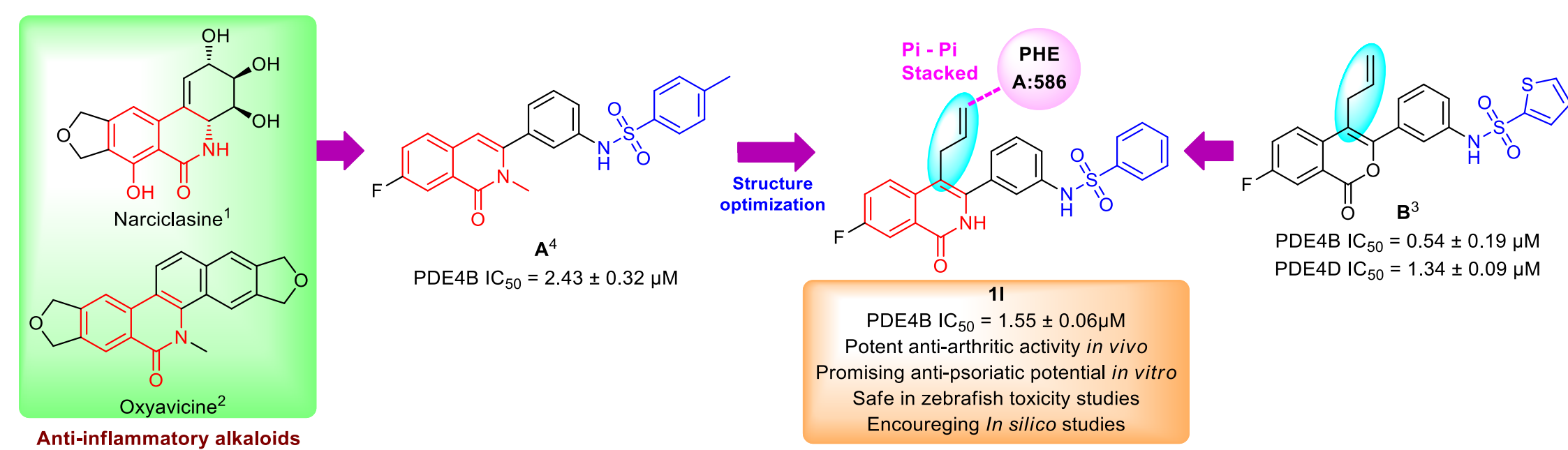
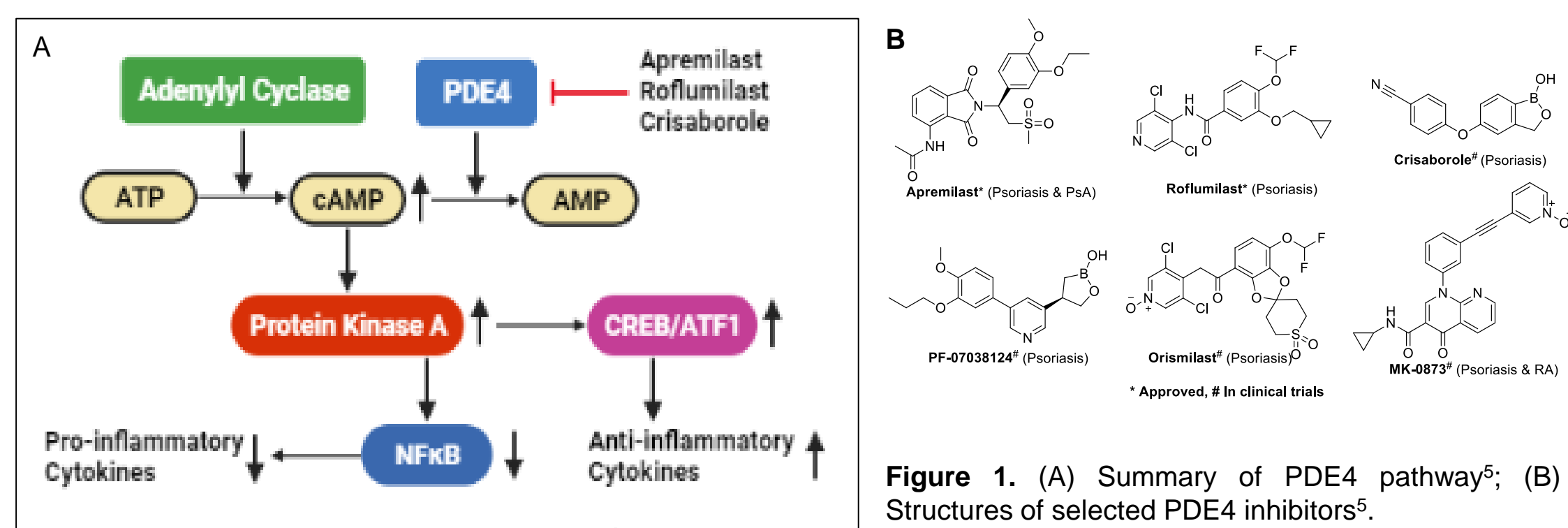


