

Supplementary Material for

Enhancing Urological Cancer Treatment: Leveraging Vasodilators Synergistic Potential with 5-FU for Improved Therapeutic Outcomes

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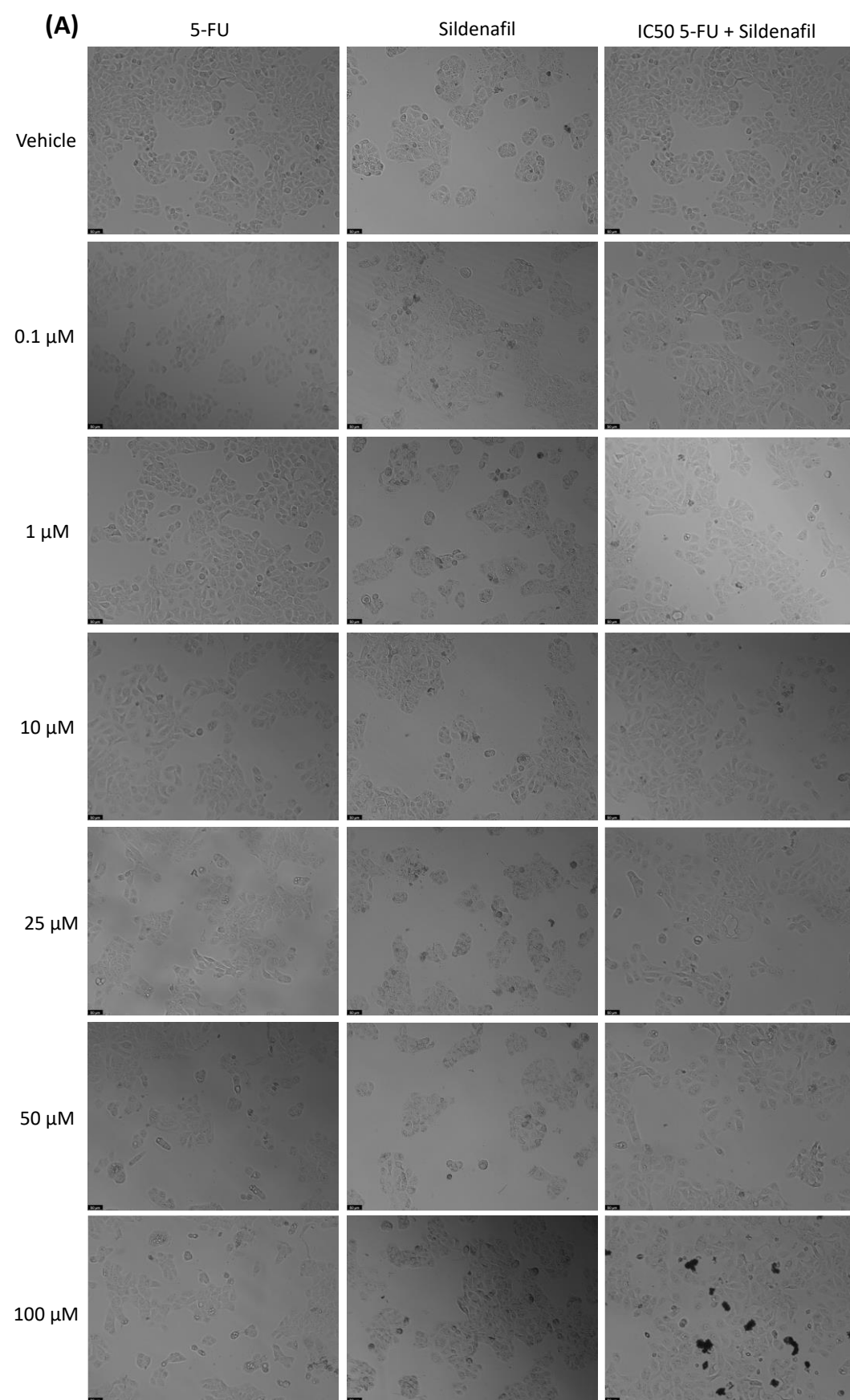
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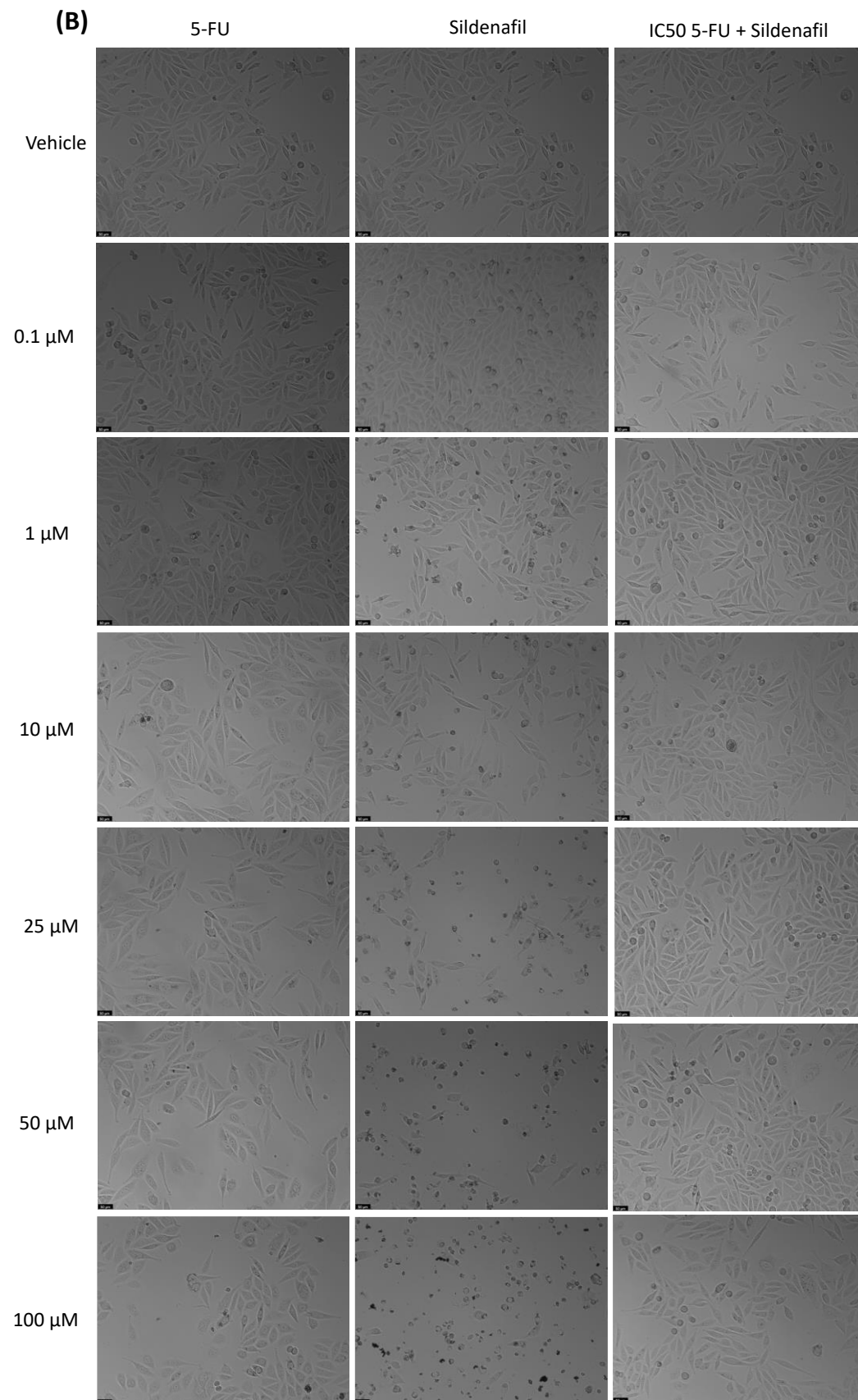
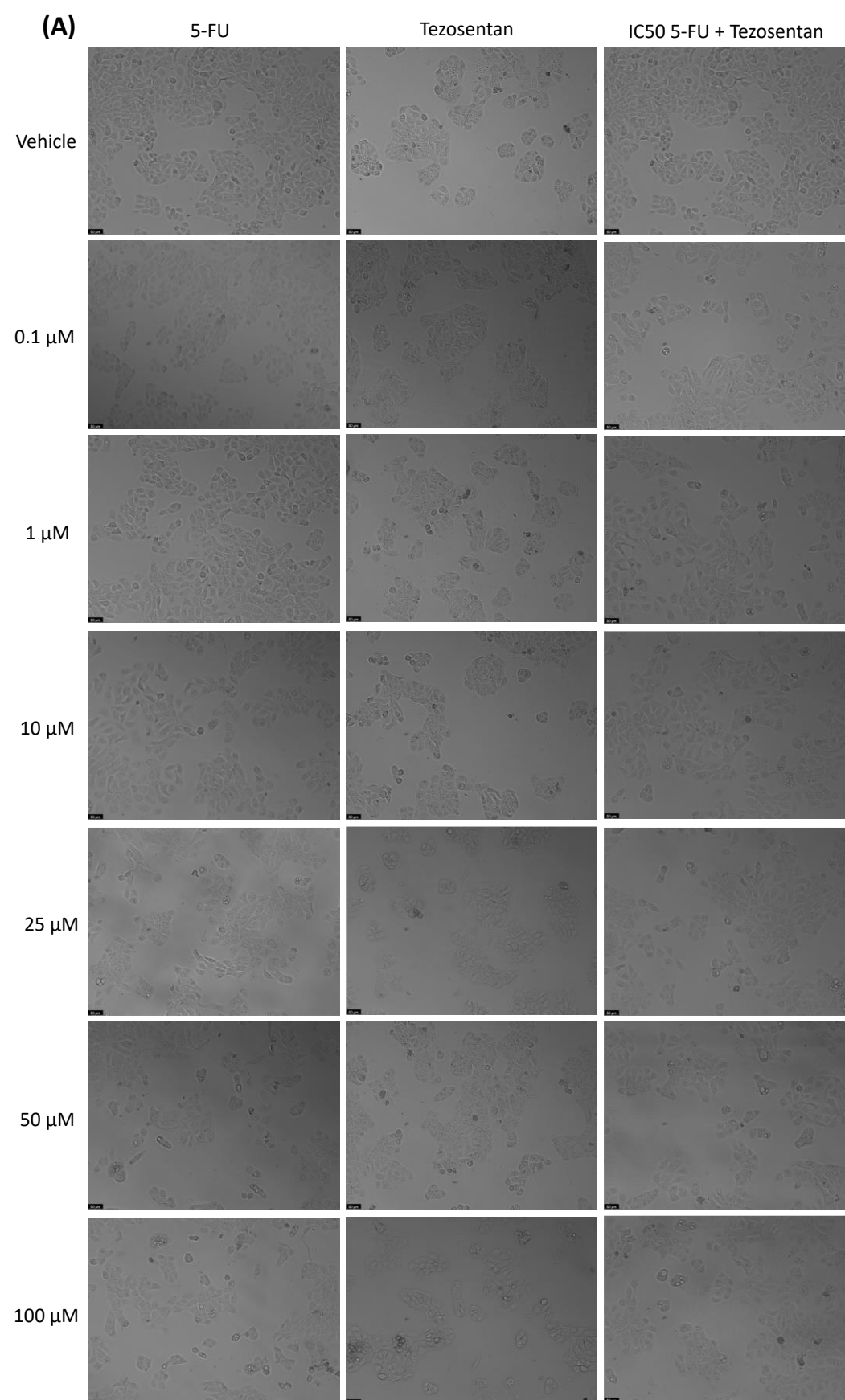


