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LETTER to EDITOR

Using Artificial Intelligence Tools to Estimate Median Lethal Dose in Animal Studies: Accuracy, Methodology, and Cautionary Notes

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Dear Editor,

Traditional toxicity studies rely on laboratory animal experimentations to estimate the median lethal dose (LD50) of medications and toxicants [1, 2]. As this approach relies on testing too many animals (e.g., up to 100) [2], alternative up-and-down methods, which use a small number of test animals (e.g., five to ten) have been advocated [3] in alignment with the three Rs (Replacement, Reduction and Refinement) to minimize animal use in testing and the associated LD50 stress [4].

Artificial intelligence has been employed to conduct and refine medical calculations by automating data manipulations that are otherwise time-consuming [5]. This commentary presents the evaluation and accuracy of AI tools in estimating LD50 values of previously published LD50 data for diazinon in chicks [6] and cadmium chloride in mice [7]. Although the sample sizes of five and six in these two studies are small, the studies remain experimentally valid [3].

The data of diazinon and cadmium LD50 experiments in animals [6, 7] were separately formulated into the form of a question to be asked from each of three AI tools, which were ChatGPT (https://chatgpt.com/), Deep Seek (https://chat.deepseek.com/sign_in), and Perplexity (https://www.perplexity.ai/) to estimate LD50 values of diazinon and cadmium. At the beginning (first case), specific information and experimental data were supplied to each AI tool regarding the LD50 experiments and the calculation method. The second case included the same experimental data, but the inquiry directed to the AI tools was of a relatively general nature. All AI tools performed LD50 calculations directly following the input question, without any interference from the author of this commentary.

Initially, in the first case, each AI tool-ChatGPT, DeepSeek, and Perplexity posed the same input of a specific question, accompanied by experimental data sufficient to calculate the LD50:

A. Calculate the median lethal dose (LD50) of diazinon in chicks by the up-and-down method (Use the part of Table 7 with a standard error of 0.61; equation: LD50 = xf + kd, where xf is the last dose used and d is the dose interval and k value is obtained from the table = -0.737) as mentioned by Dixon WJ (1980): Efficient analysis of experimental observations. Annu Rev Pharmacol Toxicol. 1980; 20:441-62. doi: 10.1146/annurev.pa.20.040180.002301), using the following experimental data: initial dose 15 mg/kg, orally; last dose 10 mg/kg, orally. The increase or decrease in the dose was 5 mg/kg, orally. Six chicks were used. The results were: XXOXOX (X = death; O = survival).

B. Calculate the median lethal dose (LD50) of cadmium chloride in mice by the up-and-down method (Use the part of Table 7 with a standard error of 0.61; equation: LD50 = xf + kd, where xf is the last dose used and d is the dose interval and k value is obtained from the table = -0.701) as mentioned by Dixon WJ (1980): Efficient analysis of experimental observations. Annu Rev Pharmacol Toxicol. 1980; 20:441-62. doi: 10.1146/annurev.pa.20.040180.002301), using the following experimental data: initial dose was 10 mg/kg, intraperitoneally; last dose was 10 mg/kg, intraperitoneally. The increase or decrease in the dose was 2 mg/kg, intraperitoneally. Five mice were used. The results were: XOXOX (X = death; O = survival).

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The AI-generated final answers were accurate when compared to the published data [6, 7], as detailed in table 1.

The figure 1 illustrates the specific components of the calculated LD50 values generated by each AI tool.