## Graphical Abstract



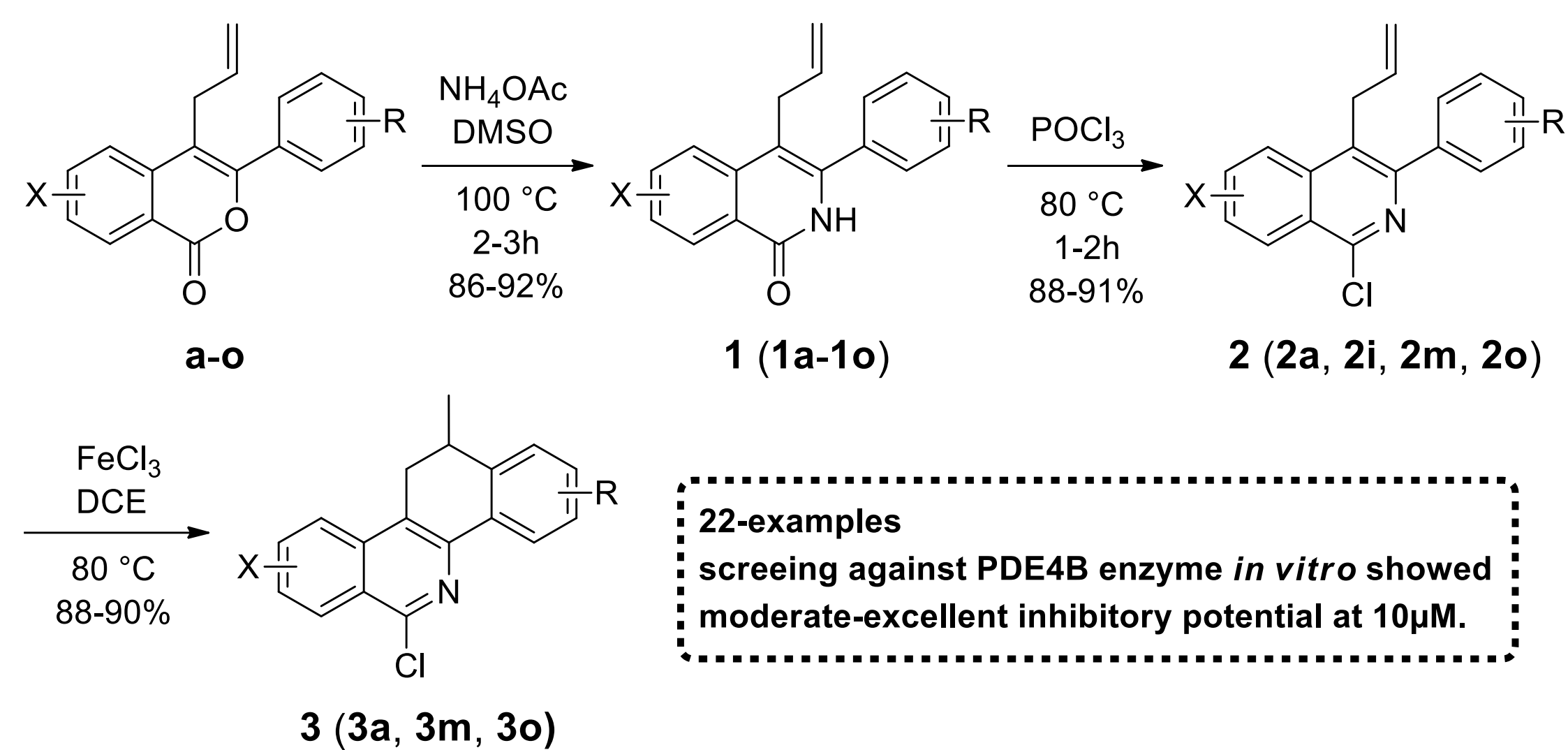
## Introduction



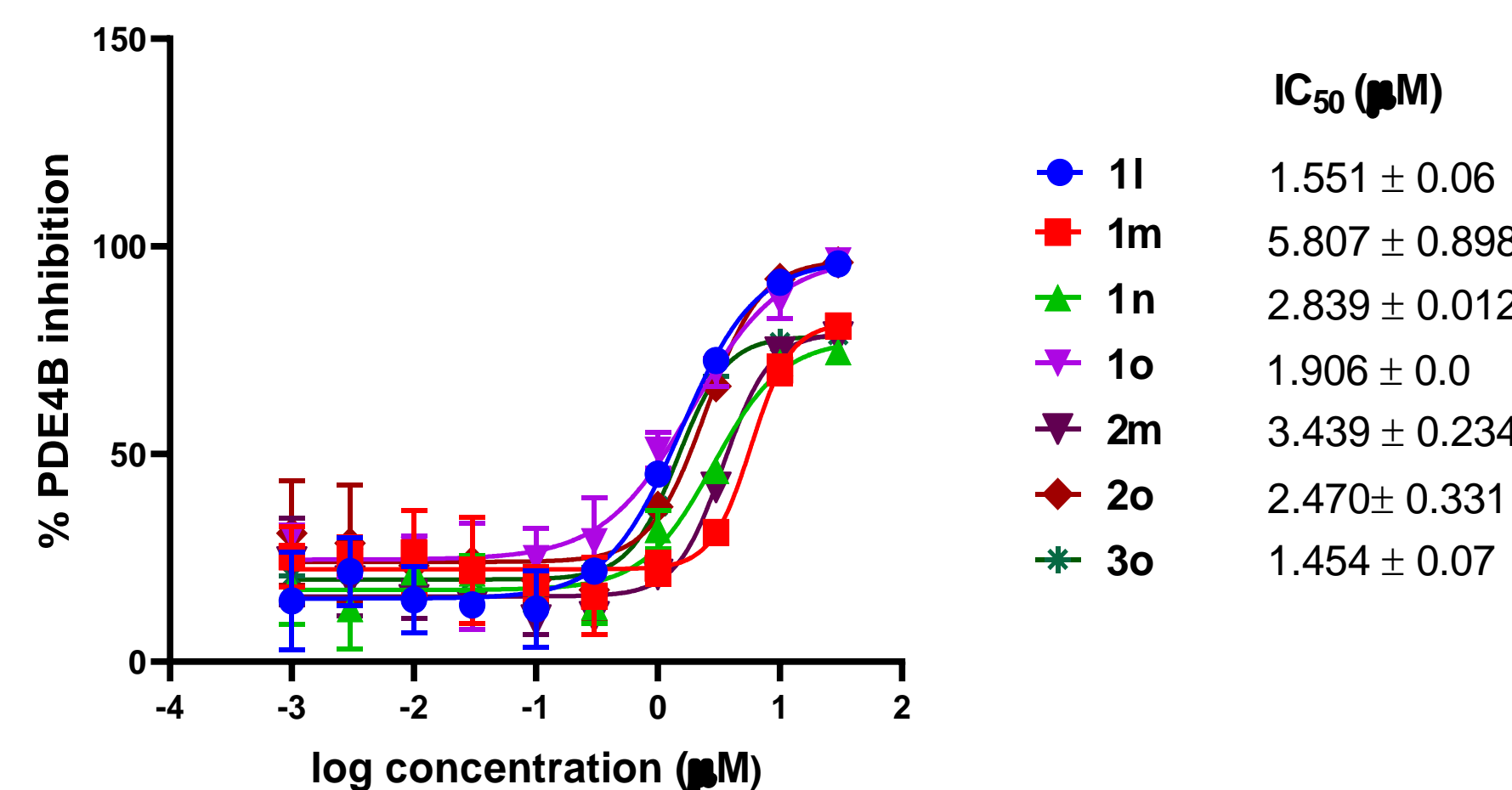
## Results and Discussion

**Table 1.** Docking scores of few selected designed isoquinolin-1(2H)-one derivatives.

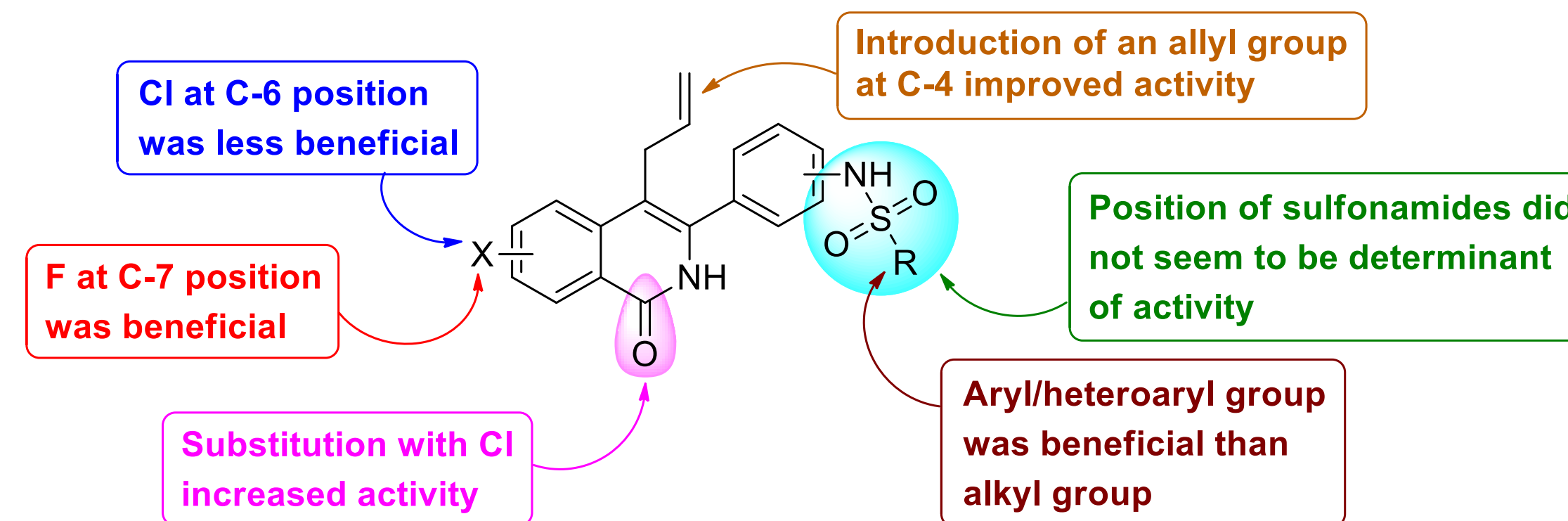
