) at fixed drug concentrations (0.5μg/ml for both MB and Dox).

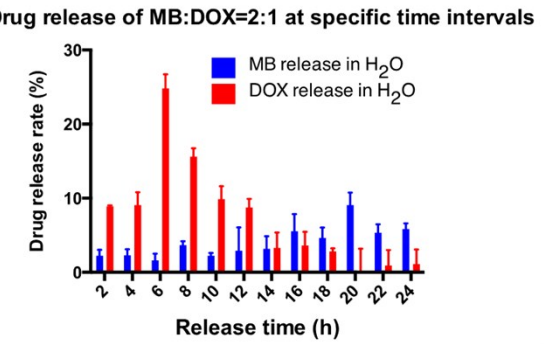
Figure SI4 showed the results taken from mAb198.3-SiO_2-DOX/MB NPs with MB/DOX loading concentration ratio as ~1:4, 1:2, 2:1 and 4:1 in the NPs. The trend of DOX and MB release was found to be similar when the NPs were dispersed in H_2O, Colo 205 cells and Mes buffer (pH 5.5), i.e., peak release of Dox were reached first, followed by that of MB. Nevertheless, different time lag between the two peak releases was found to associate with different MB/Dox ratios in the NPs. The larger the MB/Dox ratio, the smaller the difference between the two peak releases.

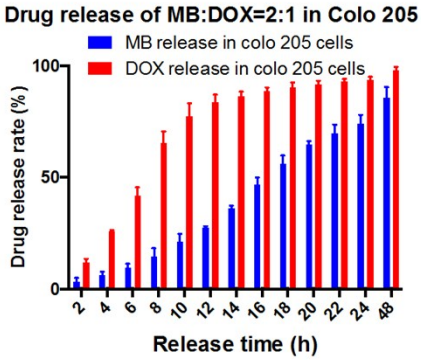


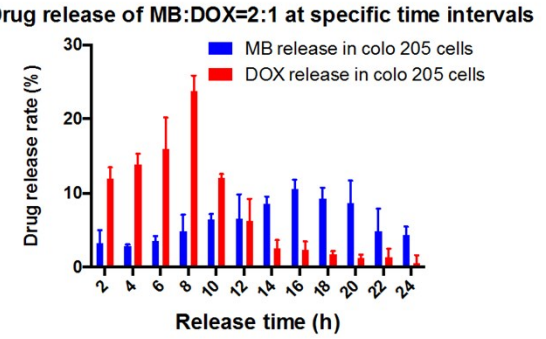

b
Drug release of MB:DOX=1:2 in H_2O
MB release in H_2O
DOX
Drug release rate (%)
Release time (h)
Drug release of MB:DOX=1:2 at specific time intervals
MB release in H_2O
DOX release in H2O
Drug release rate (%)
Release time (h)
Drug release of MB:DOX=1:2 in Colo 205 cells
MB release in colo 205 cells
DOX release in colo 205 cells
Drug release rate (%)
Release time (h)
Drug release of MB:DOX=1:2 at specific time intervals
MB release in colo 205 cells
DOX release in colo 205 cells
Drug release rate (%)
Release time (h)
Drug release of MB:DOX=1:2 in Mes buffer (pH 5.5)
MB release in Mes buffer (pH 5.5)
DOX release in Mes buffer (pH 5.5)
Drug release rate (%)
Release time (h)
Drug release of MB:DOX=1:2 at specific time intervals
MB release in Mes buffer (pH 5.5)
DOX release in Mes buffer (pH 5.5)
Drug release rate (%)
Release time (h)

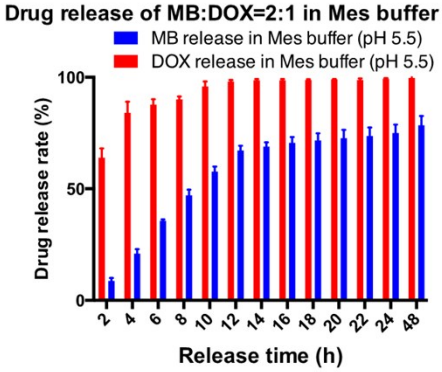
C

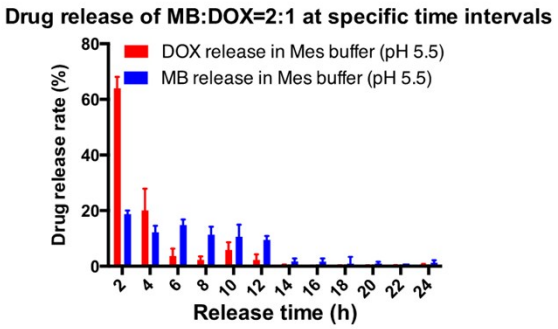

Drug release of MB:DOX=2:1 in H_2O
MB release in H_2O
DOX release in H_2O
Drug release rate (%)
Release time (h)


