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Correction

Correction: Gubič et al. Design of New Potent and Selective Thiophene-Based $K_V1.3$ Inhibitors and Their Potential for Anticancer Activity. *Cancers* 2022, *14*, 2595

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1. Error in Table

In the original publication [1], there was a mistake in **Table 3** as published. The **IC_{50} value determined based on Ltk cells for PAP-1 is 1000 times lower**. The corrected **Table 3** appears below.

Table 3. Comparison of $K_V1.3$ IC_{50} values for compounds **14**, **37**, **43**, **44**, and PAP-1 (**1**) obtained with HiClamp and manual voltage-clamp on *Xenopus laevis* oocytes (Tables 1 and 2) and with manual patch-clamp on the Ltk^- cell-line.

Compound ID	IC_{50} (Manual Voltage-Clamp Oocytes) [μM]	IC_{50} (HiClamp Oocytes) [μM]	IC_{50} (Manual Patch-Clamp Ltk^-) [μM]
PAP-1 (1)	0.78 ± 0.01	2.67 ± 0.30	**0.0004 ± 0.00002**
14	0.57 ± 0.36	1.03 ± 0.03	1.33 ± 0.20
37	3.96 ± 0.47	1.97 ± 0.14	1.35 ± 0.04
43	0.59 ± 0.15	1.20 ± 0.02	1.02 ± 0.07
44	0.47 ± 0.02	1.99 ± 0.61	0.95 ± 0.24

2. Text Correction

There was an error in the original publication. The **IC_{50} value determined based on Ltk^- cells for PAP-1 is 1000 times lower**.

A correction has been made to the following sections: **3. Results**, *3.4. Selectivity and IC_{50} Determinations of the Most Potent $K_V1.3$ Inhibitors*, first paragraph:

The most potent compounds from Tables 1 and 2 (**14**, **37**, **43** and **44**) and the reference compound PAP-1 (**1**) were tested for $K_V1.3$ inhibition with an additional independent method of manual patch-clamp procedures on Ltk^- cells (Table 3). The aim was to demonstrate the inhibition of $K_V1.3$ in a mammalian cell line and to have a direct comparison with the positive control PAP-1 (**1**), which was previously tested in L929 cells and human T-cells (IC_{50} of 2 nM) [11]. Interestingly, the reference compound PAP-1 (**1**) had an IC_{50} value of 780 nM (manual voltage clamp on oocytes) and 0.4 nM (manual patch clamp on Ltk^- cells), **PAP-1 had a much lower potency on oocytes compared with the literature data** (IC_{50} of

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2 nM, L929 cells, manual whole-cell patch-clamp) **and the IC_{50} value determined based on Ltk^- cells**. The best compound of Types I- VI had comparable potency on oocytes (Figure 3, manual voltage-clamp) and Ltk^- cells (manual patch-clamp) of 470 nM and 950 nM, respectively.

A correction has been made to the **4. Discussion**, second paragraph:

Several known small molecule $K_V1.3$ inhibitors lack selectivity for $K_V1.3$ over the closely related $K_V1.x$ family channels, which have high subtype homology. The lack of selectivity for $K_V1.5$ raises many concerns regarding potential acute cardiac toxicity. Obtaining a selective small molecule inhibitor remains a major challenge, and often the lack of selectivity prevents subsequent optimization. Based on literature data, PAP-1 (Figure 1, **1**) is selective toward K_V1 channels, whereas it has the lowest selectivity toward the $K_V1.5$ channel (i.e., 23-fold over $K_V1.5$). We also included into our testing the reference compound PAP-1 to have a direct comparison of potency and selectivity with newly designed compounds. We determined IC_{50} values for PAP-1 using three independent methods: manual voltage clamp on oocytes (IC_{50} = 0.78 ± 0.01 μM), HiClamp system on oocytes (IC_{50} = 2.67 ± 0.30 μM), and manual patch clamp on Ltk^- cells (**IC_{50} = 0.0004 ± 0.00002 μM**). Surprisingly, the IC_{50} values determined for PAP-1 **on oocytes** were approximately **390-** to 1335-fold higher than the literature IC_{50} value of 2 nM (L929 cells, manual whole-cell patch-clamp) [24]. Regarding selectivity, the PAP-1 tested at a concentration of 10 μM showed no significant effects on channels $K_V1.1$, $K_V1.2$, $K_V1.4$, $K_V1.5$, $K_V1.6$, $K_V2.1$, $K_V4.2$, and $K_V10.1$ using the HiClamp system on oocytes.

Comparing the IC_{50} values in Table 3, we can see some differences between the different test systems **can be seen**. **The IC_{50} values determined based on oocytes using the manual and HiClamp methods** are in the same order of magnitude (middle-nanomolar to low-micromolar range), **but the IC_{50} values determined based on mammalian cells are in the low-nanomolar range. These differences** can be attributed to several factors:

First, both mammalian and amphibian cells were used, which differ in size, composition, ion channel expression, and permeability to compounds [25].

Second, when comparing the **two** different methods **used on oocytes** (manual voltage clamp **and** HiClamp), it seems that IC_{50} values are generally slightly higher for the HiClamp method than for the two manual techniques. This may be due to differences in perfusion between the three systems. In the manual setup, oocytes are manually impaled in the recording chamber with two electrodes, and the test solution is either externally applied to the bath filled with ND96 (in the case of the manual voltage-clamp experiments) or applied by continuous extracellular perfusion using a pressurized fast-perfusion system (in the case of the manual patch-clamp experiments), while $K_V1.3$ currents are measured. The HiClamp, on the other hand, is a semi-automatic system, in which the oocyte is picked up from a 96-well plate, deposited in a basket and automatically impaled by two electrodes in the washing chamber. Next, the basket will submerge the oocyte in the test solution in another 96-well plate while $K_V1.3$ currents are measured. In this plate, magnets are continuously stirring the test solutions to assure homogenous perfusion. The higher IC_{50}s observed at the HiClamp could be due to adhesion of the compound to the walls of the 96-well plate or because of the continuous stirring by the magnet, which is not present in the two other experimental setups.

The authors state that the scientific conclusions are unaffected. This correction was approved by the Academic Editor. The original publication has also been updated.

Reference

1. Gubič, Š.; Hendrickx, L.A.; Shi, X.; Toplak, Ž.; Možina, Š.; Theemsche, K.M.V.; Pinheiro-Junior, E.L.; Peigneur, S.; Labro, A.J.; Pardo, L.A.; et al. Design of New Potent and Selective Thiophene-Based $K_V1.3$ Inhibitors and Their Potential for Anticancer Activity. *Cancers* **2022**, *14*, 2595. [CrossRef] [PubMed]