Compound Code	Docking Score (kcal/mol)	Compound Code	Docking Score (kcal/mol)
<b>1a</b>	-7.5	<b>1n</b>	-7.5
<b>1l</b>	-8.0	<b>2m</b>	-7.6
<b>1m</b>	-8.3	<b>Rolipram</b>	-7.6



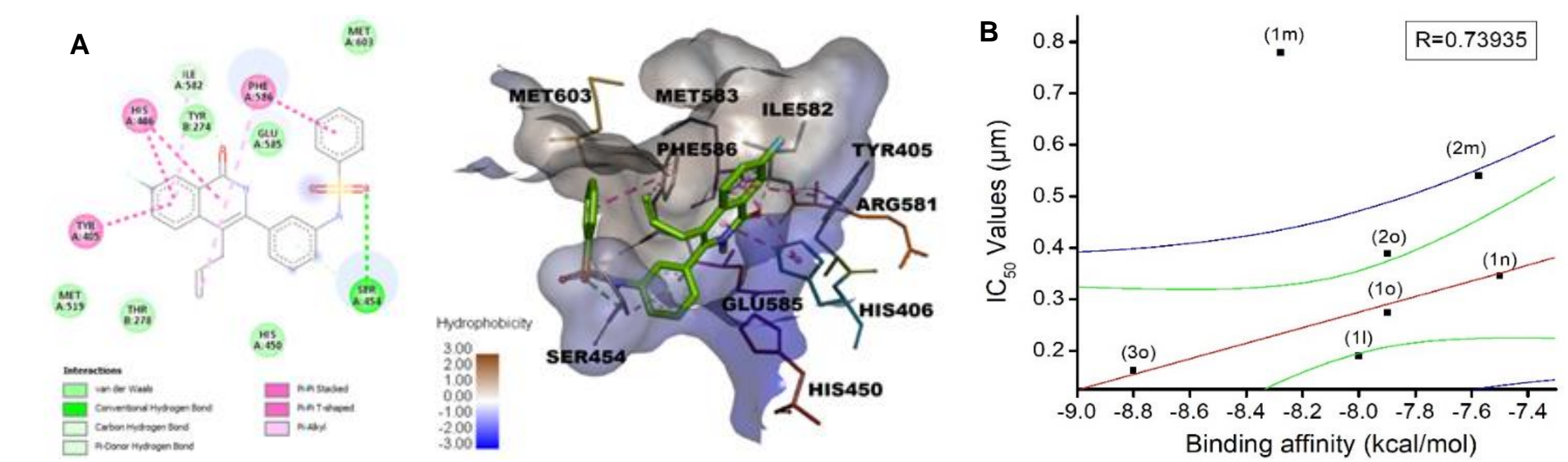
**Scheme 1.** Synthesis of targeted compounds **1**, **2** and **3**.