Figure S1. Morphological analysis of 5-FU and Sildenafil alone and in combination in (A) UM-UC-5 and (B) PC-3 cells. Cells were treated with vehicle (DMSO). Results are representative of three independent experiments. Scale bar: 50 μ m.



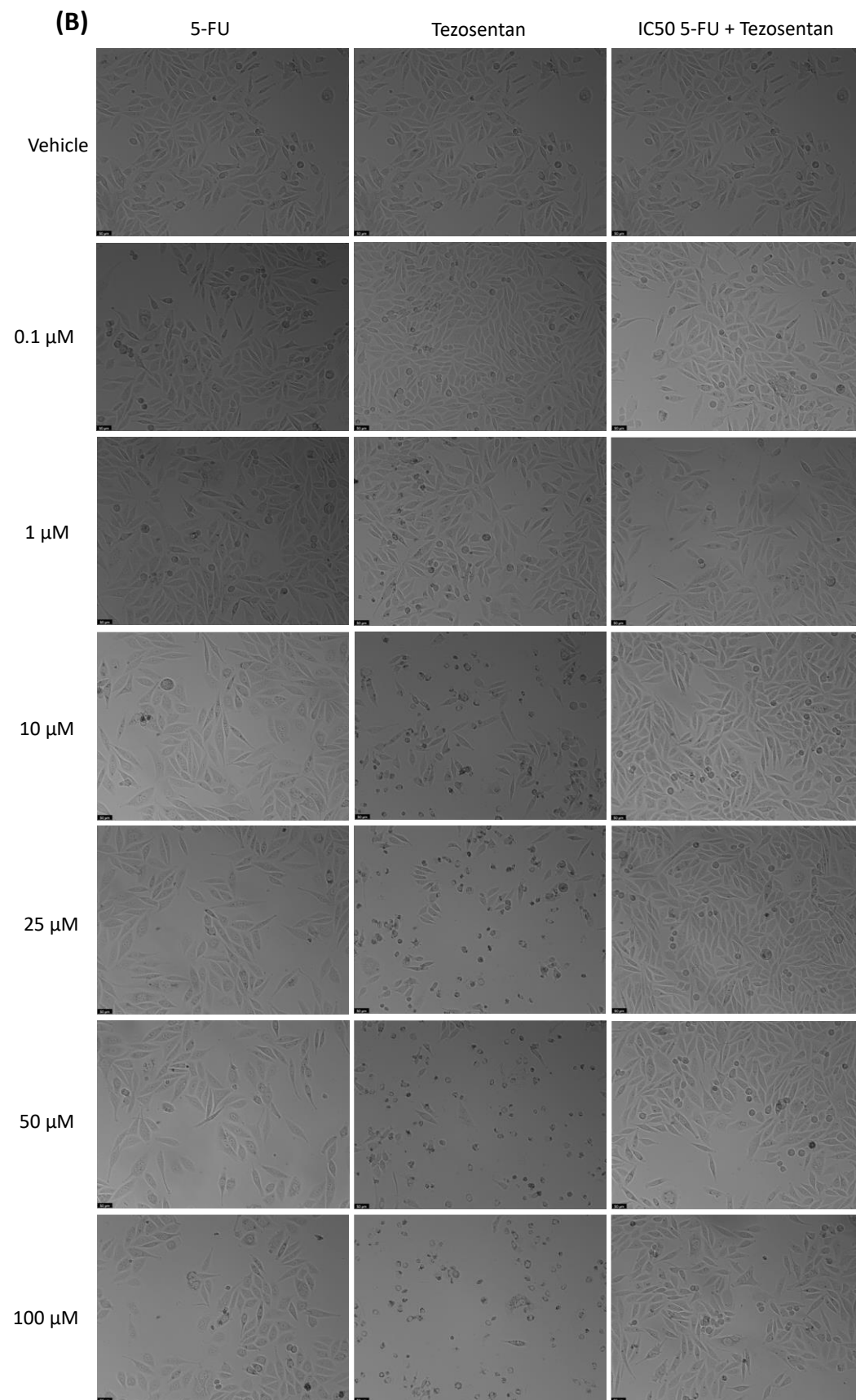
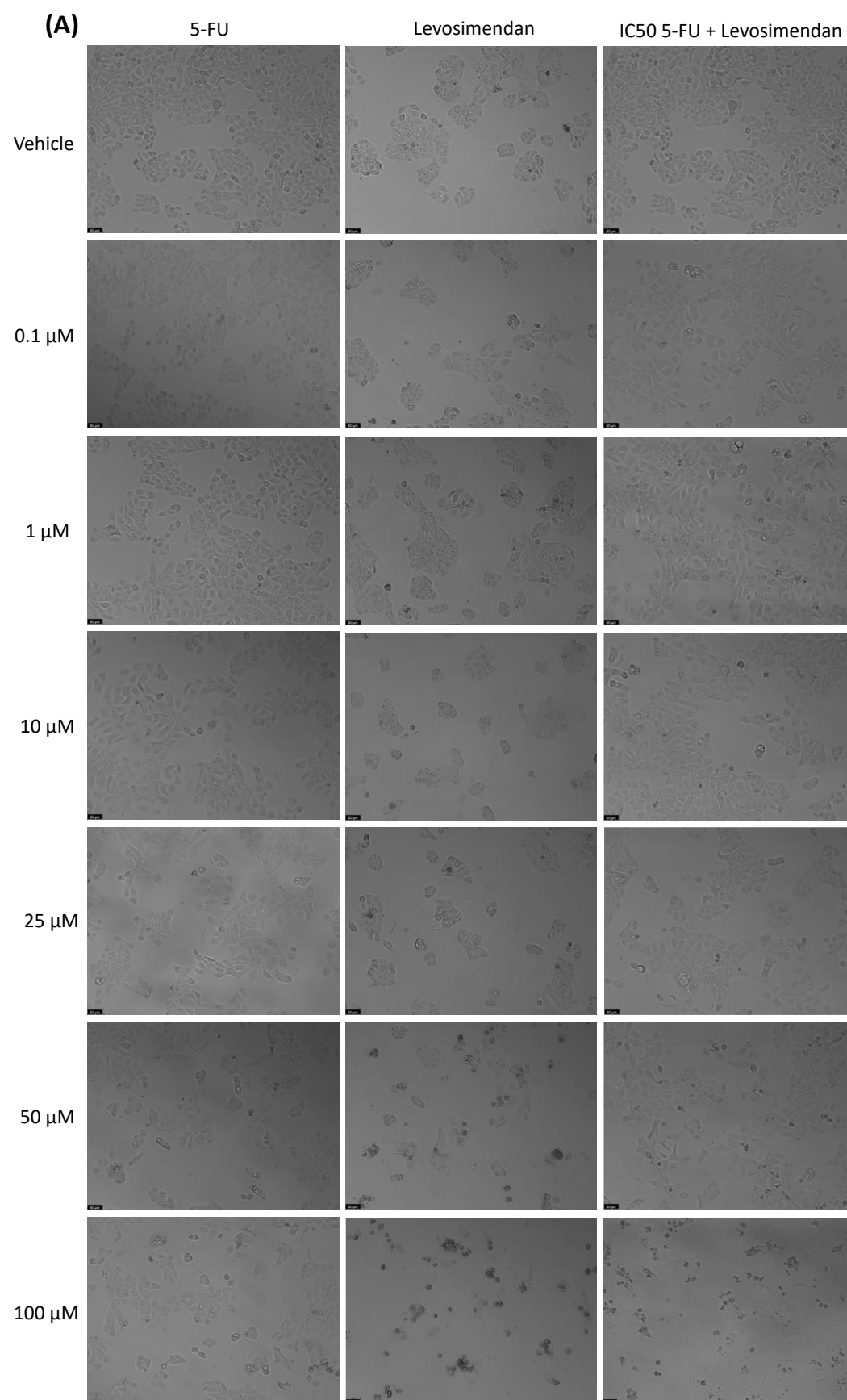


Figure S2. Morphological analysis of 5-FU and Tezosentan alone and in combination in (A) UM-UC-5 and (B) PC-3 cells. Cells were treated with vehicle (DMSO). Results are representative of three independent experiments. Scale bar: 50 μ m.



