Ethanol Fermentation Dose-Response for Sugar and Saccharine

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Introduction

In psychology, it is critical to understand the dose-response relationship and how this is graphically represented by a dose-response curve. Dose-response curves show a mathematical depiction of the relationship between the dose of an administered drug and its effects. Typically, the dose is plotted on the x-axis, and the measured result is plotted on the y-axis. This comparison shows us how the measured response to a drug changes as the dose increases. However, dose-response curves carry much more information with them. Median effective dose (ED50), median lethal dose (LD50), efficacy, potency, therapeutic index, and margin of safety are all crucial factors with significant implications that can be calculated from a dose-response curve. Understanding dose-response relationships is foundational across scientific fields, but within neuropharmacology, we can use these graphs to compare well-understood drugs, learn about a novel drug, or even when analyzing other methods of treatment.

Measuring drug effects is a foundational part of understanding drugs and behavior. The drug-response curve proves to be an essential tool when comparing the potency and efficacy of different drugs. Jakubovski and colleagues used dose-response curves to compare the effectiveness of selective serotonin reuptake inhibitors (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SNRIs) in treating anxiety disorders. The 2018 review performed a meta-analysis of 52 previous studies on the efficacies of various SSRIs and SNRIs using dose-response curves. Points of interest included symptom improvement, likelihood and time course of treatment response, tolerability, pharmacological agent, and diagnostic indication dose. The review found that although both kinds of medication are successful in treating anxiety disorders, SSRIs are more effective than SNRIs, meaning an increase in the dose of an SSRI (within therapeutic range) is associated with greater therapeutic benefit, and higher doses of SNRIs are

not (Jakubovski et al., 2018). These findings have substantial implications for guiding the treatment of anxiety disorders in adults and highlight the utility of the dose-response curve.

Beyond examining psychotherapeutic medications, dose-response curves are also essential when analyzing illicit drugs, especially considering the potential for abuse, tolerance, and lethal dose. Marusich and Branch's 2006 study, *Stability of cocaine dose-response functions at different inter-dose intervals,* aimed to examine the pattern of tolerance in daily cocaine use and behavioral factors that may influence it. The authors discuss the importance of using dose-response curves when evaluating drug tolerance because they show the range of effects brought on by different doses. Marusich and Branch used operant conditioning procedures in four phases to examine the self-administration of cocaine hydrochloride in pigeons. Phases varied in reinforcement schedule, and a dose-response curve was generated for each, with tolerance defined as a right shift in the curve. In only one of the four phases was tolerance developed. The authors suggest that previous experience with different doses may inhibit the development of tolerance (when cocaine use becomes frequent). These results may be useful when trying to understand cocaine tolerance in humans and further emphasize the importance of understanding the functions and implications of dose-response curves.

It is important to note that dose-response curves are frequently used to examine less understood elicit substances as well. A 2017 study by Gannon et al. on "bath salts", an amphetamine-related cathinone, utilized a dose-response curve when studying rats to show how these drugs can have a high potential for abuse in humans—again, showing that dose-response curves are a first step in learning about any drug (Gannon et al., 2017).

Being able to produce and analyze a dose-response curve is endlessly valuable beyond neuro and behavioral pharmacology; they may also be used to examine other forms of treatment. A 2010

Australian study by Harnett and colleagues examined the dose-response relationship of psychotherapy, showing that we can use mathematical relationships in unexpected ways. A dose-response curve was created to determine the number of psychotherapy sessions necessary for a participant to improve or return to a normal state of functioning. Participants were adults who qualified for psychological treatment; each attended between 2 and 34 therapy sessions throughout the study; the Kaplan-Meier survival analysis procedure was used to estimate subjects' improvement. Harnett et al. found that it would take eight sessions for 50% of participants or 21 sessions for about 85% of participants to meet the criteria for "reliable improvement". To reach full clinical recovery, it is expected that one would need a minimum of 14 sessions, but 23 would be effective in more people (Harnett et al., 2010). Dose-response curves have proved a practical analysis outside of the typical dose-response research. Other studies have used a similar approach to examine the dose-response of cognitive behavioral therapy for anxiety disorders (Levy et al., 2020) or even to show how exercise can be an effective treatment for depression (Dunn et al., 2005).

Grasping the function and importance of the dose-response relationship through current literature is essential. Understanding and drawing information from dose-response curves is foundational in studying drug effectiveness and potency. The present study aims to show this significance by using the process of fermentation to effectively model dose-response, hypothesizing that fermentation reactions of sugar and saccharine when each is combined with yeast will be an insightful model of dose-response, specifically when comparing efficacy and potency.

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