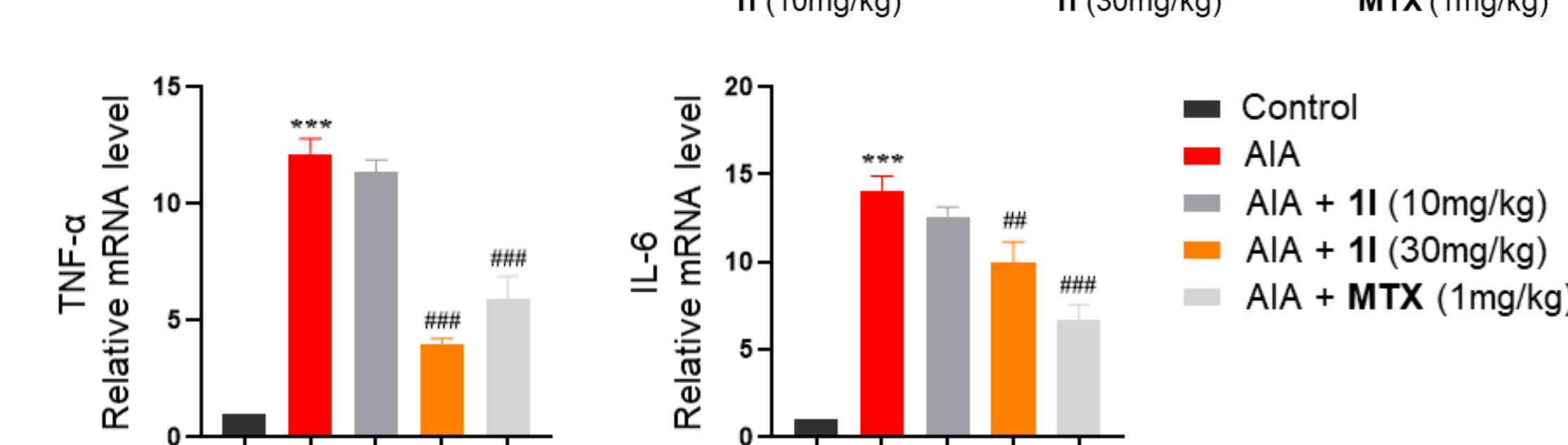
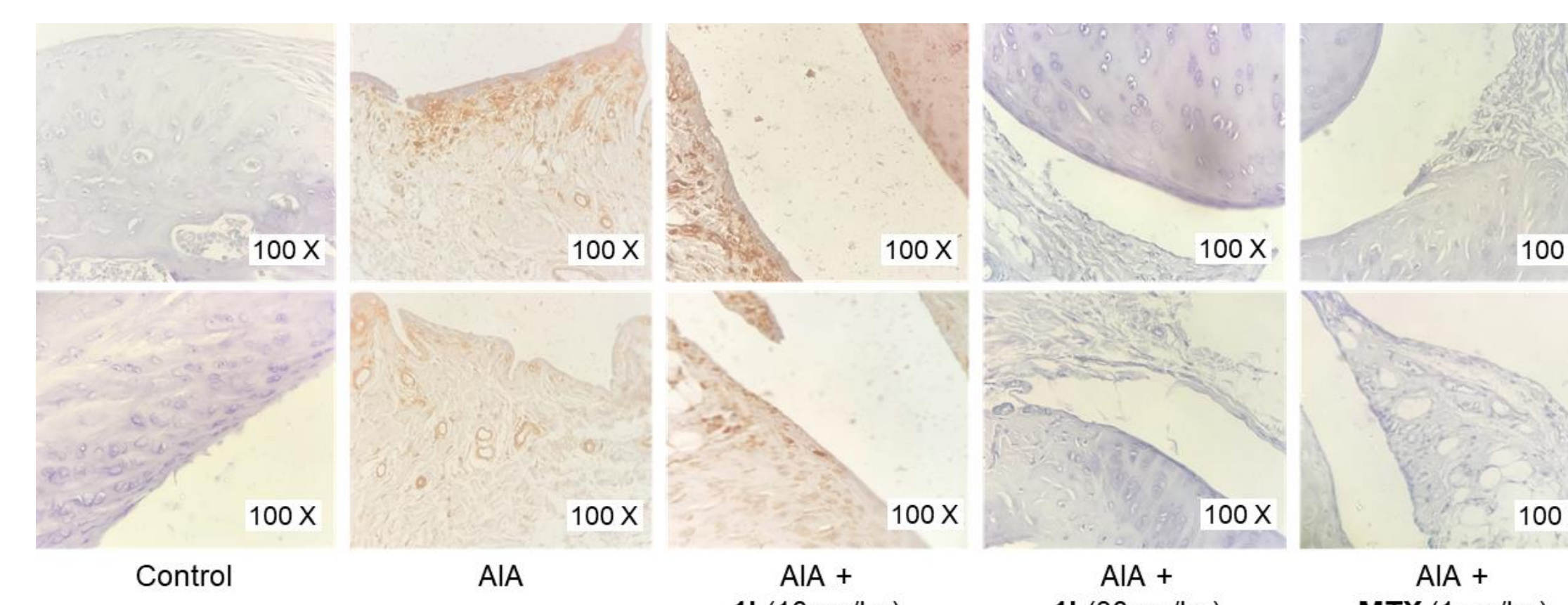
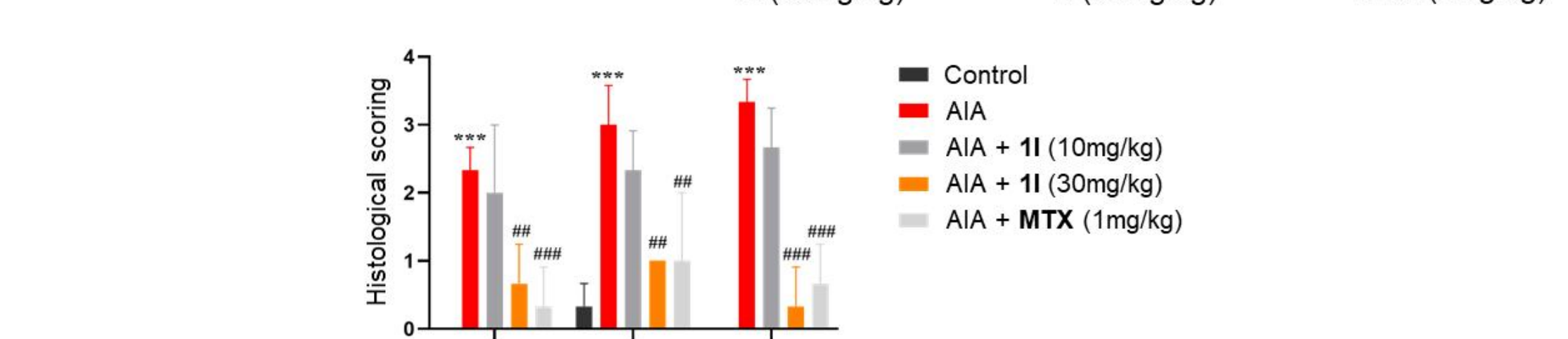
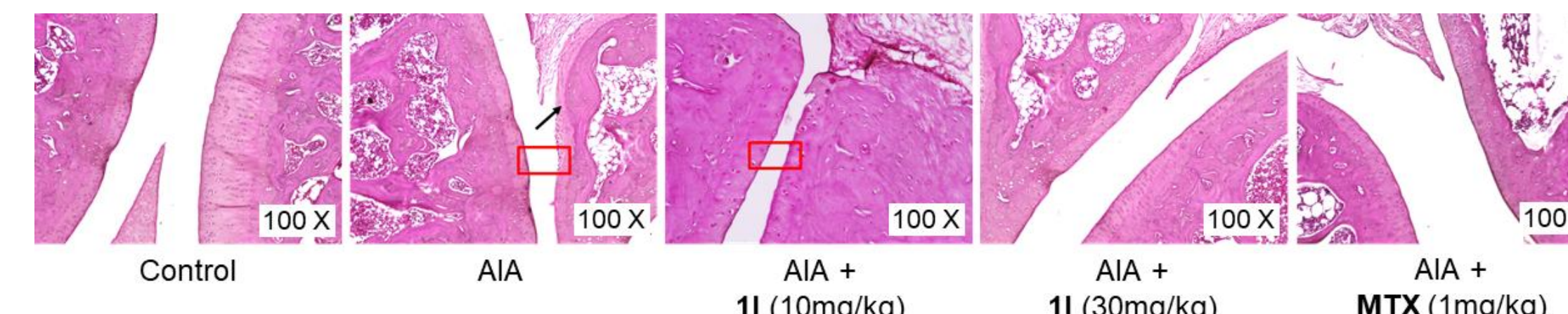
