Toxicology Tutorial – Dose Response

Dose-Response Curves

When we graph the dose of a substance and the percentage of a population that responds to that dose, the result is called the dose-response curve. The x-axis is the dose, typically in a logarithmic scale. This means units on the x-axis increase by a power of 10, allowing us to compare a very wide range of doses on a single graph. The y-axis is the response, or the percentage of subjects that show a response.

When plotting the response at various doses, the dose-response curve normally takes the form of a sigmoid curve that is shaped like the letter "S", much like the example in Figure 1. It conforms to a smooth curve as close as possible to the individual data points.

For most effects, small doses are not toxic. The point at which toxicity first appears is known as the threshold dose level.

From that point, the curve increases with higher dose levels. In this hypothetical example, no toxicity or response is exhibited at just over 10 mg, but as the dose approaches 100 mg, 100% of the individuals exhibit a response.

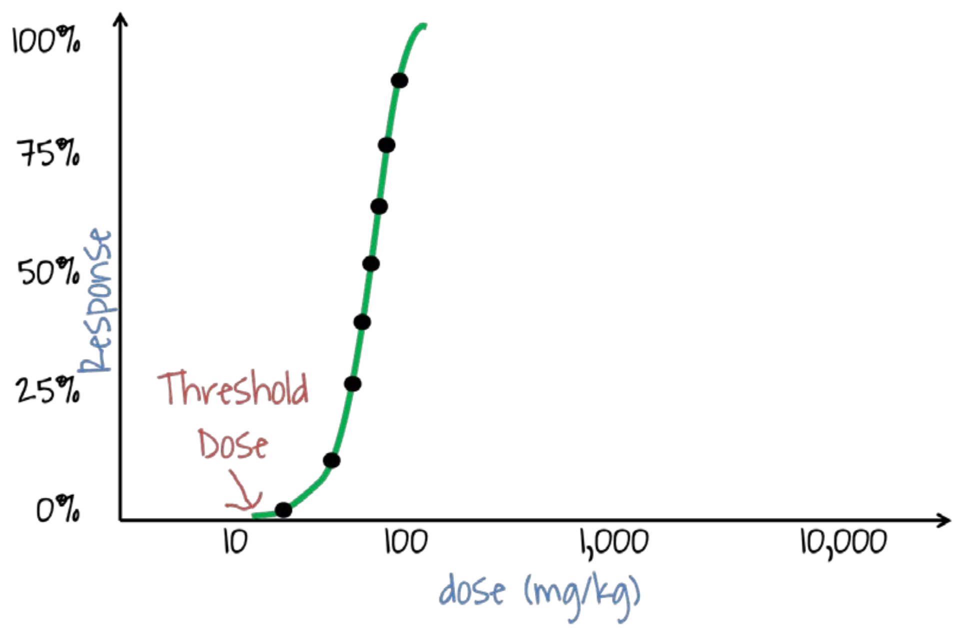

Figure 1 – Typical dose-response curve for a substance. The threshold dose is the point at which effects are first seen.

It's important to know the shape and slope of the dose-response curve for predicting the toxicity of a substance at specific dose levels. The slope of the curve indicates the change in the percent of the population responding as the dose increases.

Take, for instance, the new example (Figure 2), which we will call Chemical A. A sharp increase in the slope of a dose-response curve indicates that as the dose increases, there are increasingly higher risks of toxic responses. In this hypothetical example, notice the steep slope of the curve with relatively small increases in the dose.

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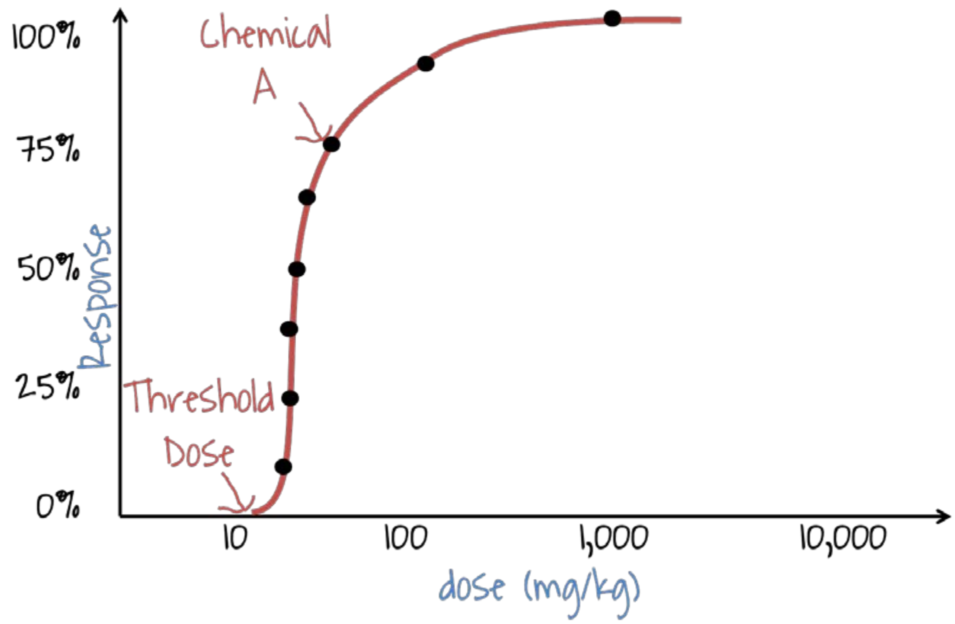