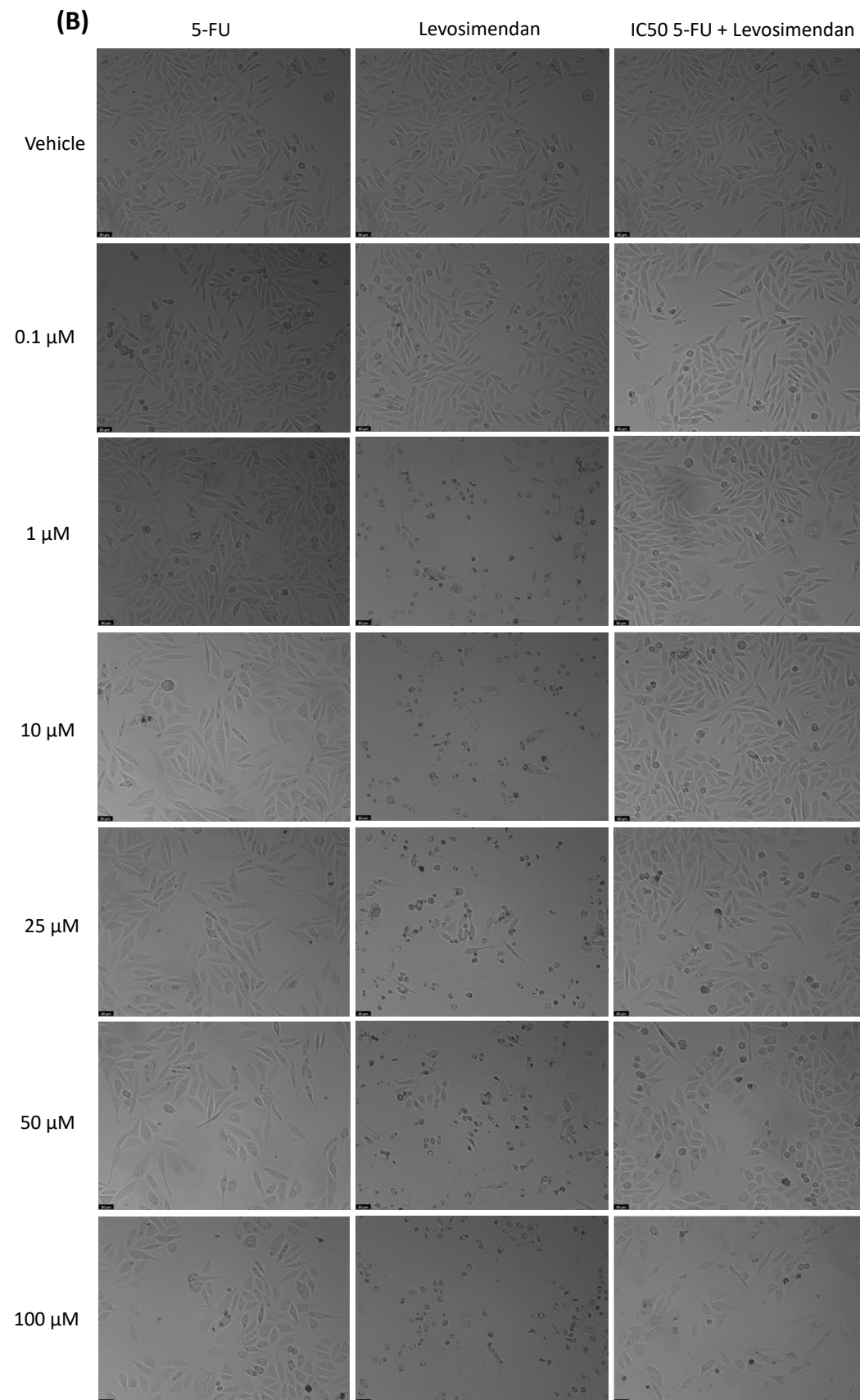


Figure S3. Morphological analysis of 5-FU and Levosimendan alone and in combination in (A) UM-UC-5 and (B) PC-3 cells. Cells were treated with vehicle (DMSO). Results are representative of three independent experiments. Scale bar: 50 μ m.

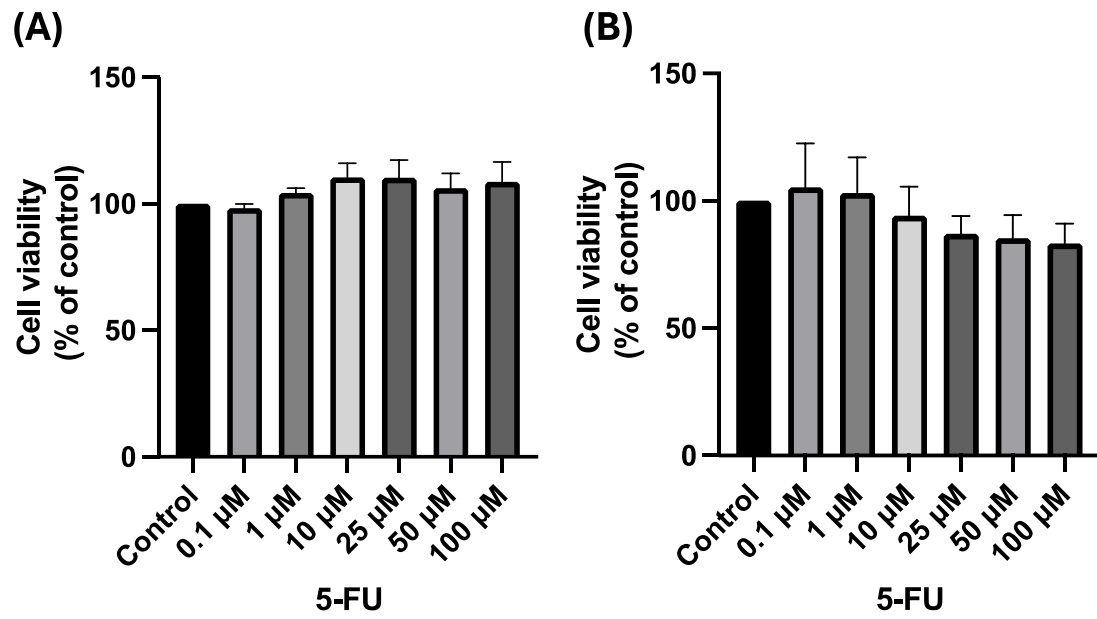


Figure S4. Biosafety evaluation of 5-FU at (A) 24 h and (B) 72 h in MRC-5 cell line. MRC-5 were treated with 0.1% DMSO and increasing concentrations (0.1-100 μ M) of 5-FU. Values are expressed as percentages of control and represent means $\pm$ SD. Each experiment was done three times independently (n = 3).