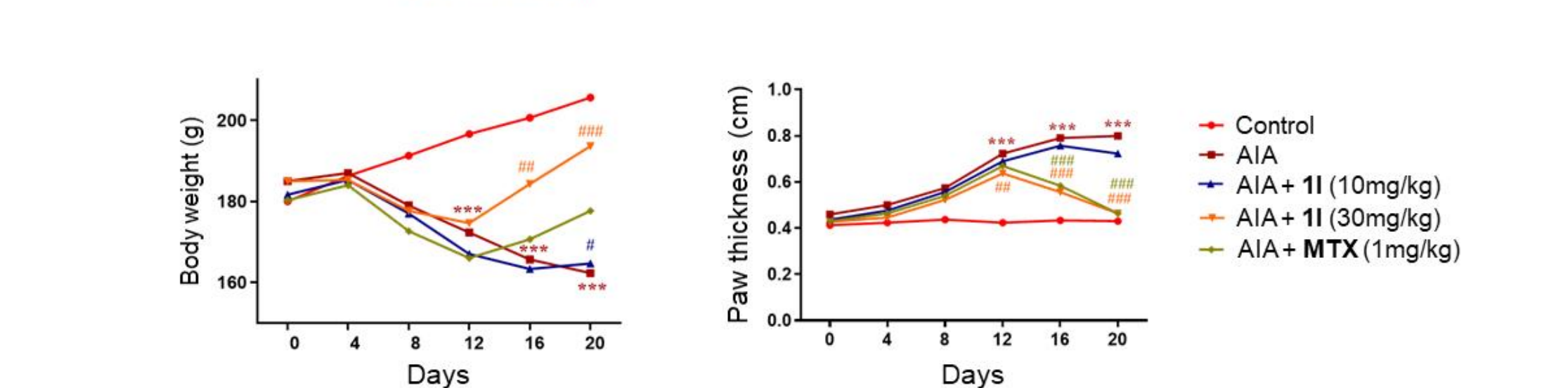
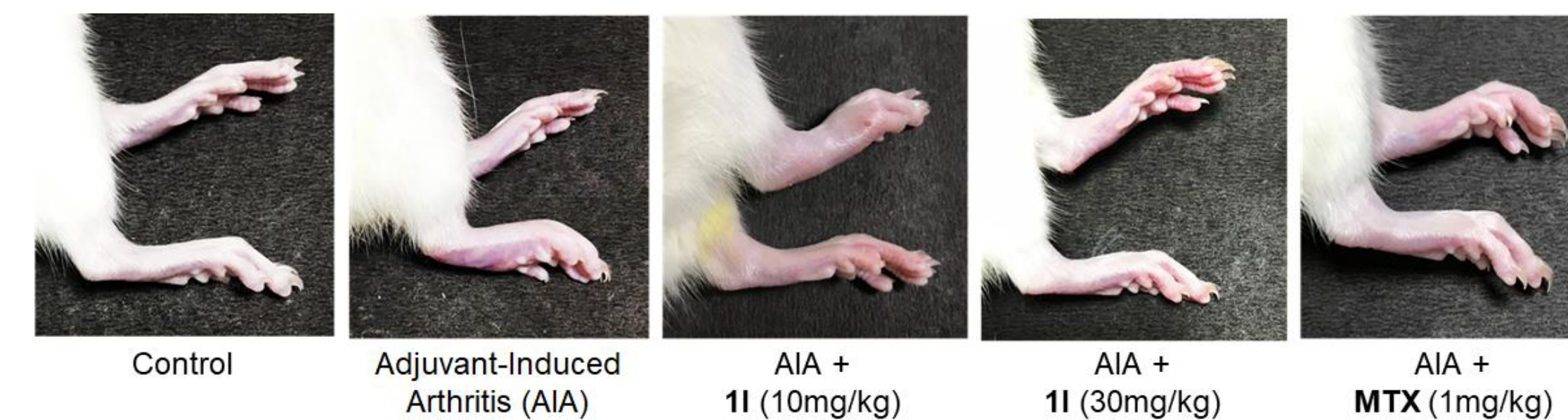
**Figure 2.** Dose-response curves of compound **1l**, **1m**, **1n**, **1o**, **2m**, **2o** and **3o**.