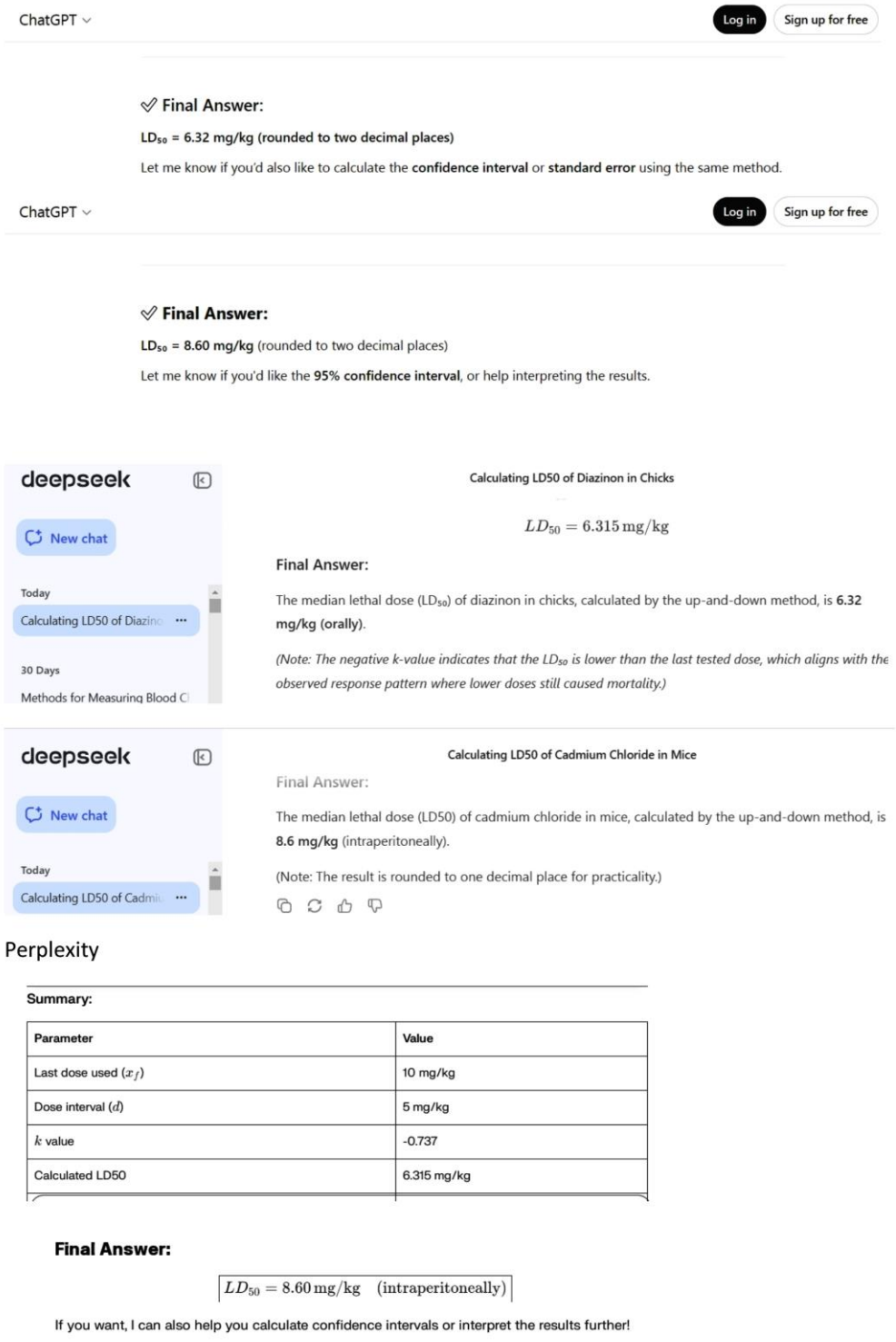

Figure 1. Components of the calculated LD50 values for diazinon (6.32 mg/kg, orally) in chicks and cadmium chloride (8.6 mg/kg, intraperitoneally) in mice generated by artificial intelligence tools

Table 1. Median lethal doses (LD50) of diazinon and cadmium chloride calculated by artificial intelligence tools in response to a specified question with sufficient experimental data

Artificial intelligence tool	Diazinon LD50 (mg/kg, orally) in chicks	Cadmium Chloride LD50 (mg/kg, intraperitoneally) in mice
ChatGPT	6.32	8.6
Deep Seek	6.315	8.6
Perplexity	6.315	8.6

These results demonstrate the accuracy of the calculations performed by the three AI tools, as they closely align with the previously published data and the methods used to determine the LD50 values of diazinon and cadmium [6, 7]. However, in the second instance involving the three AI tools, the same experimental data were provided, but the input questions were designed to include fewer details than those in the first instance mentioned above:

A. Calculate the median lethal dose (LD50) of diazinon in chicks by the up-and-down method using the following experimental data: initial dose 15 mg/kg, orally; last dose 10 mg/kg, orally. The increase or decrease in the dose was 5 mg/kg, orally. Six chicks were used. The results were: XXOXOX (X= death; O=survival).

B. Calculate the median lethal dose (LD50) of cadmium chloride in mice by the up-and-down method using the following experimental data: initial dose was 10 mg/kg, intraperitoneally; last dose was 10 mg/kg, intraperitoneally. The increase or decrease in the dose was 2 mg/kg, intraperitoneally. Five mice were used. The results were: XOXOX (X= death; O=survival).

In the second case, the answers obtained from the AI tools became inaccurate (table 2). The inaccurate results in this case suggest that the three AI tools used different calculation methods. This difference likely arose because the input information was less complete than in the first case, even though the experimental results provided to the AI tools were identical. However, the closest answers to those of the first case were those of Deep Seek for diazinon and cadmium. This could be further validated by performing additional LD50 calculations using data obtained from the literature.

Table 2. Median lethal doses (LD50) of diazinon and cadmium chloride calculated by artificial intelligence tools after identical data input as in table 1, but with lesser inquiry details

Artificial intelligence tool	Diazinon LD50 (mg/kg, orally) in chicks	Cadmium Chloride LD50 (mg/kg, intraperitoneally) in mice
ChatGPT	14.39	8.24
Deep Seek	7.50	9.0
Perplexity	11.20	11.2

The LD50 values were not estimated manually; instead, AI tools generated them almost instantly, provided that the input question includes sufficient information and experimental data, as demonstrated in the first example. The differences between accurate and inaccurate outcomes (a limitation) stem from insufficient data input in the latter case. The small sample sizes for diazinon and cadmium did not affect the accuracy of the AI tools in estimating LD50 values using the up-and-down method [3].

A word of caution is warranted when using AI tools to estimate toxicity outputs such as LD50, instead of performing the traditionally cumbersome manual calculations. From a toxicological perspective, AI holds valuable educational potential in the fields of medicine and pharmacy, which merits further exploration.

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