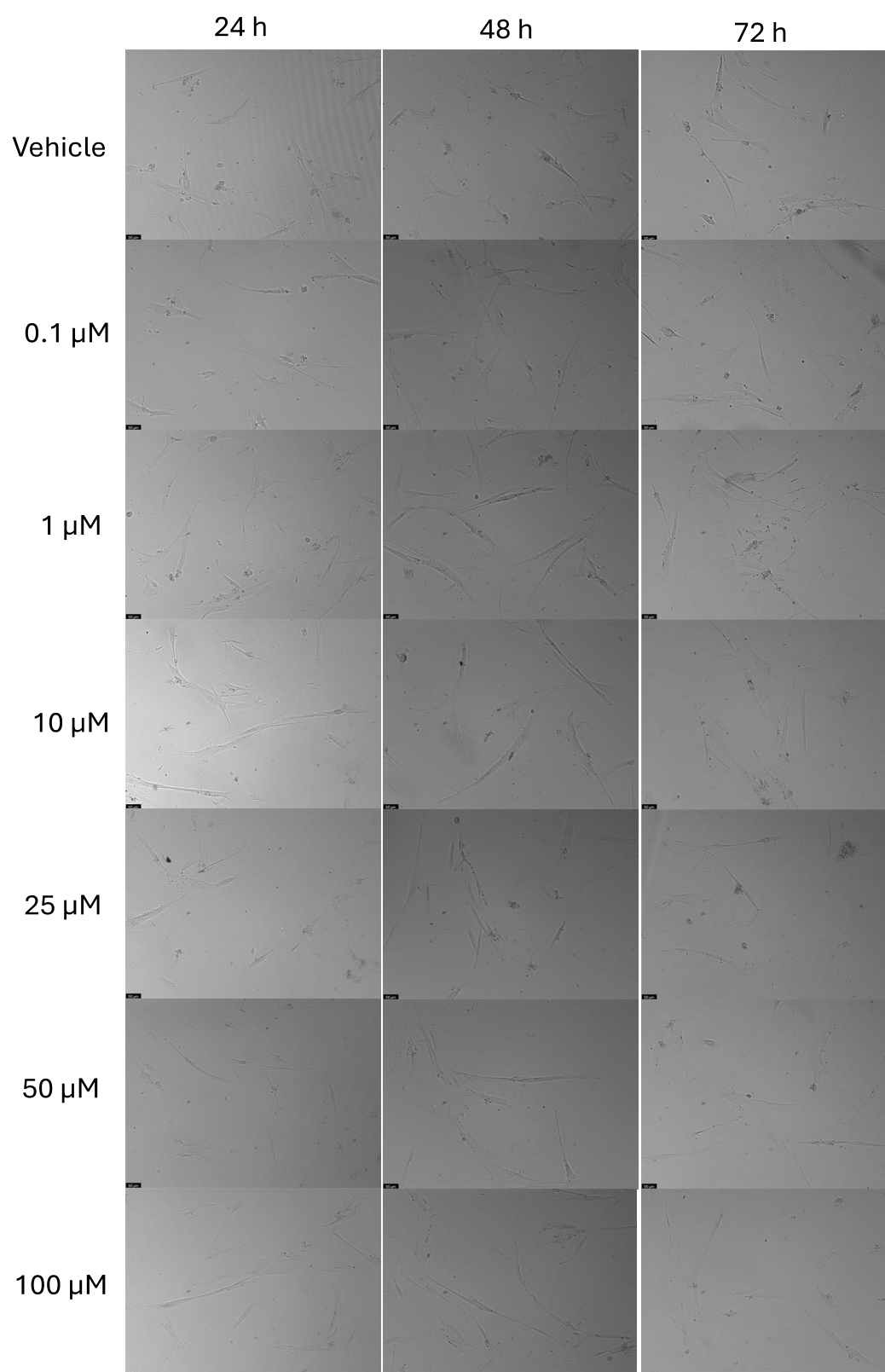


Figure S5. Morphological evaluation of MRC-5 cells treated with 5-FU. MRC-5 were treated with vehicle (DMSO) and increasing concentrations (0.1-100 μ M) of 5-FU for 24, 48 and 72 h. Results are representative of three independent experiments. Scale bar: 50 μ m.