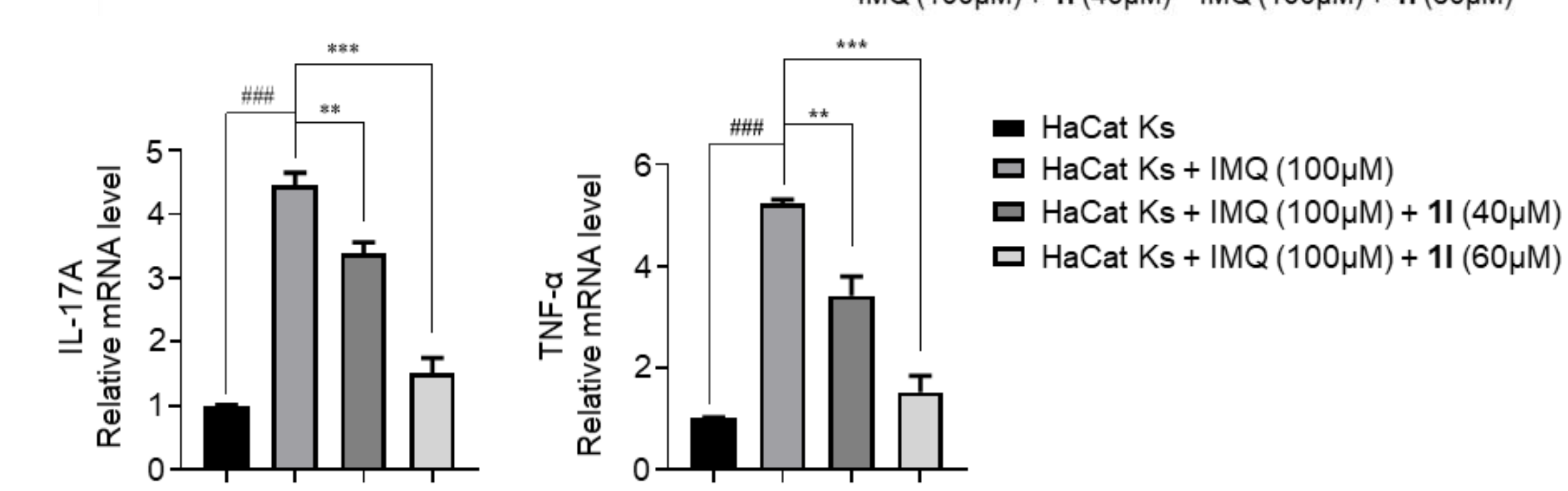
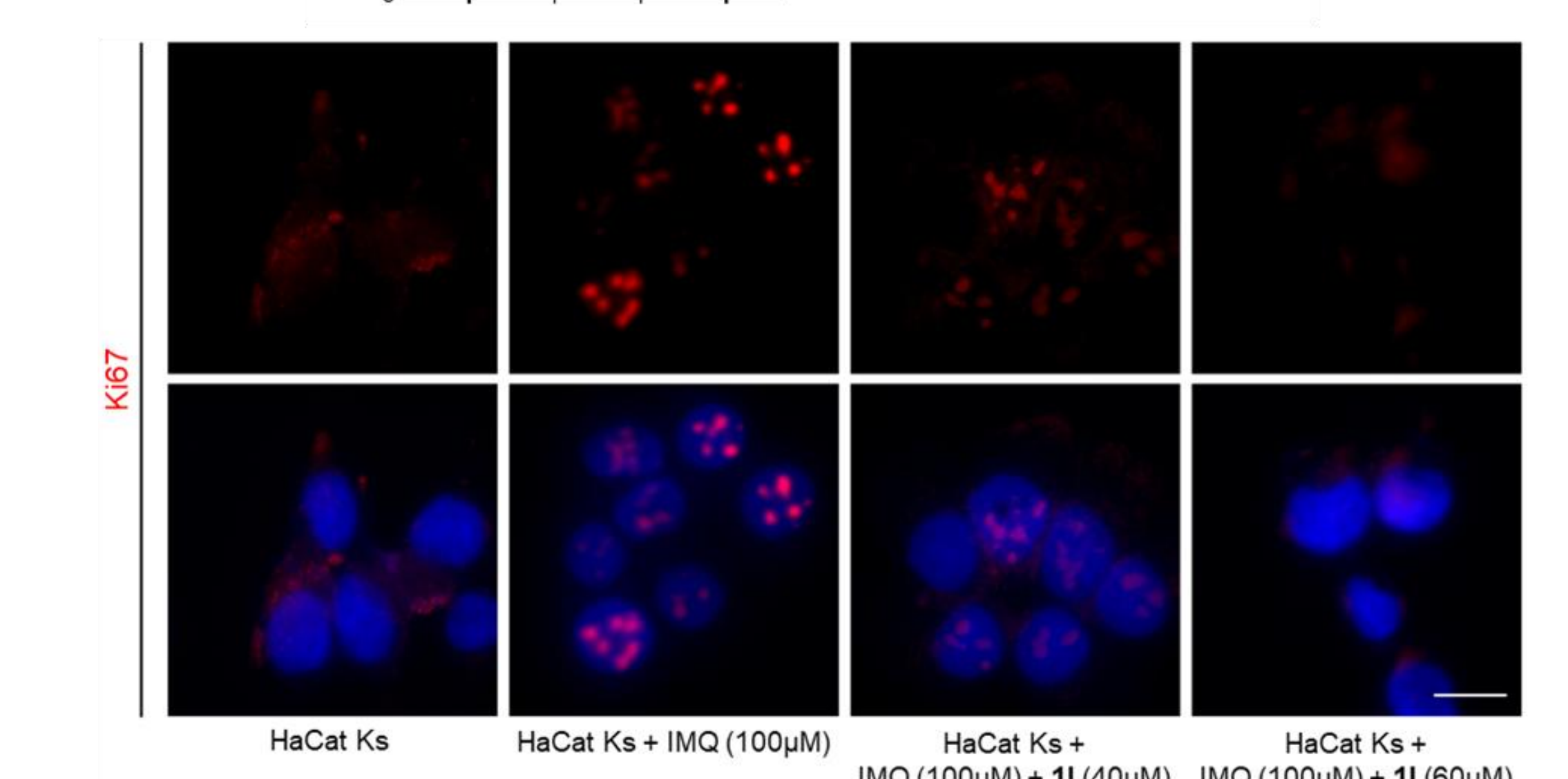
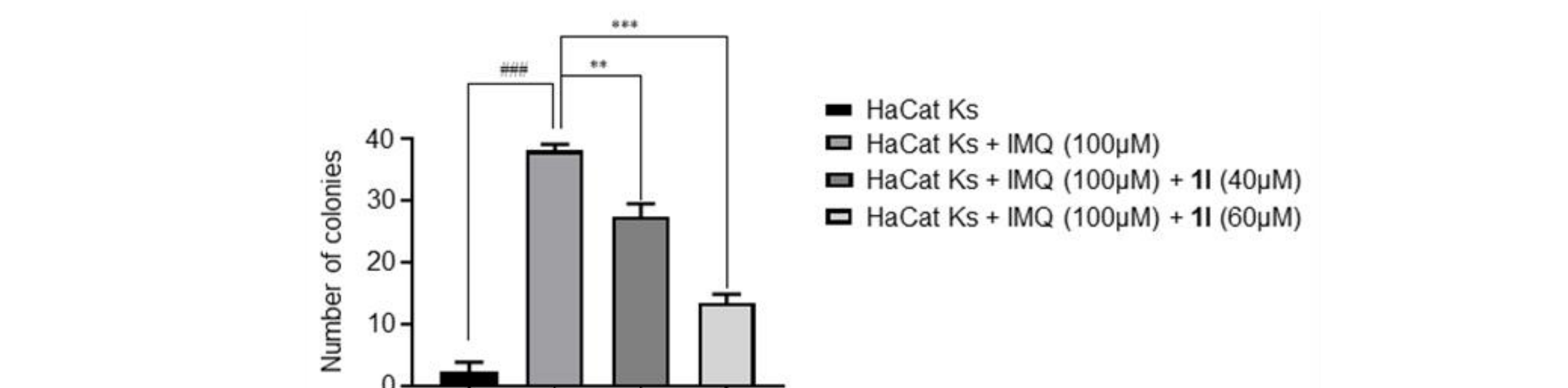