Drug release of MB:DOX=2:1 at specific time intervals
MB release in H_2O
DOX release in H_2O
Drug release rate (%)
Release time (h)


Drug release of MB:DOX=2:1 in Colo 205
MB release in colo 205 cells
DOX release in colo 205 cells
Drug release rate (%)
Release time (h)


Drug release of MB:DOX=2:1 at specific time intervals
MB release in colo 205 cells
DOX release in colo 205 cells
Drug release rate (%)
Release time (h)


Drug release of MB:DOX=2:1 in Mes buffer (pH 5.5)
MB release in Mes buffer (pH 5.5)
DOX release in Mes buffer (pH 5.5)
Drug release rate (%)
Release time (h)


Drug release of MB:DOX=2:1 at specific time intervals
DOX release in Mes buffer (pH 5.5)
MB release in Mes buffer (pH 5.5)
Drug release rate (%)
Release time (h)

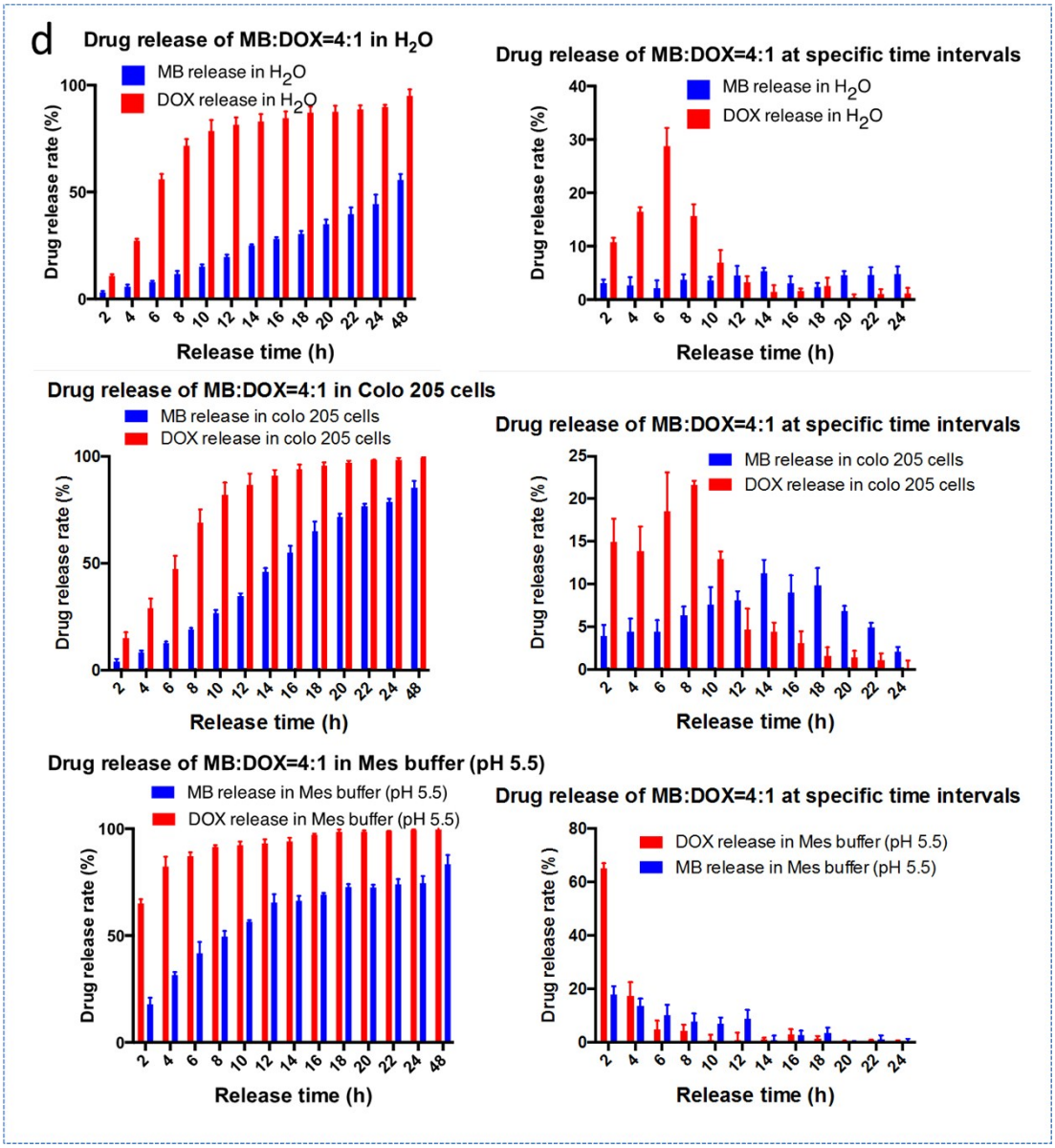


Figure SI4 The cumulative drug release profiles and those plotted at specific time points in H_2O, Colo 205 cytoplasm, and Mes buffer (pH 5.5) at different MB/DOX ratios (1:4(a), 1:2(b), 2:1(c) and 4:1(d)).

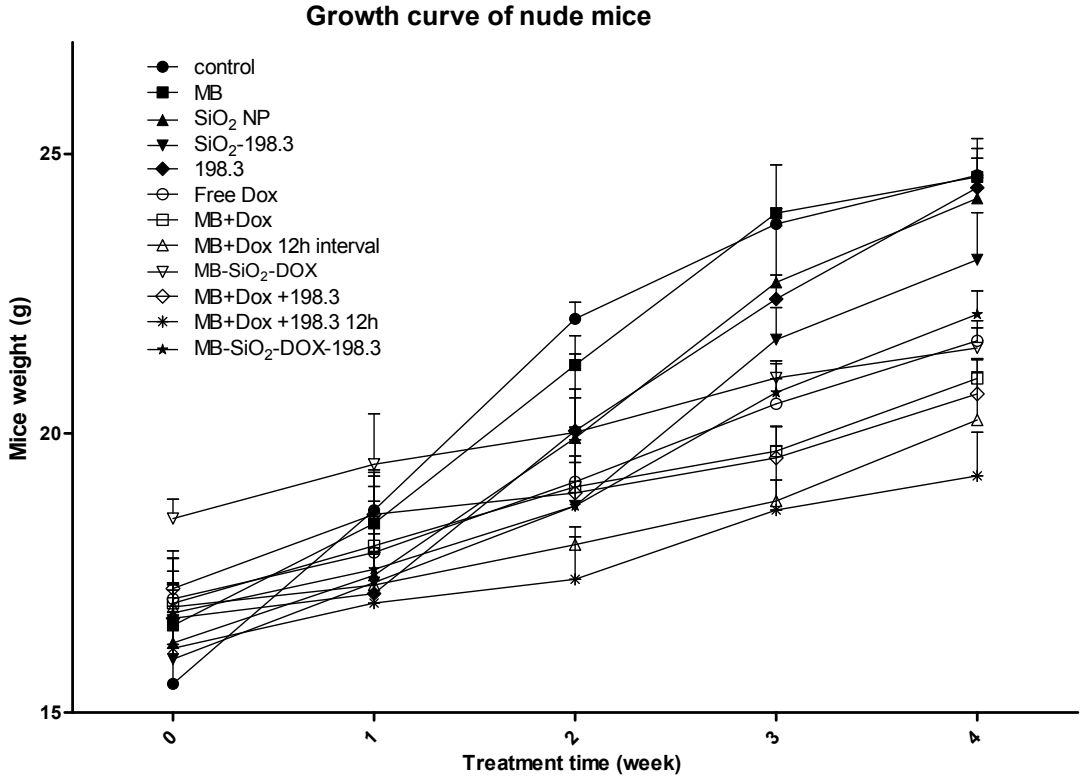


Figure SI5 Mice weight of 12 treatment groups during administration period. The results represent the means ± SDs (n = 5).

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