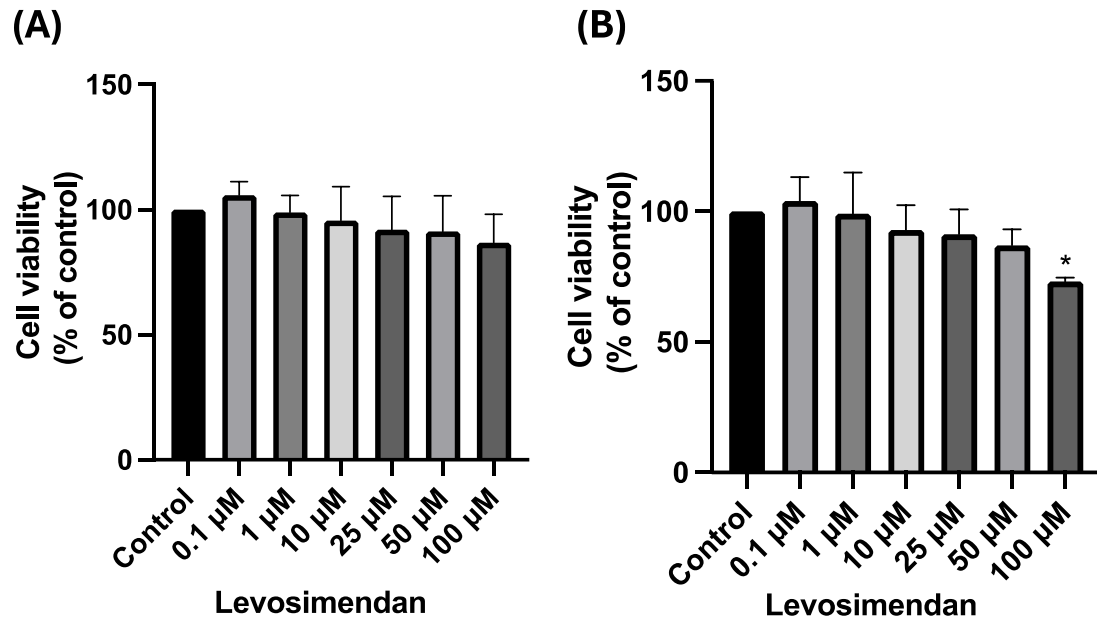


Figure S6. Biosafety evaluation of Levosimendan at (A) 24 h and (B) 72 h in MRC-5 cell line. MRC-5 were treated with 0.1% DMSO and increasing concentrations (0.1-100 μM) of Levosimendan. Values are expressed as percentages of control and represent means $\pm$ SD. Each experiment was done three times independently ($n = 3$). * Statistically significant vs. control at $p < 0.05$.

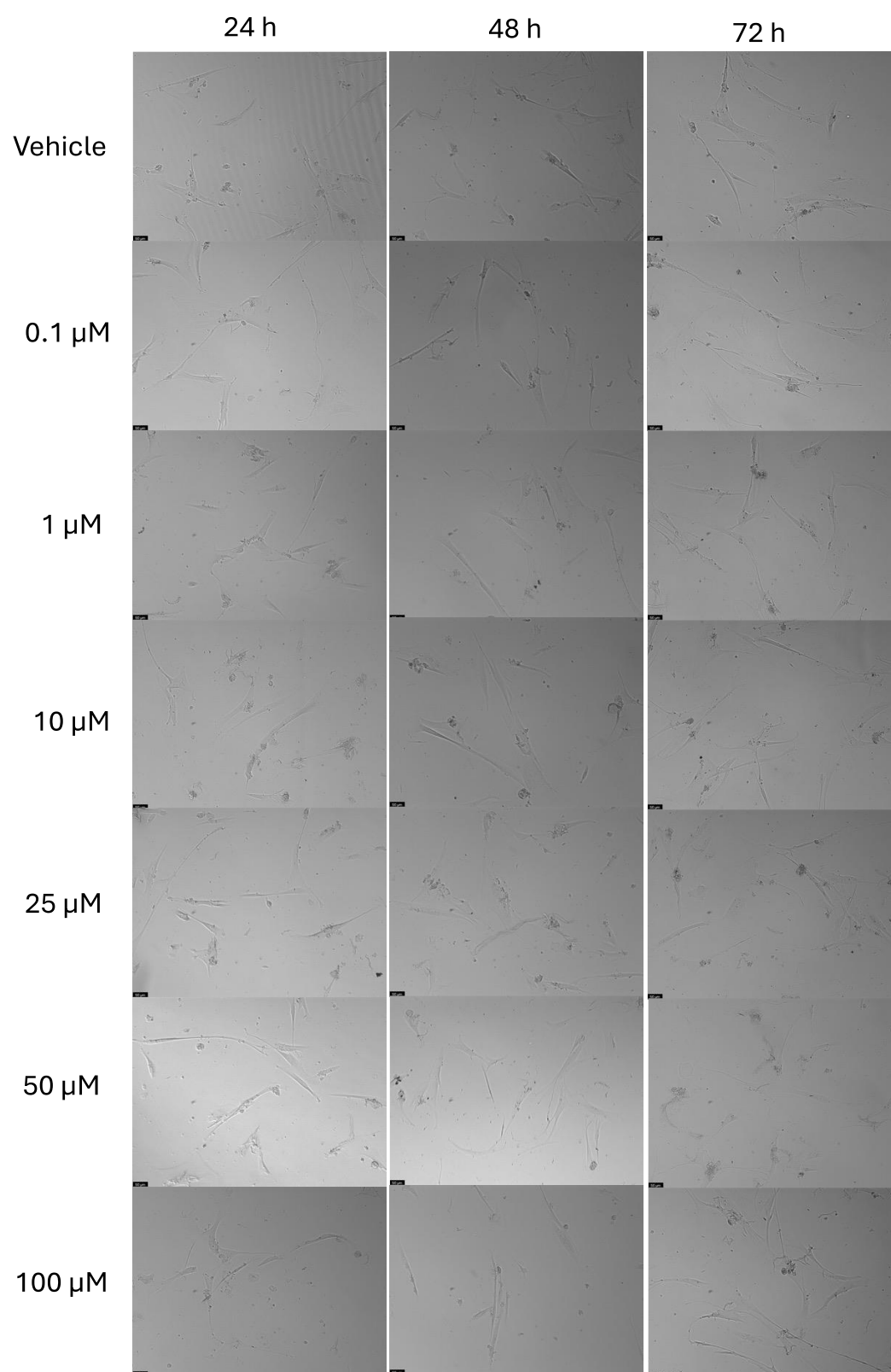


Figure S7. Morphological evaluation of MRC-5 cells treated with Levosimendan. MRC-5 were treated with vehicle (DMSO) and increasing concentrations (0.1-100 μ M) of Levosimendan for 24, 48 and 72 h. Results are representative of three independent experiments. Scale bar: 50 μ m.