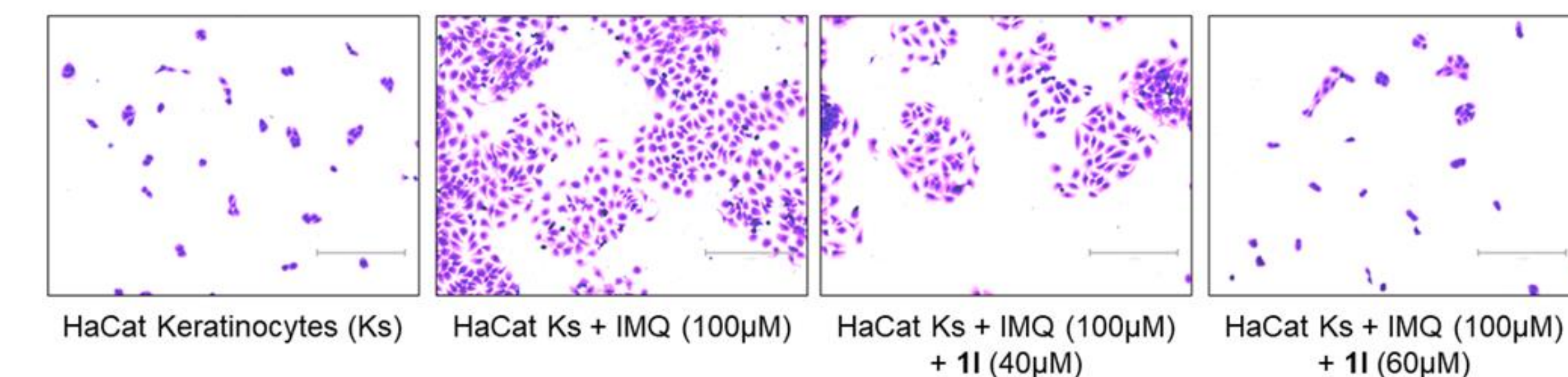
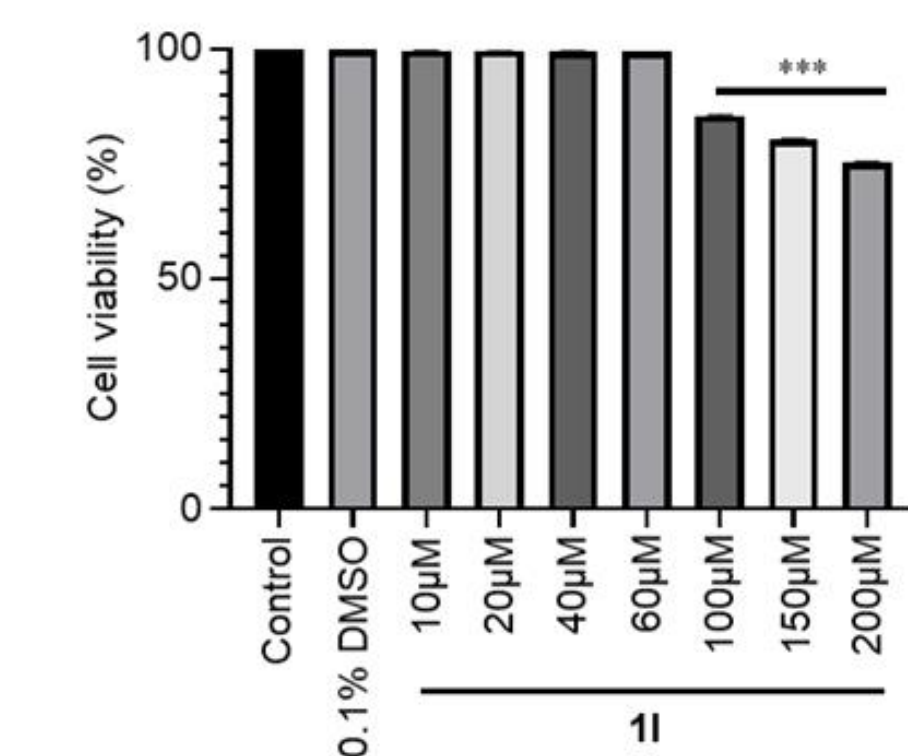
**Figure 3.** SAR presentation of the present series.