Figure 2 – Dose-response curve for hypothetical Chemical A, with a threshold dose slightly above 10 mg.

In Figure 3, the response curve has been added for another hypothetical example, which we will call Chemical B. In this second example, the slope of the response curve for Chemical B is initially not as steep as Chemical A. This suggests that the effect of increasing dose is relatively minimal until the dose reaches about 100 mg. As we move beyond 100 mg, the slope begins to steepen, suggesting that the response is greatly impacted as the dose continues to increase.

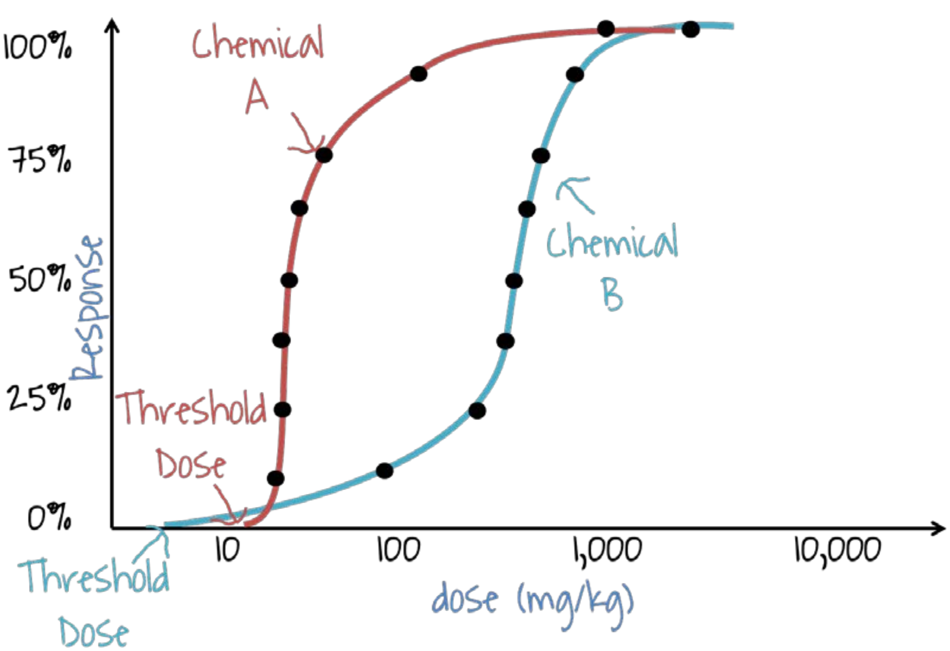

Figure 3 – The dose-response curve for hypothetical Chemical B is added, with a slope initially much lower than Chemical A until the dose reaches beyond 100 mg.

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Major differences among toxicants may exist not only in the slope, or potency, but also in the point at which the threshold is reached. So in these two hypothetical examples, Chemical A has a higher threshold, which means it takes a larger dose to begin seeing effects when compared to Chemical B.

Comparing dose-response curves among chemicals in this way can help toxicologists understand more about them. A curve with a steep slope indicates the chemical has a high potency, or toxic strength, compared to other chemicals. The greater the slope, the greater the potency.

When we compare these two hypothetical examples, what can we conclude by looking at the shape and slope of the curves? We can see that it takes a much lower dose of Chemical B to begin seeing effects when compared to Chemical A. As the dose approaches 100 mg for both chemicals, notice what happens. More than 75% of people responded to Chemical A, but less than 25% of people responded to Chemical B at this same dosage.