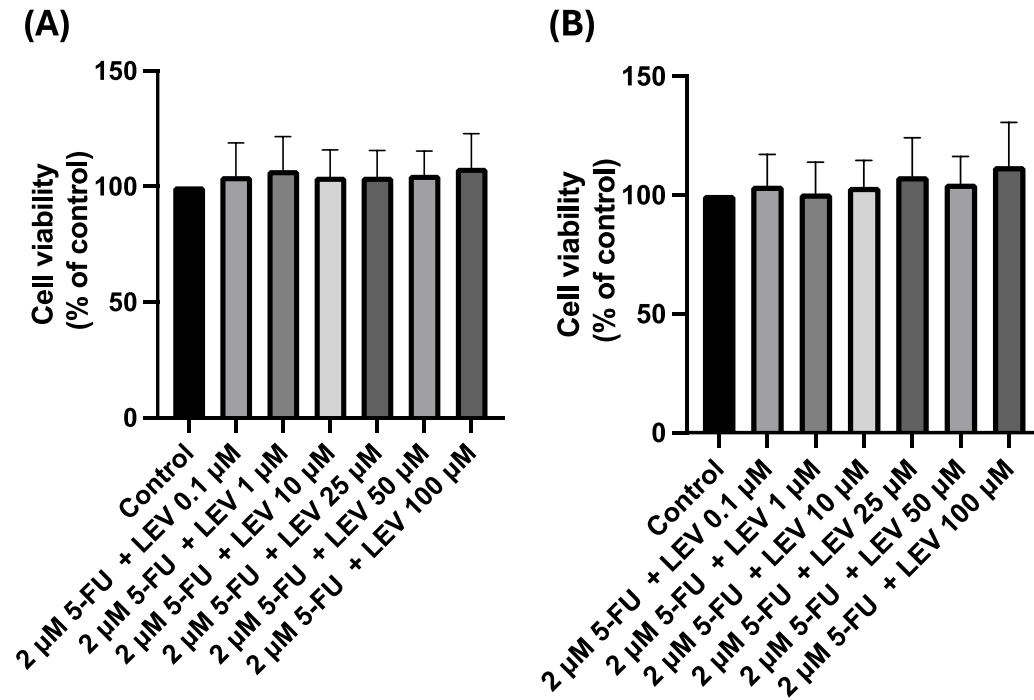


Figure S8. Biosafety evaluation of Levosimendan + 5-FU at (A) 24 h and (B) 72 h in MRC-5 cell line. MRC-5 were treated with 0.1% DMSO, increasing concentrations (0.1-100 μ M) of Levosimendan combined with 2 μ M 5-FU. Values are expressed as percentages of control and represent means $\pm$ SD. Each experiment was done three times independently ($n = 3$).

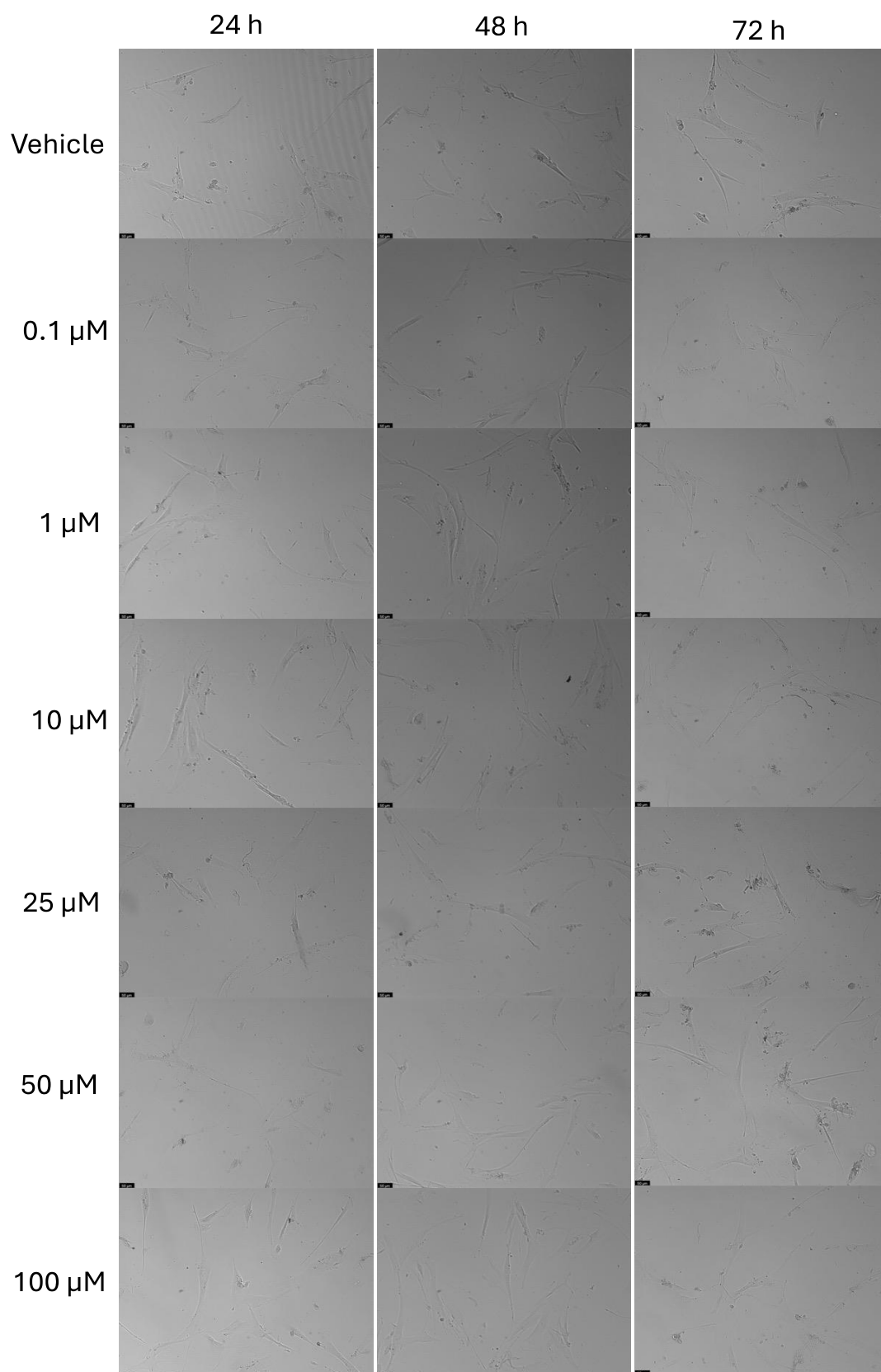


Figure S9. Morphological evaluation of MRC-5 cells treated with Levosimendan + 2 μM 5-FU. MRC-5 were treated with vehicle (DMSO) and increasing concentrations (0.1-100 μM) of Levosimendan combined with 2 μM 5-FU for 24, 48 and 72 h. Results are representative of three independent experiments. Scale bar: 50 μm .