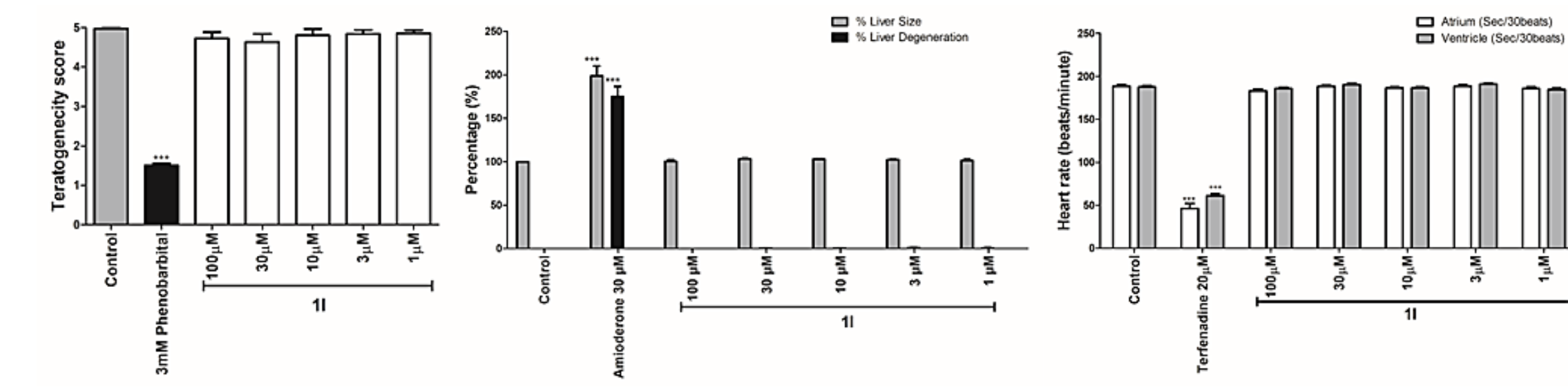
**Figure 4.** (A) Protein-ligand interactions of **1l** molecule; (B) Correlation study: binding affinity vs experimental IC<sub>50</sub> values.



**Figure 5.** Anti-arthritis activity of compound **1l** in the adjuvant-induced arthritis (AIA) rat model.



**Figure 6.** Anti-psoriatic potential of compound **1l** in the imiquimod (IMQ)-induced psoriatic keratinocytes.



**Figure 7.** Toxicity assessment of **1l** in Zebrafish embryo model.

## Conclusions

The present study facilitated the identification of new isoquinolin-1(2H)-one derivatives as potent inhibitors of PDE4B. The identified molecule **1l** exhibited potent anti-arthritis and anti-psoriatic potential with broad safety profile. Thus, compound **1l** can serve as a potential lead for arthritis and psoriasis.

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