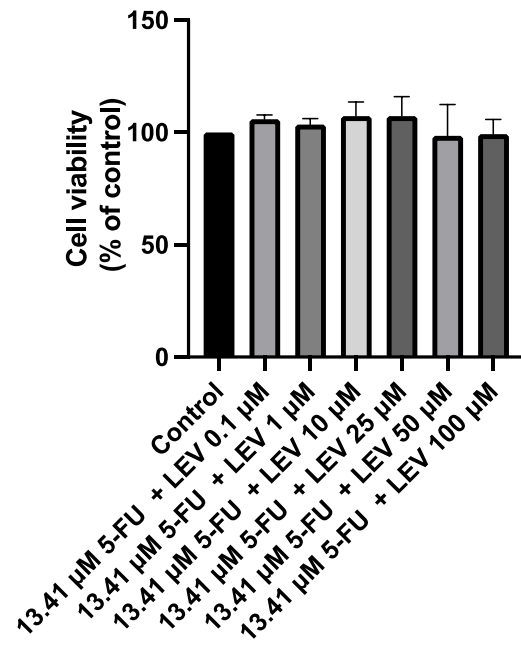
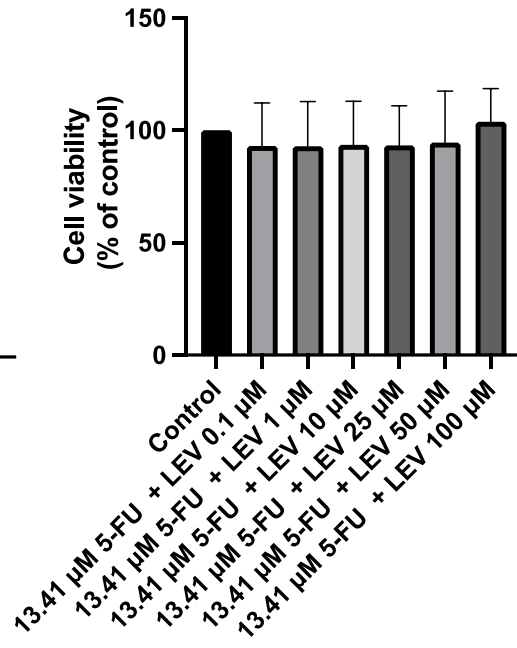
(A)**(B)**

Figure S10. Biosafety evaluation of Levosimendan + 5-FU at (A) 24 h and (B) 72 h in MRC-5 cell line. MRC-5 were treated with 0.1% DMSO, increasing concentrations (0.1-100 μ M) of Levosimendan combined with 13.41 μ M 5-FU. Values are expressed as percentages of control and represent means $\pm$ SD. Each experiment was done three times independently ($n = 3$).

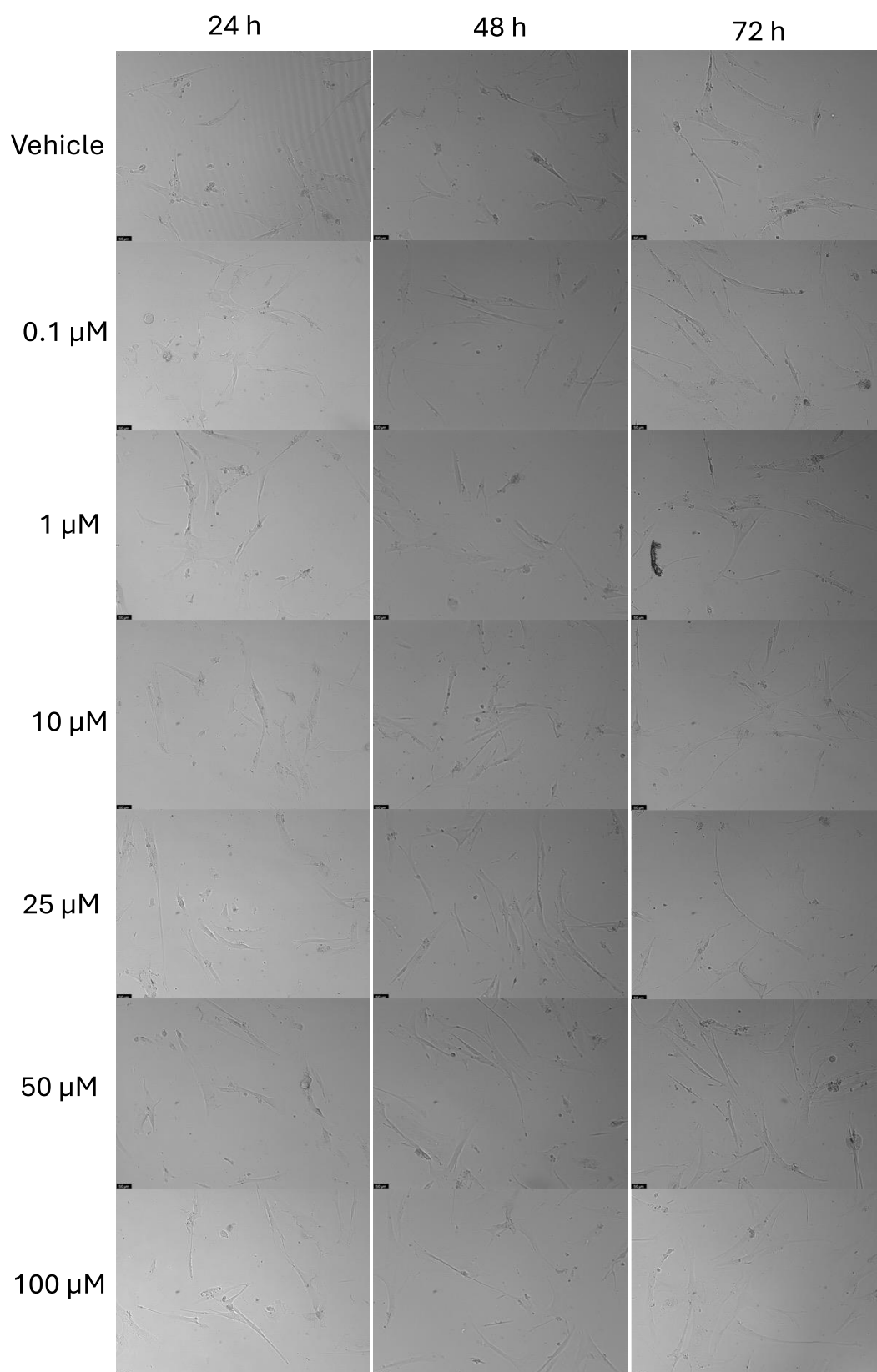


Figure S11. Morphological evaluation of MRC-5 cells treated with Levosimendan + 13.41 μM 5-FU. MRC-5 were treated with vehicle (DMSO) and increasing concentrations (0.1-100 μM) of Levosimendan combined with 13.41 μM 5-FU for 24, 48 and 72 h. Results are representative of three independent experiments. Scale bar: 50 μm .